"A COMPARATIVE STUDY OF DEXMEDETOMIDINE VERSUS MIDAZOLAM FOR MONITORED ANAESTHESIA CARE IN MIDDLE EAR SURGERIES"

By

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Dr. Ramya K

LIST OF ABBREVIATIONS

ASA = American Society of Anaesthesiologists	S No. = Serial number
MAC = Monitored Anesthesia care	Inj. = Injection
GA = General anesthesia	IV = Intravenous
LA = Local anesthesia	mm Hg = Millimetres of mercury
ENT = Ear, nose, throat	gm = Gram
HR = Heart rate	kg = Kilogram
SBP = Systolic blood pressure	mcg = Microgram
DBP = Diastolic blood pressure	ng = Nanogram
MAP = Mean arterial pressure	ml = Millilitres
RR = Respiratory rate	lit = Litres
ECG = Electrocardiogram	mins = Minutes
PACU = Post anesthesia care unit	hr = Hour
RSS = Ramsay sedation score	% = Percentage
VAS = Visual analog score	FDA = Food & Drug administration
PONV = Post operative nausea vomiting	SD = Standard deviation

ABSTRACT

BACKGROUND: Monitored anaesthesia care (MAC) involves administration of local anaesthesia in combination with intravenous sedatives, anxiolytic and/or analgesics, which is a common practice during ENT procedures that are superficial, less invasive and can be done under local anesthesia in well counselled patients. Midazolam has been in use for MAC because of a number of beneficial effects. Recent studies suggest that α_2 agonists provide adequate sedation and analgesia and also improve surgical field visibility. Dexmedetomidine, a highly selective α_2 agonist is emerging as a preferred choice for MAC.

AIM: To compare the efficacy of Inj. Dexmedetomidine and Inj. Midazolam for Middle ear surgeries under Local Anaesthesia with Monitored Anaesthesia Care in terms of sedation, analgesia and hemodynamic stability in the perioperative period.

METHODS:96 patients of either sex, aged between 18-60 years of ASA grade I & II undergoing Middle ear surgeries under local anaesthesia with Monitored Anaesthesia Care were divided into two groups of 46 patients each to receive either Inj. Dexmedetomidine (Group D)1 µg/kg IV bolus over 10 minutes followed by continuous infusion @ 0.5 µg/kg/hr. or Inj. Midazolam (Group M)40 µg/kg IV bolus over 10 minutes followed by continuous infusion @ 20 µ/kg/hr for sedation during surgery. Sedation as titrated to Ramsay sedation score of 3. Vital parameters like Heart rate, Blood pressure, SpO_2, Respiratory rate were recorded every 5 minutes for up to 120 minutes in the intraoperative period and for 120 minutes in post operative period. Need for rescue

sedation (Inj. Propofol), rescue analgesic (Inj. Fentanyl) and surgeon satisfaction scores were assessed.

RESULTS: Sedation with Dexmedetomidine was more profound compared to Midazolam ($p<0.05$). Analgesic effects of Dexmedetomidine were better than Midazolam ($p<0.001$). Fall in Heart Rate was significantly more in Group D compared to baseline value and compared to Group M.. Blood Pressure was maintained within normal limits in both the groups but the fall in SBP, DBP and MAP was significantly more in Group D than in Group M ($p < 0.05$).

CONCLUSION: Dexmedetomidine is a safe and attractive agent for sedation in patients undergoing middle ear surgeries under local anaesthesia with monitored anaesthesia care as it provides a calm patient, causes better analgesia and rapid recovery.

KEYWORDS: Dexmedetomidine; Midazolam; Monitored anaesthesia care; Middle ear surgery; conscious sedation.

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INTRODUCTION

Monitored anaesthesia care (MAC) involves administration of local anaesthesia in combination with intravenous sedatives, anxiolytic and/or analgesics, which is a common practice during ENT procedures that are superficial, less invasive and can be done under local anaesthesia in well counselled patients. "American society of Anaesthesiologists (ASA) defines monitored anaesthesia care as instances in which an anaesthesiologist has been requested to provide specific anaesthesia services to a particular patient undergoing a planned procedure, in connection with which a patient receives local anaesthesia or in some cases no anaesthesia at all"[1,2]. Primary objective in providing monitored anaesthesia care is to ensure patient comfort, safety and satisfaction during surgery.[3]

Monitored anaesthesia care can be used for middle ear surgeries and has many advantages like less bleeding, postoperative analgesia, ability to test hearing intra operatively, cost effectiveness and rapid recovery. Middle ear surgeries like Tympanoplasty and Mastoidectomy that address pathology of tympanic membrane and middle ear respectively can be performed under local anaesthesia without sedation. Local anaesthesia is cost effective but better pre operative counselling is needed. However local anaesthesia alone has been reported to be associated with anxiety, dizziness, claustrophobia etc[4, 5]. Patients may be uncomfortable and move due to pain, noise of suction, manipulation of instruments and position of head and neck. Pain during surgery may lead to sympathetic stimulation and a restless patient may have tachycardia and hypertension, leading to increased bleeding in surgical field. Therefore MAC is an

attractive option as it causes less pharmacological disturbance, allows more rapid recovery than General anaesthesia and is cost effective.

Several drugs have been used for sedation under monitored anaesthesia care like Benzodiazepines, Opioids and Propofol. Since the approval of Midazolam by FDA in 1985,practitioners of all medical disciplines embraced the versatility of Midazolam. It is the most frequently used sedative and has been reported to be well tolerated in monitored anaesthesia care. Despite having a number of beneficial effects like quick onset, limited duration of action, it is far from being an ideal agent due to untoward effects like prolonged sedation after repeated administration, restlessness, cognitive impairment, respiratory depression.[6]

Recently α-2 adrenoreceptor agonists like Clonidine and Dexmedetomidine have been in use for their sedative, analgesic, anxiolytic, sympatholytic and cardiovascular stabilising effects.[7] Dexmedetomidine is a selective alpha-2 adrenoreceptor agonist with 8 times more potency than Clonidine. It is being used as a single agent in many painful procedures likeawake intubation, shockwave lithotripsy, endoscopic examinations etc. It is also used for ICU sedation and as an adjuvant to local anaesthetics. It decreases sympathetic outflow and has been reported to reduce bleeding significantly in ENT surgeries.It provides excellent sedation and analgesia with minimal respiratory depression and can be safely and effectively used for surgeries under MAC.[7]Use of continuous intravenous infusion of short acting sedative-hypnotics is associated with stable level of sedation, fewer side effects and shorter recovery time than traditional intermittent bolus techniques.[8]

This study was undertaken to evaluate and compare the efficacy of Inj. Dexmedetomidine with Inj. Midazolam in terms of sedation, analgesia and hemodynamic stability in patients undergoing middle ear surgeries under local anaesthesia with monitored anaesthesia care.

AIMS & OBJECTIVES

To compare the efficacy of Inj. DEXMEDETOMIDINE and Inj. MIDAZOLAM for Middle ear surgeries under Local Anaesthesia with Monitored Anaesthesia Care in terms of -

1. Intraoperative sedation.
2. Intraoperative and Postoperative Analgesia.
3. Intraoperative hemodynamic stability.
4. Surgeon’s satisfaction.
5. Side effects, if any.

HISTORY & REVIEW OF LITERATURE

The first defining role of α_2 agonists in clinical anaesthesia was described by **Kaukinen SKaukinen L, Eerola R** [9] in 1979. This was soon followed by a description of reduction in minimum alveolar concentration of halothane by Clonidine by **Bloor BC,Flacke WE**[10] in 1982. Role of alpha 2 agonists in anaesthesia was later supported by **Maze M,Tranquilli W** [11] in 1991.

Dexmedetomidine was introduced in 1999 in USA and was approved only as a short term (< 24 hours) sedative for ICU patients on mechanical ventilation.

Dexmedetomidine is now used as a sedative, analgesic and adjuvant to regional and general anaesthesia in operating room and in diagnostic and procedure units[3] and for other uses such as withdrawal, detoxification, amelioration in adult and pediatric patients.[12,13] Various studies have been done to evaluate its sedative and analgesic effects in various procedures. Some of these studies are as follow:

Nociti JR, Serzedo PS, Zuccoloto EB, Sebben F, GonzalesRF(2003)[14] studied the effects of Dexmedetomidine on Propofol requirements and cardiovascular and respiratory stability for sedation during plastic surgery under local anaesthesia. 40 patients scheduled for elective face, nose and breast plastic surgeries under local anaesthesia were divided into groups of 20 each: C (Control) and D (Dexmedetomidine). Sedation was achieved in both groups with 1 mg/kg bolus Inj. Propofol followed by continuous infusion to provide conscious sedation. Group D patients received Inj. Dexmedetomidine at the rate of 0.01µg/kg/min plus Inj. Propofol infusion. Blood pressure, pulse rate, oxygen saturation, $ETCO_2$, perioperative bleeding control and post anaesthetic recovery features were

assessed. They found that mean Propofol infusion rate was lower in group D as compared to group C. Mean blood pressure values, pulse rate, mean duration to open eyes were also lower in group D and they also showed better bleeding control compared to group C. They concluded that Dexmedetomidine-Propofol combination is safe and has the advantages of decrease in Propofol requirements, good cardiovascular stability, and excellent perioperative bleeding control without causing any depression in ventilation.

Turan A, Sapolyo O, Karamanlioglu B, Kurt I, Pamukcu Z(2004)[15] compared Dexmedetomidine and Propofol for monitored anaesthesia care in patients undergoing Septoplasty and Endoscopic sinus surgeries in terms of hemodynamic, analgesic and sedative effects. 40 patients were randomly divided into two groups to receive either Inj. Propofol 0.8 mg/kg loading dose followed by infusion at 2 mg/kg/h (Group I) or Inj. Dexmedetomidine 1 µg/kg IV loading dose over 5 minutes followed by maintenance at 0.4 µg/kg/h (Group II). Infusion rates were adjusted according to sedation scale in both groups. All the patients received Inj. Fentanyl 1 µg/kg after loading dose and received Inj. Fentanyl 0.5-1 µg/kg when visual rating scale (VRS) was > 4. Mean blood pressure, Heart rate, SpO_2 and Visual rating scale were assessed during surgery. At the end of surgery, VAS and Aldrete scores were recorded. They found that VAS, intraoperative sedation scores and additional analgesic requirement was higher in Group I. They concluded that Dexmedetomidine causes a more profound sedation and better postoperative analgesia and is a better alternative to Propofol in MAC.

Ustün Y, Gündüz M, Erdoğan O, Benlidayi ME (2006)[16] compared Dexmedetomidine and Midazolam sedation in third molar removal surgery. 20 patients with impacted mandibular third molars on both sides were included in this study to receive Inj. Dexmedetomidine (Group D) 4 µg/kg/h or Midazolam (Group M) 0.4 mg/kg/hr 15 minutes before start of the first surgery. The other agent was given for second surgery. Hemodynamic parameters, sedation scores, patient cooperation and pain scores were assessed during both surgeries. Patients were asked about their experience and preference at the end of the second surgery. They found that mean HR and BP measurements were significantly lower in group D. Patients in Group M had amnesia and higher pain scores. 65% patients showed preference for Dexmedetomidine sedation. They concluded that Dexmedetomidine sedation was more preferred by patients and is a great alternative to Midazolam for intravenous sedation as it provides satisfactory sedation and analgesia without causing amnesia and any side effects for third molar removal.

Alhashemi JA (2006)[7] conducted a comparative study of Dexmedetomidine versus Midazolam for monitored anaesthesia care in patients undergoing cataract surgery under peribulbar block. 44 patients were divided into two groups to receive either Inj. Dexmedetomidine 1 µg/kg loading dose over 10 min followed by 0.1 - 0.7 µg/kg/h IV as maintenance (Group D) or Inj. Midazolam 20 µg/kg loading dose followed by 0.5 mg IV boluses as and when required (Group M). Pulse rate, Mean arterial pressure, Aldrete score, patients and surgeons' satisfaction score were assessed during surgery. They found that Group D had lower MAP, PR, better patient satisfaction score but delayed PACU discharge in comparison to Midazolam. They concluded that Dexmedetomidine is not

suitable for sedation in cataract surgery as it was associated with cardiovascular depression and delayed Post Anaesthesia Care Unit (PACU) discharge.

O'Daniel TG, Shanahan PT(2006) [17] conducted a study to determine the efficacy of Dexmedetomidine as a multifunctional sedative agent for patients undergoing extended superficial musculo aponeurotic system (SMAS) face lift surgery. This retrospective study was conducted on 50 non intubated patients undergoing face lifts by the same surgeon. All patients received Dexmedetomidine as the primary sedative agent. Heart rate, Respiratory rate, postoperative emergence rates and adverse events were recorded. They found that Dexmedetomidine infusion controlled systolic blood pressure to < 120 mm Hg and provided adequate sedation in 42 out of 50 patients. They concluded that in their population of non-intubated patients undergoing facial rejuvenation surgery, Dexmedetomidine fulfilled the properties sought in a sedative agent.

Mc Cutcheon CA, Orme RM, Scott DA, Davies MJ, Mc Glade DP (2006)[8] compared Dexmedetomidine with Midazolam- Fentanyl for sedation during carotid endarterectomy (CEA) done under regional anaesthesia. This study was done in 56 patients undergoing CEA. The number of drug interventions required to treat deviations of blood pressure and heart rate out of pre-determined range were compared. They also compared patient satisfaction and recovery. They found that patients in Dexmedetomidine group required fewer interventions and less likely to need intervention for treatment of tachycardia and hypertension and also less likely to have them. There was no difference in both groups in terms of hypotension or bradycardia intraoperatively. The number of patients requiring additional pain relief in the post anaesthesia care unit was significantly higher in Midazolam-Fentanyl group. They concluded that, Dexmedetomidine is a good alternative

but not superior to standard Midazolam-Fentanyl technique for sedation during carotid endaraterectomy.

Karaaslan K, Yilmaz F, Gulcu N, Colak C, Sereflican M, Kocoglu H(2007)[18] compared Dexmedetomidine with Midazolam in combination with Tramadol patient-controlled analgesia in endoscopic nasal surgeries under MAC. 70 patients undergoing Septoplasty or Endoscopic sinus surgery were randomly divided into 2 groups to receive either Inj. Dexmedetomidine 1 µg/kg over 10 minutes followed by continuous infusion of 0.5 µg/kg/h (Group D) or Inj. Midazolam 40 µg/kg over 10 minutes followed by 50 µg/kg/h (Group M). 1-minute bolus Inj. Tramadol (1.5 mg/kg) was given in both groups 10 minutes after the primary drug infusion and continued with infusion using PCA device. Vital parameters, VAS, RSS were recorded at 10-minute intervals during the surgery and at 5 minutes of arrival in PACU and 5 minutes before discharge. Hemodynamic parameters were higher in Midazolam group but pain and sedation scores were comparable. Amount of rescue dosing with Inj. Tramadol was higher in Group M. They concluded that both drugs provide adequate sedation and analgesia for FESS under MAC but better analgesic effect was seen with Dexmedetomidine.

Demiraran Y, Korkut E, Tamer A, Yorulmaz I, Kocaman B, Sezen G (2007)[19] compared Dexmedetomidine with Midazolam for sedation in patients undergoing Upper GI endoscopy. 50 adult patients aged between 18 - 60 years were divided into 2 groups. Heart rate, Mean arterial pressure, respiratory rate, SpO_2 was measured every minute during the procedure. Patients were asked to rate their anxiety and satisfaction after the procedure. Hemodynamic parameters were comparable in both groups. Patient and Endoscopist satisfaction was better with Dexmedetomidine than Midazolam and

Midazolam group had more adverse effects than Dexmedetomidine group (P<0.05). They concluded that Dexmedetomidine is a better alternative to Midazolam for sedation in patients undergoing upper GI endoscopy.

Ayoglu H, Yapakci O, Ugur MB, Uzeen L, Altunkaya H, Ozer Y (2008)[20] studied the effectiveness of Dexmedetomidine in reducing bleeding during Septoplasty and Tympanoplasty operations. 80 patients, aged 18- 65 years of which 40 patients were scheduled for Septoplasty (S) and 40 to undergo Tympanoplasty (T) operations, were randomly divided into 4 groups - SD, TD, S and T. Patients in group SD and TD were given Inj. Dexmedetomidine 1 µg/ kg as bolus dose followed by 0.7 µg/ kg/ h as maintenance dose. Groups S and Group T were control groups and were given normal saline. If blood pressure was > 20% of preoperative values, Inj. Fentanyl 1 µg/kg was given. Intraoperative blood loss was assessed with gauze count. Patients in Group SD had less bleeding and lower bleeding scores and lower need of Inj. Fentanyl. Patients in Group TD required less Fentanyl as compared to Group T. They concluded that, Dexmedetomidine reduces bleeding and reduces intraoperative Fentanyl requirement in patients undergoing Septoplasty under General anaesthesia.

Goksu S, Arik H, Demiryurek S, Mumbuc S, Oner U, Demiryurek AT (2008)[21]conducted a study to understand haemodynamic effects of perioperatively administered Dexmedetomidine for Functional endoscopic sinus surgery under local anaesthesia. 62 patients were divided into 2 groups to receive either Inj. Dexmedetomidine initial loading dose of 1 µg /kg given for a 10-min period followed by 0.7 µg /kg /h (Treatment group) or Normal Saline (Control Group). Maintenance infusion was stopped 15 minutes before the end of the surgical procedure. HR, SBP, DBP & mean

arterial BP markedly decreased in Dexmedetomidine group. Dexmedetomidine also provided appropriate levels of sedation. They concluded that Dexmedetomidine provides analgesia, adequate sedation and surgical comfort without adverse effects in patients undergoing functional endoscopic sinus surgery under local anaesthesia.

Kaygusuz K, Gokce G, Gursoy S, Ayan S, Mimaroglu C, Gultekin Y (2008)[22] conducted a randomised control trial to compare Inj. Dexmedetomidine and Inj. Propofol in terms of sedation in patients undergoing Extra corporeal shockwave lithotripsy (ESWL). 46 patients posted for elective ESWL were divided into two groups to receive either Inj. Dexmedetomidine infused at 6 µg /kg /h as loading dose over 10 minutes followed by maintenance at 0.2 µg /kg/h or Inj. Propofol given at 6 mg/kg/h as loading dose for 10 minutes followed by an infusion at 2.4 mg/kg/h. Inj. Fentanyl 1 µg/kg was given to all patients 10 minutes before start of ESWL. The Observer's Assessment of Alertness/ Sedation scores, RR and VAS were recorded at 5 minute intervals. Visual analog scale values, RR, SpO_2 were low in Dexmedetomidine group. They concluded that Dexmedetomidine-Fentanyl is effective for sedation in ESWL.

Eren G, Cukurova Z, Demir G, Hergunsel O, Kozanhan B, Emir NS (2011)[23] compared Dexmedetomidine with three different doses of Midazolam for sedation. 125 patients were divided into three groups: Group I (n = 40) for control, Group II (n = 40) for Dexmedetomidine (1 µg/kg/h), and group III was the Midazolam group (n = 45). Group III patients were further divided into A, B, C subgroups to receive 0.02 mg/kg, 0.04 mg/kg, and 0.06 mg/kg of Midazolam respectively. Drugs were given over 10 minutes. Ramsay and visual analog scores, HR, Blood pressure, SpO_2, respiratory rates were measured every 5 minutes upto 30 minutes. Sedation and anxiolysis was better in

Group II and III C. They concluded that Dexmedetomidine was as effective at lower doses in comparison to Midazolam at higher doses in terms of sedation. They also concluded that although Dexmedetomidine caused significant decrease in the blood pressure and heart rate, it probably just normalized increased levels caused by preoperative stress.

Candiotti KA, Bergese SD, Bokesch PM, Feldman MA, Wisemandle W, Bekker AY (2010)[24] conducted a study on Monitored Anaesthesia Care with Dexmedetomidine. 326 patients were randomized 2:2:1 to receive Inj. Dexmedetomidine 0.5 µg/kg, Dexmedetomidine 1 µg/kg, or Normal Saline as loading dose, followed by a maintenance infusion of 0.2–1.0 µg/kg/h of Dexmedetomidine or equivalent volume of saline titrated to achieve sedation level 4 on the Observer's Assessment of Alertness/Sedation Scale [OAA/S], 15 minutes before placement of block. Inj. Midazolam was given if sedation score was ≤ 4 and Inj. Fentanyl given for pain. Patients not requiring rescue Midazolam were noted. Fewer patients in the 0.5 and 1 µg/kg Dexmedetomidine groups required Midazolam and Fentanyl supplementation compared with placebo. They concluded that Dexmedetomidine is an effective sedative for patients undergoing surgeries under MAC as it provides better patient satisfaction, less opioid requirements and less respiratory depression.

Vyas DA, Hihoriya NH, Gadhavi RA (2013)[25] compared Dexmedetomidine versus Midazolam for sedation during Tympanoplasty and Modified radical mastoidectomy under local anaesthesia. 50 patients were divided into two groups to receive either Inj. Dexmedetomidine 1µg/kg loading dose over 15 minutes and 0.5µg/kg/h (n= 25) as maintenance or Inj. Midazolam 0.05 mg/kg loading dose and 0.01mg/kg/h (n= 25)

maintenance. Blood pressure, heart rate, sedation level, patient and surgeon satisfaction scores were measured. Sedation was comparable in both groups but Surgeon's satisfaction score and patient's satisfaction score were higher in group D. They concluded that Dexmedetomidine is a suitable alternative to Midazolam for ENT surgeries done under MAC.

Parikh DA, Kolli SN, Karnik HS, Lele SS, Tendolkar BA(2013)[26] compared Dexmedetomidine with Midazolam-Fentanyl for Tympanoplasty under local anaesthesia. Patients were divided into 2 groups to receive either Inj. Dexmedetomidine 1 µg/kg over 10 minutes loading dose and 0.2 µg/kg/hr maintenance infusion (Group D) or Inj.Midazolam 0.06 mg/kg plus Inj. Fentanyl 1 µg/kg loading dose (Group MF) followed by Normal saline infusion at 0.2 ml kg/h. Sedation was titrated to RSS of 3. Vital parameters, rescue analgesics and sedatives, patient and surgeon satisfaction scores were recorded. Patient and surgeon satisfaction score was better in Group D than Group MF. Patients requiring rescue Fentanyl and Midazolam was higher in Group MF than Group D. They concluded that Dexmedetomidine is better than Midazolam-Fentanyl for sedation during Tympanoplasty with better surgeon and patient satisfaction.

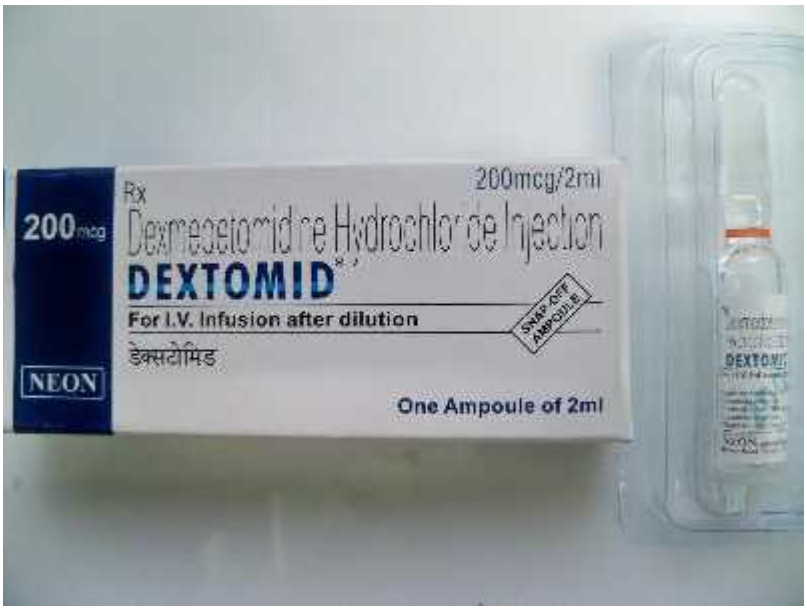
Verma R, Gupta R, Bhatia VK, Bogra J, Agarwal SP (2014)[27] conducted a study comparing Dexmedetomidine versus Propofol for MAC in patients undergoing middle ear surgeries. Patients in Group Dexmedetomidine received 1 µg/kg infusion over 10 minutes and 0.4 µg/kg/hr. Patients in Propofol group received 75 µg/kg/min for 10 minutes and 50 µg/kg/min infusion. Patients were monitored for hemodynamic parameters and sedation. They concluded that both drugs provide adequate sedation but

Propofol group was associated with more requirement of rescue analgesia and poor patient and surgeon satisfaction.

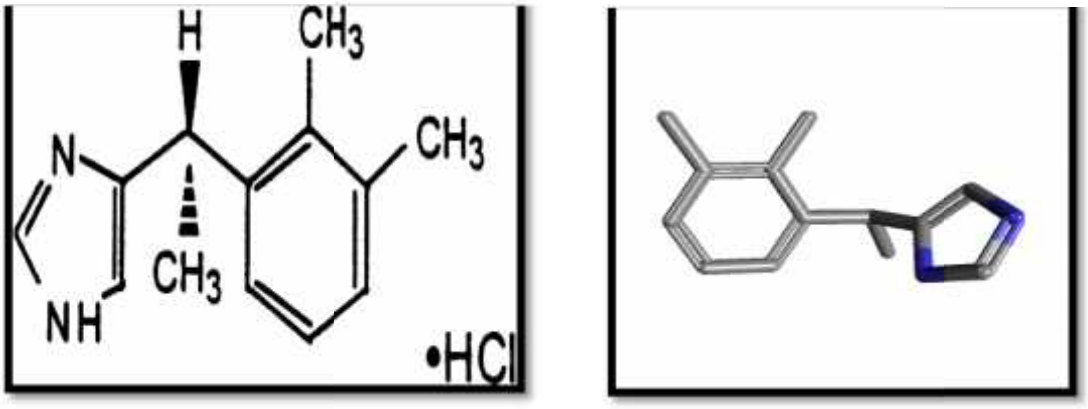
Gupta K, Bansal M, Gupta PK, Pandey MN, Agarwal S (2015)[28] conducted a study on 64 patients undergoing middle ear surgery under General anaesthesia to assess better operating conditions, bloodless field and depth of anaesthesia and rapid emergence. Patients were divided into 2 equal groups to receive either Dexmedetomidine infusion @ 0.5µg/kg/h or placebo infusion of normal saline. Patients were assessed intra operatively for bleeding at site, hemodynamics, awakening and postoperative recovery. They concluded that Dexmedetomidine infusion provides oligemic field thereby providing better visualisation with operating microscope for middle ear surgery.

Padmaja A, Varma T, Darshini PP(2015) [29] conducted a study comparing efficacy of Midazolam versus Dexmedetomidine in 40 patients undergoing minor ENT procedures under MAC in terms of sedative properties, rescue analgesic doses needed and hemodynamics. They concluded that Midazolam and Dexmedetomidine are comparable in terms of sedation but Dexmedetomidine reduces dose of rescue analgesic and decreases MAP, thereby reducing bleeding at surgical site making it a more favourable choice for ENT surgeries.

PHARMACOLOGY OF DEXMEDETOMIDINE



Dexmedetomidine hydrochloride belongs to imidazole subclass of α 2 receptor agonists and is a S- enantiomer of Medetomidine, an agent previously used as a veterinary anesthetic . It is described chemically as (+)- 4 - (s) [2, 3- (dimethyl phenyl) ethyl]-11 - imidazole monohydrochloride. Empirical formula is $C_{13}H_{16}N_2HCl$ and it has a molecular weight of 236.72.



Structure of Dexmedetomidine

MECHANISM OF ACTION:

Dexmedetomidine is a nonselective α_2 agonist with α_2/α_1 binding ratio of 1620:1[2,30] compared to Clonidine, α_2/α_1 200:1, making it a complete α_2 agonist.[31] (8 times more specificity for α_2 receptors). The α_2 adrenoceptor selectivity of Dexmedetomidine is dose-dependent i.e at low to medium doses or at slower rates of infusion, high levels of α_2 receptor selectivity are observed, while high doses or rapid infusions of low doses are associated with both α_1 and α_2 activities.

$\alpha_2$receptors are G protein coupled receptors. Intracellular pathways include inhibition of Adenylate cyclase and modulation of ion channels. 3 homologous subtypes of α_2 have been identified in humans namely $\alpha_{2A,}$ α_{2B} andα_{2C} .

$\alpha_2$adrenoceptors are found in CNS in highest densities in the locus ceruleus which is the predominant noradrenergic nuclei of brainstem and an important modulator of vigilance. Presynaptic activation of α_{2A} adrenoceptor in locus ceruleus inhibits the release of nor-epinephrine and results in sedation and hypnosis.[32] Stimulation of α_2 adrenoceptors in descending medullospinal noradrenergic pathway terminates the propagation of pain signals leading to analgesia, sympatholysis and neuroprotection. Postsynaptic activation of α_2 receptors results in decreased sympathetic activity that leads to hypotension and bradycardia.[33] Stimulation of α_{2B} receptor suppresses shivering, promotes analgesia at spinal cord and induces vasoconstriction of peripheral vasculature. The α_{2C} receptors are associated with modulation of cognition, sensory processing, mood, stimulant-induced locomotor activity and regulation of epinephrine outflow from the

adrenal medulla. Inhibition of nor epinephrine release appears to be equally affected by all three α_2 receptor subtypes.[34]

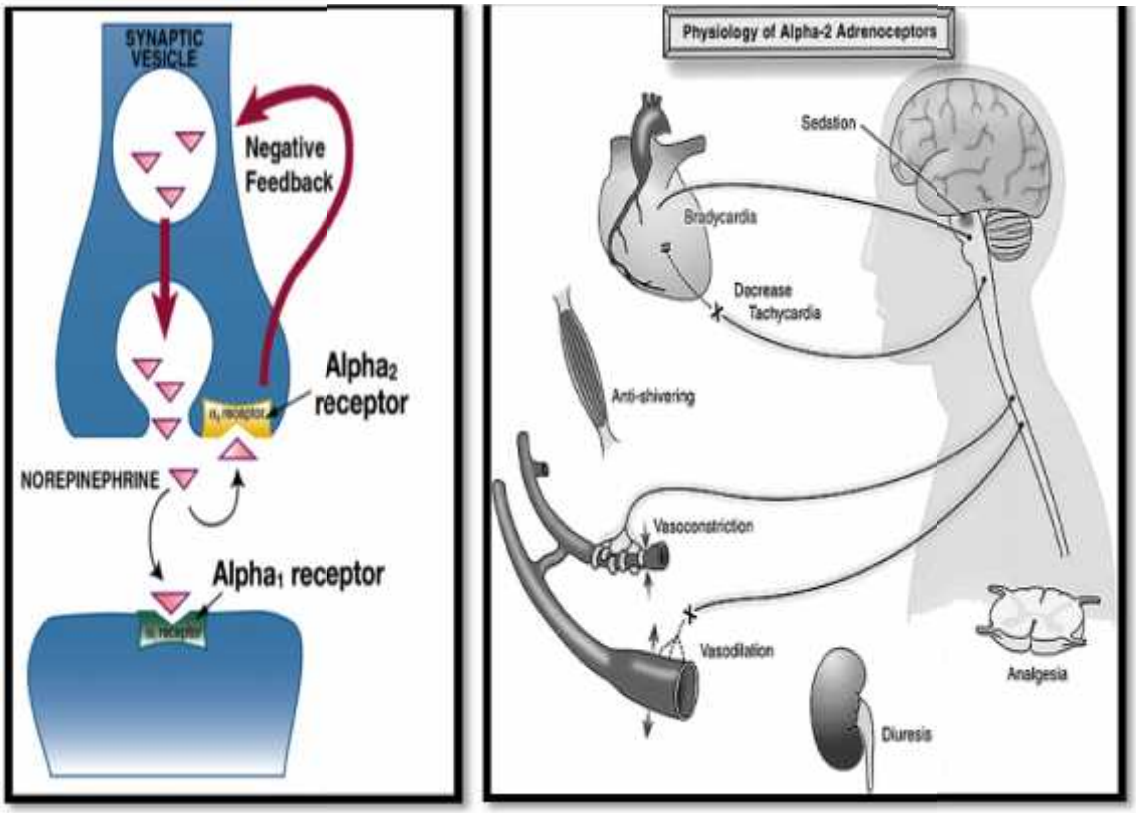


Fig.2.a. Alpha receptor, b. Physiology of Alpha-2 Adrenoreceptor

PHARMACOKINETICS:

After intravenous injection, Dexmedetomidine has an onset of action after approximately 15 minutes. Peak concentrations are usually achieved within 1 hour after continuous infusion. It has a rapid distribution phase with half-life (t ½ α) of 6 minutes, terminal elimination half-life (t ½ β) of 2-2.5 hours, and volume of distribution (V_d) of 118 litres. Clearance is approximately 39L/h. It exhibits linear kinetics in the dose of 0.2-

0.7 µg/kg/h when given for less than 24 hours. It has context-sensitive half-life ranging from 4 minutes after a 10-minute infusion to 250 minutes after an 8-hour infusion.

Dexmedetomidine is rapidly distributed and extensively metabolized in the liver and undergoes near complete biotransformation through direct glucuronidation and cytochrome P_{450} metabolism. Metabolites of biotransformation are excreted in the urine (95%) and faeces. Metabolites possess some intrinsic activity. Total plasma clearance is age independent, thus similar rates of infusion can be used in children and adults. The average protein binding of Dexmedetomidine is 94% with a 6% free fraction. The dose should be reduced in patients with liver or renal impairment. It crosses the placenta and should be used during pregnancy only if the potential benefits outweigh the risk to fetus.

Dexmedetomidine is absorbed through transdermal, buccal or intramuscular routes, with a mean bioavailability from the latter two routes of 82% and 104% respectively. After intramuscular administration, the time to t_{max} in the blood is 1.6-1.7 hours, with a bioavailability of 73%. After transdermal administration, the t_{max} is around 6 hours with a bioavailability of 88%.

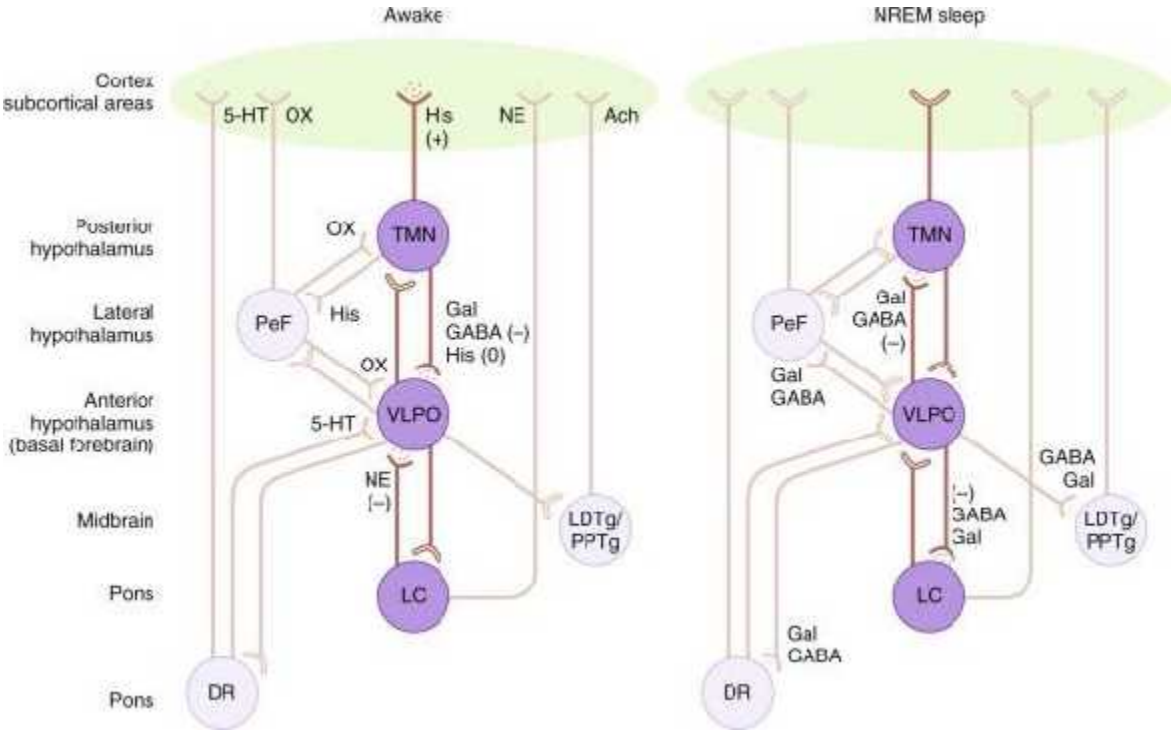
EFFECTS ON ORGAN SYSTEMS:

CENTRAL NERVOUS SYSTEM:

i) Sedation:

The α_2 agonists produce their hypnotic[2, 35,36]effects by an action on α_2 receptors in the locus ceruleus, sedative effects through the endogenous sleep-promoting pathway. The quality of sedation produced by Dexmedetomidine seems different compared to that produced by other sedatives acting through the GABA systems.

Dexmedetomidine decreases projections of the locus ceruleus to the ventrolateral preoptic nucleus. This increases GABAergic and galanin release in the tuberomammillary nucleus which causes a decrease in level of histamine release in cortical and subcortical projections. α_2 agonists possibly inhibit ion conductance through L-type or P-type calcium channels and facilitate conductance via voltage-gated calcium-activated potassium channels. The type of sedation is described as “cooperative or arousable”, to distinguish it from sedation induced by drugs acting on the GABA system, such as Midazolam or Propofol which produce a clouded consciousness.[37] The similarity between natural sleep (non–rapid eye movement) and Dexmedetomidine-induced hypnosis has been tried to maintain cognitive and immunologic function in the sleep-deprived patients in ICU. Dexmedetomidine at a dose 10 times normal range causes profound sedation and can be used for total intravenous anaesthesia.



Dexmedetomidine causes non–rapid eye movement sleeping pattern (NREM). The stimulation of the locus ceruleus (LC) by Dexmedetomidine (*Right*) releases the inhibition over the ventrolateral preoptic nucleus (VLPO). The VLPO subsequently releases γ-aminobutyric acid (GABA) onto the tuberomammillary nucleus (TMN). This inhibits the release of the arousal-promoting histamine on the cortex and forebrain, thereby inducing loss of consciousness. *(From Ebert T, Maze M: Dexmedetomidine: Another arrow for the clinician's quiver. Anaesthesiology 101:569-570, 2004.)*

ii) Analgesia:

$\alpha_2$agonists produce analgesia when given via the intra thecal or epidural route.[38] This is due to inhibition of firing of nociceptive neurons in substantia gelatinosa of the dorsal horn of the spinal cord[39] which are stimulated by peripheral Aδ and C fibers and also inhibition of release of the nociceptive neurotransmitters like substance P, encephalins. Dexmedetomidine use has been shown to decrease opioid requirement.[40,41]

iii) Cerebroprotection:

Dexmedetomidine reduces intra cerebral catecholamine outflow during injury and results in less neural tissue damage with better neurologic outcome. Neuro protective effects may be due to modulation of pro apoptotic and anti apoptotic proteins and reduction of glutamate that is produced during injury.

CARDIOVASCULAR SYSTEM:

Dexmedetomidine has no direct effects on heart. It shows a biphasic, dose-dependent blood pressure effect. At low doses, it reduces sympathetic tone which is mediated by decrease in norepinephrine release at the neuro effector junction and inhibition of neurotransmission in sympathetic nerves[42]. The net effect is significant reduction in circulating catecholamines with a slight decrease in blood pressure and a modest reduction in heart rate[43]. When administered as a continuous infusion it causes a stable haemodynamic response. Significant hypotension is usually seen in hypovolemic patients. Bradycardia is common in patients with high vagal tone. It is due to central sympatholytic action, partly by baroreceptor reflex and enhanced vagal activity. The administration of 1 µg/kg body weight bolus (high dose) produces transient increase in blood pressure and reflex decrease in heart rate caused by activation of α_{2b} receptors located on vascular smooth muscle cells.

RESPIRATORY SYSTEM:

Dexmedetomidine reduces minute ventilation while retaining the slope of the ventilatory response to increasing carbon dioxide at doses that cause significant sedation.[44]Ventilation changes produced by Dexmedetomidine are similar to those seen

during normal sleep. Dexmedetomidine has also been shown to block histamine-induced bronchoconstriction in some studies done in dogs.[45]

ENDOCRINE FUNCTION:

Dexmedetomidine at high doses or prolonged use causes decrease in level of circulating catecholamines. It causes attenuation of stress response by inhibition of secretion of Adrenocorticotropic hormone (ACTH) and Cortisol.[46] The ratio of levels of inhibition caused by Etomidate and Dexmedetomidine was shown to be in the order of 100:1, suggesting that inhibitory activity of Dexmedetomidine is not clinically relevant. Stimulation of α_2 adrenoreceptors on pancreatic β cells inhibits the release of insulin however this effect has not been proved clinically, because hyperglycemia has not been reported to be significant in patients who received α_2 agonists.

RENAL FUNCTION:

Dexmedetomidine exerts a diuretic effect by decreasing secretion of Vasopressin and inhibiting its action at the collecting duct. This results in reduced expression of aquaporin-2 receptors thereby decreasing salt and water absorption. α_2 agonists also increase release of Atrial natriuretic peptide that results in natriuresis[46].

THERMOREGULATION:

Dexmedetomidine lowers shivering threshold and rates of shivering but does not change the sweating threshold. Thermoregulatory response is inhibited within a wider range of temperature, possibly by its activity at α_{2B} receptors in the hypothalamic thermoregulatory centre of the brain.

USES:

1. **Monitored anaesthesia care (MAC):** Dexmedetomidine causes arousable sedation with anxiolysis, analgesia and ease of orientation without causing respiratory depression.
2. **Premedication:** Dexmedetomidine at dose of 0.33 to 0.67 mcg/kg given 15 minutes prior to surgery has anxiolytic, sedative, analgesic, antisialagogue and sympatholytic effects.[47]
3. **Adjuvant during General Anaesthesia:** Dexmedetomidine can be used as an adjuvant to General anaesthesia due to its analgesic, sedative and sympatholytic properties. It reduces dose of Thiopentone, inhalational agents and Opioids.[48] It also effectively attenuates the hemodynamic stress response to endotracheal intubation[2]. It decreases oxygen consumption in intraoperative and postoperative period[49].In postoperative period, Dexmedetomidine infusion can be continued in extubated and spontaneously breathing patients. The ongoing sedation and sympatholytic effect is beneficial in reducing myocardial ischemic events in post operative period in patients undergoing non-cardiac surgery.
4. **Adjuvant in Regional Anaesthesia:** Highly lipophilic nature of Dexmedetomidine allows rapid absorption into cerebrospinal fluid and binding to α_2 receptors of spinal cord is responsible for its analgesic action. It prolongs both duration of sensory and motor blockade induced by local anaesthetics when given via Intrathecal, Epidural, Caudal route [50-52]. Intrathecal Dexmedetomidine at a dose of 3 μg causes significant prolongation of sensory and motor blockade. Epidural Dexmedetomidine at a dose of 100 μg has been shown to decrease the

incidence of postoperative shivering. Addition of Dexmedetomidine 2 μg/kg body weight to Bupivacaine for caudal analgesia in pediatric patients promotes post operative analgesia. Addition of 0.5 μg/kg body weight of Dexmedetomidine to Lidocaine for intravenous regional anaesthesia improves the quality of anaesthesia and perioperative analgesia.

5. **Cardiac Surgery:** Dexmedetomidine blunts haemodynamic response to endotracheal intubation and also reduces myocardial ischemia during cardiac surgery[53]. Dexmedetomidine causes reduction in pulmonary vascular resistance, pulmonary artery pressure and pulmonary capillary wedge pressure and has been successfully used to manage pulmonary hypertension in patients undergoing mitral valve replacement.
6. **Neurosurgery:** Dexmedetomidine maintains stable cerebral haemodynamics without causing sudden increase in ICP during intubation, extubation and head pin insertion. It attenuates the neurocognitive impairment like delirium and agitation. It does not interfere with neurological monitoring and allows immediate postoperative neurological evaluation. It exerts neuroprotective effect during cerebral ischemia. Dexmedetomidine has been safely used in awake craniotomy procedures[17] and implantation of deep brain stimulators for Parkinson's disease.
7. **ICU Sedation:** Dexmedetomidine is a popular agent in the ICU due to its ability to produce sedation while keeping the patient awake, calm and being able to communicate their needs. Patients receiving Dexmedetomidine infusions as part of their sedation regimen in the postoperative ICU setting have been described as being very easy to wake up and having the ability to follow commands and

cooperate while being tracheally intubated. Undisturbed patients were noted to fall asleep right away[54]. Despite sound levels of sedation, there is limited respiratory depression, providing wide safety margins [55] .This characteristic allows for "daily wake up" tests to be done in a safe fashion. This critical test is done when ventilated ICU patients are taken off all sedatives to assess their mental status and sedation is titrated accordingly. It facilitates early weaning from ventilator and thereby reducing overall stay in ICU[56] It is approved by FDA for ICU sedation for not more than 24 hours.

8. **Procedural Sedation:** Dexmedetomidine is an excellent agent for short term procedural sedation and has been safely used in Trans-esophageal echocardiography, Colonoscopy, Awake fiberoptic intubation[43], pediatric patients undergoing MRI[57-59]etc. The usual dose of dexmedetomidine is 1 mcg/kg for 10 minutes followed by infusion of 0.2 mcg/kg/hr. Its onset of action is 5 minutes and peak effect is seen at 15 minutes.
9. **Controlled Hypotension:** Dexmedetomidine is an effective agent for controlled hypotension and this is mediated by its central and peripheral sympatholytic action. It is a near ideal hypotensive agent due to its ease of administration, predictability with anaesthetic agents, ability to maintain adequate perfusion to vital organs and lack of toxic side effects. Controlled hypotension using Dexmedetomidine has been safely used in Spinal surgeries for Scoliosis correction, Septoplasty, FESS, Tympanoplasty, Maxillofacial surgeries etc.
10. **Analgesia:** Dexmedetomidine causes activation of α_2 receptors in spinal cord and thereby reduces transmission of nociceptive signals like substance P. It has

significant opioid sparing effect and is useful in intractable neuropathic pain. Intra-articular administration during knee surgery improves postoperative analgesia and less analgesic is required compared to IV route. Suggested mechanisms are activation of α_{2A} receptors, inhibition of the conduction of nerve signals through C and A δ fibres and the local release of encephalin.

11. **Obesity:** Dexmedetomidine can be used as 0.7mcg/kg infusion preoperatively as an alternative to narcotics to avoid respiratory depression in morbidly obese patients.

ADVERSE EFFECTS:

Hypotension, hypertension, nausea, vomiting, bradycardia and hypoxia are common after loading dose of Dexmedetomidine.[60]A frequently reported side effect of is dry mouth which is due to its antisialagogue action.

Overdose may cause rare adverse effects like First or second-degree Atrioventricular block, Atrial fibrillation, Dystonia, Atelectasis, Hemorrhage, Confusion, Agitation and Rigors. Most of these events occur during or briefly after loading dose of drug. By omitting or reducing the loading dose, adverse effects can be reduced.

Withdrawal phenomenon is reported after abrupt discontinuation with prolonged administration of Dexmedetomidine, leading to development of hypertension, tachycardia, emesis, agitation, dilated pupils, diarrhea, increased muscle tone and tonic clonic seizures.

Effects of α_2 agonists are readily reversed by $\alpha_2$adrenergic antagonists like Atipamezole[37]. Similar to other adrenergic receptors, the α_2 agonists also show tolerance after prolonged administration.

DOSAGE AND ADMINISTRATION:

The recommended loading dose of Dexmedetomidine is 1 μg/kg body weight IV given over a period of ten minutes, followed by a continuous IV infusion of 0.2-0.7 μg/kg/hr. The maintenance dose is titrated until the sedation goal is reached.

DRUG INTERACTIONS:

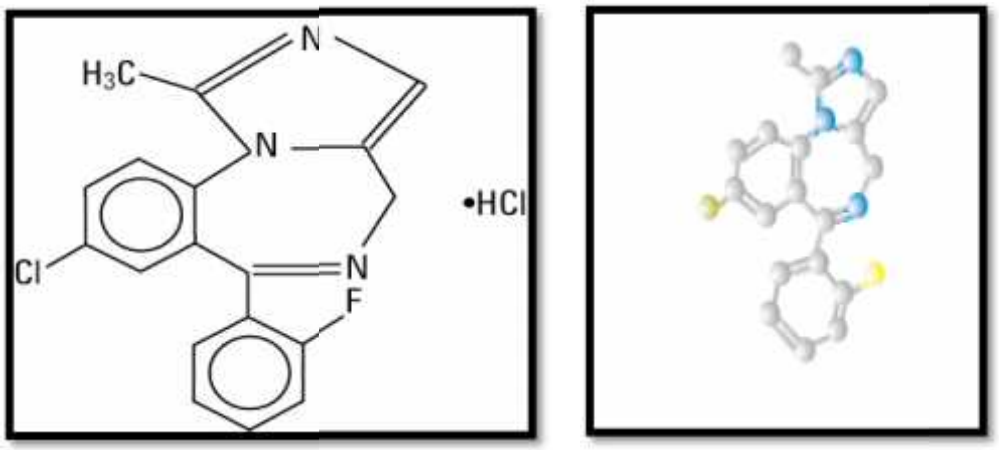
Studies have shown that Dexmedetomidine inhibits CYP2 D6 in vitro, but the clinical significance is still not known. Dexmedetomidine has minimal interaction with drugs metabolized by the Cytochrome P 450 system.

Sedative, hypnotic or anaesthetic effects of Dexmedetomidine are enhanced during co-administration with Isoflurane, Sevoflurane, Propofol , Midazolam.

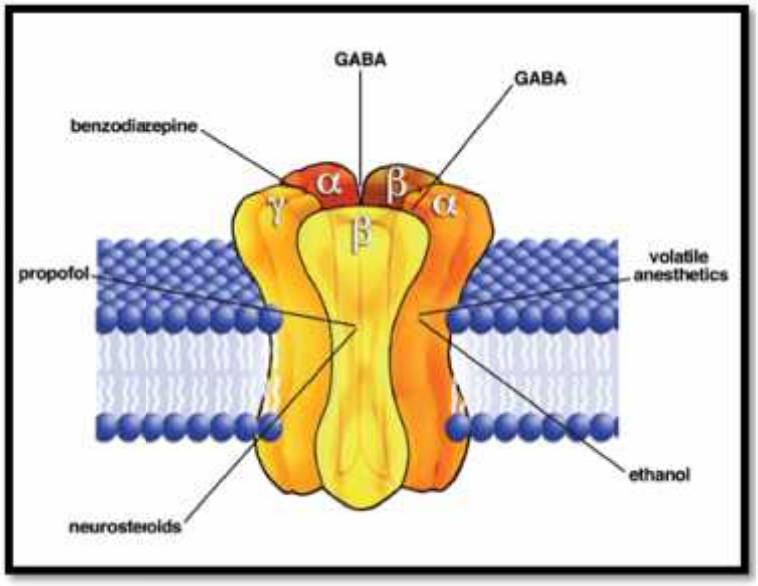
PHARMACOLOGY OF MIDAZOLAM

Midazolam is an imidazobenzodiazepine derivative with imidazole ring in its structure[5] that accounts for stability in aqueous solution & rapid metabolism. It is described chemically as 8-Chloro-6-(2-fluorophenyl)-1-methyl-4H-imidazo [1,5-a][1,4] benzodiazepine. Its empirical formula is $C_{18}H_{13}ClFN_3$ and it has a molecular weight of 362 D. The drug was synthesized in 1976 by Fryer and Walser. The unique structure of midazolam confers a number of physicochemical properties that distinguish it from other benzodiazepines in terms of its pharmacologic and pharmacokinetic characteristics.

Midazolam is 2-3 times more potent and has twice the affinity for benzodiazepine receptors compared to Diazepam. Midazolam is a short acting drug and is used as premedication, sedative and induction agent. It produces dose-dependent anxiolysis, hypnosis, anterograde amnesia and conscious sedation. It has anticonvulsant and spinally mediated muscle relaxant properties. Compared to other benzodiazepines its amnestic effects are more potent than sedative effects.



Structure of Midazolam



Structure of GABA receptor

MECHANISM OF ACTION

Midazolam produces its pharmacologic effects by facilitating the actions of γ-aminobutyric acid (GABA), the principal inhibitory neurotransmitter in the CNS. The benzodiazepine receptors are found in highest densities in the olfactory bulb, cerebral cortex, cerebellum, hippocampus, substantia niagra, and inferior colliculus, lower densities are found in the striatum, lower brainstem, and spinal cord. $GABA_A$ receptor is a large macro molecule that contains physically separate binding sites (alpha, beta & gamma subunits) not only for GABA and Benzodiazepines but also for Barbiturates, Etomidate, Propofol, neurosteroid and alcohol. Therefore benzodiazepines, barbiturates and alcohol can produce synergistic effects on CNS. Benzodiazepines have built in ceiling effect that prevents them from exceeding the physiological maximum of GABA inhibition.

Benzodiazepines do not cause activation of $GABA_A$ receptors but rather enhance the affinity of the receptors for inhibitory neurotransmitter, GABA .This causes an enhanced opening of chloride gated channels resulting in increased chloride conductance, thus producing hyperpolarization of the postsynaptic cell membrane and rendering postsynaptic neurons more resistant to excitation.

Sedation, anterograde amnesia, and anticonvulsant properties are mediated via α_1 subunit (more abundant receptor situated in cerebral cortex, cerebellar cortex, and thalamus) whereas anxiolysis and muscle relaxation is due to α_2 subunit of $GABA_A$[61](less abundant & present principally in hippocampus and amygdala). Midazolam receptor occupancy of less than 20% is sufficient to produce the anxiolytic effect, sedation is

observed with 30% to 50% receptor occupancy, and unconsciousness requires 60% or greater occupation of benzodiazepine agonist receptors.

PHARMACOKINETICS:

Midazolam has a rapid onset of action of 30-60 seconds compared to other benzodiazepines. The high lipophilic nature of Midazolam at physiologic pH causes its rapid onset of activity and equilibration between plasma and CSF occurs within 2-3 minutes after IV administration.[62,63] This lipophilicity accounts for rapid CNS effect and large volume of distribution of 1-1.5 litres/ kg. Elderly and morbidly obese patients have an increased volume of distribution resulting from enhanced distribution of drug into peripheral adipose tissues.[64,65] Its very high metabolic clearance and rapid rate of elimination causes it to have a short duration of action. Midazolam is extensively bound to plasma proteins (96-98%)[66] and this binding is independent of plasma concentration. Distribution half life is 7-15 minutes. Elimination half time of midazolam is 1-4 hours. The termination of action after single doses is caused both by distribution into peripheral tissues and by metabolic biotransformation. The context-sensitive half-times for Diazepam and Lorazepam are very long, therefore, only Midazolam should be used by continuous infusion to avoid excessive accumulation**.**

Midazolam is rapidly metabolized by hepatic & small intestine cytochrome-P_{450} (CYP3A4) enzyme to inactive metabolites. Only about 50% of an orally administered dose reaches the systemic circulation, reflecting a substantial first pass hepatic effect. The principal metabolite is 1-hydroxymidazolam which has approximately half the activity of parent compound. This active metabolite is rapidly conjugated to 1-

hydroxymidazolam glucuronide and subsequently cleared by kidneys.[67] Renal clearance of midazolam is 6-8ml/kg/min. The elimination half time, V_d, the clearance of midazolam are not altered by renal failure. This is consistent with the extensive hepatic metabolism of midazolam. Metabolism of Midazolam is slowed in the presence of drugs like Cimetidine, Erythromycin, calcium channel blockers, anti fungal agents which inhibit cytochrome P_{450} resulting in unexpected CNS depression.

EFFECTS ON ORGAN SYSTEMS:

1. **CENTRAL NERVOUS SYSTEM:**

Midazolam like other benzodiazepines produces decreases in cerebral metabolic oxygen requirements ($CMRO_2$) and cerebral blood flow analogous to barbiturates and Propofol[68]. However unlike these compounds Midazolam does not produce a burst suppression pattern on EEG, emphasizing that there is a ceiling effect with respect to the decrease in $CMRO_2$ produced by increasing doses of Midazolam. Plasma levels required for hypnosis and amnesia during surgery are 100 to 200ng/ml, with awakening usually occurring at levels less than 50 ng/ml.

It causes dose related changes in regional cerebral blood flow in brain regions associated with the normal functioning of arousal, attention and memory. The cerebral vasomotor response to carbon dioxide is preserved. In patients with severe head injury, a bolus dose of Midazolam may decrease CPP with little effect on ICP. Although Midazolam may improve neurologic outcome after incomplete ischemia in animal experiments, benzodiazepines have not been shown to possess neuroprotective activity in humans.

Midazolam is also potent anticonvulsant, effective in treatment of status epilepticus. Paradoxical excitement occurs in less than 1% of all patients receiving midazolam and is effectively treated by benzodiazepine antagonist Flumazenil.

2. RESPIRATORY SYSTEM:

Midazolam produces dose dependent decrease in ventilation.[69] Patients with COPD experience a greater depression of ventilation. Synergistic depressant effects occur when Midazolam is co-administered with opioid analgesics. Transient apnea may occur after rapid injection of large doses > 0.15mg/kg IV and respiratory depression may remain for 60-120 minutes[70], especially in presence of preoperative medication that includes Opioids. Benzodiazepines also depress swallowing reflex and decrease upper airway activity.

3. CARDIOVASCULAR SYSTEM:

Midazolam used alone has modest hemodynamic effects. The predominant hemodynamic change is a slight reduction in arterial blood pressure, resulting from a decrease in systemic vascular resistance. Midazolam maintains relatively stable hemodynamics by preservation of homeostatic reflex mechanisms. The hemodynamic effects of Midazolam are dose related, the plateau plasma level for Midazolam is 100 ng/mL, above which little change in arterial blood pressure occurs. The effects of Midazolam on systemic blood pressure are more in presence of hypovolemia. Heart rate, ventricular filling pressures, and cardiac output are maintained after induction of anaesthesia with Midazolam. In patients with elevated left ventricular filling pressures, Midazolam produces a “nitroglycerin-like” effect by decreasing the filling pressure and

increasing cardiac output. Despite the hypotension, Midazolam even in doses of 0.2 mg/kg is safe and effective for induction of anaesthesia even in patients with severe aortic stenosis.

USES:

Midazolam is the most commonly used benzodiazepine for preoperative medication[68] in pediatric patients, for IV sedation and for MAC. In combination with other drugs it can be used for maintenance of anaesthesia. Like Diazepam, it is a potent anticonvulsant for the treatment of grand mal seizures which may occur with systemic toxicity produced by local anesthetics.

1. **Premedication:**

It is the most commonly used oral premedication drug for children. Oral Midazolam syrup (2mg/ml) is effective for producing sedation and anxiolysis at a dose of 0.25mg/kg with minimal effect on ventilation and oxygen saturation even when administered at doses as large as 1mg/kg. In adults, Midazolam administered IV prior to induction, provides reliable sedation, anterograde amnesia and anxiolysis without causing delay in awakening.

Midazolam can be administered by various routes with following dosages:

- Oral 0.5mg/kg
- Intravenous 0.04 -0.08 mg/kg
- Intramuscular route 0.05- 0.1 mg/kg
- Trans mucosal-
    i) Intranasal 0.2- 0.5 mg/kg
    ii) Sublingual 0.2- 0.5mg/kg

2. Sedation and Monitored Anaesthesia Care:

Midazolam in doses of 1- 2.5mg IV (onset within 30-60 seconds, time to peak effect 3-5 minutes, duration of sedation 15-80 minutes) is effective for sedation during short procedures and regional anaesthesia. Compared to Diazepam, it produces a more rapid onset of action with greater anterograde amnesia and less postoperative drowsiness. Sedation occurs without loss of airway reflexes or significant cardiovascular changes. Caution should be exercised while sedating elderly patients because of its pharmacokinetics. Midazolam on injection is less veno-irritant compared to diazepam because of its water soluble property. Midazolam produces a conscious sedation, relief of anxiety and anterograde amnesia when administered prior to short procedures which require sedation like Tympanoplasty, Dental procedures, Upper GI endoscopy, Bronchoscopy, Cath lab procedures etc.

3. Induction of Anaesthesia

Anaesthesia can be induced by administration of Midazolam 0.1-0.2mg/kg over 30-60 seconds.[71] Onset of unconsciousness is facilitated when small dose of Opioid (Fentanyl 50-100 µg IV or its equivalent) precedes injection of Midazolam by 1-2 min. When midazolam is used in appropriate doses, induction occurs less rapidly than with Thiopentone, but amnesia is more reliable. Midazolam induction dose is less if preoperative medication includes CNS depressant drugs. Elderly patients require lesser dose due to increased sensitivity of Midazolam on CNS with increasing age. Awakening after general anaesthesia with Midazolam is 1-2.5 times longer than that of Thiopentone.

4. Maintenance of Anaesthesia:

Midazolam may be administered to supplement Opioids, Propofol and /or inhaled anesthetics during maintenance of anaesthesia. The context sensitive half time for Midazolam increases modestly with increase in duration of administration of the continuous infusion of these. Anesthetic requirements for inhalational anesthetics are decreased in a dose dependent manner by Midazolam. Infusions of Midazolam have been used to ensure a constant and appropriate depth of anaesthesia. Plasma level of > 50 ng/mL is achieved with a bolus loading dose of 0.05 to 0.15 mg/kg and a continuous infusion of 0.25 to 1 μg/kg/min. This plasma level is sufficient to keep the patient asleep and amnesic but arousable at the end of surgery.

ADVERSE EFFECTS:

Benzodiazepines have fewer side effects. The most significant problem with Midazolam is respiratory depression when it is used as sedative. When given for induction and maintenance of anaesthesia, benzodiazepines can produce an undesirable postoperative amnesia, sedation, and rarely respiratory depression. These effects can be reversed with Flumazenil. Rare side effects are loss of balance, blurring of vision and dysphoria.

ANTAGONIST: Flumazenil is a benzodiazepine antagonist. Elimination half time of 0.7-1.3 hours. Its half-life is shorter than those exhibited by benzodiazepines and as a result it would be possible to reverse benzodiazepines-mediated respiratory depression only to have it recur upon Flumazenil elimination. Consequently either repetitive

Flumazenil dosing or continuous infusion (0.5-1 µg/kg/min) may be required to ensure sustained recovery from benzodiazepine mediated effects.

DRUG INTERACTIONS:

Ethanol, Barbiturates and other central nervous system depressants potentiate the sedative effects of the benzodiazepines. Erythromycin, Ranitidine, Diltiazem, Fluconazole, Verapamil and Roxithromycin increase serum levels and toxic effects.

MONITORED ANAESTHESIA CARE

Monitored anaesthesia care (MAC) has been described as a specific anaesthesia service for diagnostic or therapeutic procedures performed under local anaesthesia along with sedation and analgesia, titrated to a level that preserves spontaneous breathing and airway reflexes, according to the latest American Society of Anesthesiologists (ASA) update in 2008. MAC alone or with local anaesthesia accounts for a relatively high percentage of anaesthesia services nationwide. MAC essentially comprises of three basic components: A safe conscious sedation, measures to allay patient's anxiety and effective pain control. MAC results in less physiologic disturbance and a more rapid recovery than general anaesthesia. MAC is suitable for day care procedures. Presently, MAC is the first choice in 10-30% of all surgical procedures.[72]

Monitored anaesthesia care (MAC) may be applied in varies ENT surgeries in which an adequate sedation and analgesia are desirable for the comfort of both the patient and surgeon. MAC includes support of vital functions, management of possible intraoperative problems, and provision of psychological support.

American Society of Anesthesiologists (ASA) Standards for Basic Anesthetic Monitoring applicable to all levels of anaesthesia care include monitored anaesthesia care too. It includes pulse Oximetry (SpO_2), Electrocardiography (ECG), NIBP Monitor, Capnography (most effective in intubated patients but can be adapted [side stream] to MAC). It is important to continually evaluate patient's response to verbal stimulation to titrate the level of sedation and to allow early detection of neurologic or cardiopulmonary dysfunction and to prevent awareness or excessive anaesthetic depth and thereby

promoting patient safety and early recovery. Bispectral index (BIS) is effective to measure the depth of consciousness during MAC. The incidence of apnea during MAC is high, and the incidence increases as BIS decreases[73].There is a poor correlation between BIS value and observational sedation scale scores for different sedative drugs[74], which emphasizes the use of both BIS and sedative scales to evaluate patient's response to sedation.

The American Society of Anesthesiologists along with the American Dental Association has dichotomized anaesthesia into 4 different levels – minimal, moderate, and deep sedation, and general anaesthesia.

Minimal sedation, also referred to as anxiolysis, describes a depressed levelof consciousness, but allows a patient to respond appropriately to verbal commands and light tactile stimulation. They often seem relaxed, but are fully aware of their surroundings. They also maintain their protective airway reflexes, thus are able to swallow, cough, and breathe without assistance.

Moderate sedation - the level consciousness is further depressed andpatients are less aware of their surroundings than during minimal sedation. Patients may require light tactile stimulation or repeated verbal commands to respond and also be able to maintain their protective airway reflexes and respiration.

Deep sedation - patients cannot be easily aroused and may respondpurposefully to repeated or painful stimulation. Their ability to protect their airway reflexes and maintain adequate spontaneous ventilation may be impaired.

A level of sedation that allows verbal communication should be optimal for the patient's comfort and safety. If the level of sedation is deepened to the extent that verbal communication is lost, most of the advantages of monitored anaesthesia care are also lost, and the risk of this technique almost approaches to general anaesthesia with an unprotected and uncontrolled airway. Arterial hypoxemia as a result of alveolar hypoventilation is a risk after the administration of sedatives, hypnotics, or analgesics. A patient who is receiving minimal supplemental oxygen may have acceptable oxygenation despite significant alveolar hypoventilation.

An ideal sedative agent should be consistently effective in having rapid onset, easy titration, high clearance, and minimal side-effects; particularly a lack of cardiovascular and respiratory depression. Due to dearth of an ideal agent, sedation techniques for MAC often utilizes a combination of agents to provide analgesia, amnesia, and hypnosis with complete and rapid recovery that suits a particular operative procedure with minimum side effects like postoperative nausea and vomiting (PONV), prolonged sedation, and cardiorespiratory depression. Fewer sedative drugs are required in geriatric population, as chances of desaturation and cardiovascular instability are more[75].

Targeting the effect-site concentration rather than blood concentration provides faster onset and better predictability of drug effect. Drug titratability can be achieved with the use of a wide variety of drug delivery techniques including intermittent boluses, target-controlled infusion, variable-rate infusion, and patient-controlled sedation (PCS). The patient maintained sedation (PMS) is found to be more effective than PCS in terms of patient satisfaction and minimizing side effect[76]. Use of continuous intravenous infusion

of short acting sedative – hypnotic drugs has been found to be associated with fewer intraoperative side effects and shorter recovery times than traditional intermittent bolus techniques as this provides stable level of sedation.

Several drugs have been used for sedation during surgery under local anaesthesia with monitored anaesthesia care including Propofol, Benzodiazepines and Opioids. However, Propofol[11] may cause over sedation and disorientation, benzodiazepines may result in confusion, particularly in elderly and opioids are associated with increased risk of respiratory depression[35] and oxygen desaturation. All of these untoward effects may hamper patient's cooperation during surgery and would make these agents less ideal for intraoperative management of sedation in MAC.

Midazolam is most commonly used for sedation in MAC and reported to be well tolerated by patients. Despite having a number of beneficial effects like quick onset, limited duration of action, it is far from being an ideal agent due to untoward effects like prolonged sedation after repeated administration, restlessness, cognitive impairment, respiratory depression.

Dexmedetomidine, a novel alpha-2 adrenergic receptor agonist, provides adequate sedation and analgesia with minimal respiratory depression. The sedative effect is rapid, stable and maintains patient arousability. It acts primarily on the sleep pathway and does not inhibit the activity of the orexinergic neurons, which is the basis of its arousable sedation[77]. Moreover it has sympatholytic action which not only decreases the stress response to surgery but also the surges in heart rate and blood pressure. Hypotension and bradycardia have been observed in studies done earlier with

Dexmedetomidine[78-80]. These effects are known to be related to the dose, route of administration and infusion rate (in intravenous administrations)[8,43,81,82]. Reports of its use state that, alpha-2 agonist effect is observed, but not alpha-1 effect, on administration of low and moderate doses and slow rates of infusion. Consequently, peripheral vasoconstriction and hypertension would not be expected in these instances[61-63]

A multicentric trial on 321 patients undergoing a broad range of surgical or diagnostic procedures under MAC revealed that Dexmedetomidine provides greater patient satisfaction, less opioid requirements, and less respiratory depression. Dexmedetomidine was well- tolerated over different age groups and the hypotension and bradycardia caused by its infusion were easily manageable. Dexmedetomidine with Fentanyl has been used safely and effectively for sedation and analgesia during extracorporeal shockwave lithotripsy[23]. Thus despite higher cost, Dexmedetomidine appears to be an attractive alternative and effective substitute of opioids, primarily due to its property of arousable sedation with analgesic sparing effect, preservation of better airway reflexes, and ventilatory drive.

Contrary to the popular belief, intravenous sedatives may actually increase the pain perception during procedural sedation. **Frolich MA** et al concluded that the pain perception during procedural sedation not only depends on the type of sedative administered but also the gender and race of the patient. This knowledge may actually help to guide us to provide analgesia and sedation to facilitate medical procedure.

MATERIALS AND METHODS

SOURCE OF DATA: This study was carried out in the Department of Anaesthesiology, B.L.D.E.U's Shri B.M Patil Medical College, Hospital and Research centre, Vijayapur.

STUDY PERIOD: One and half years, from December 2015 to August 2017.

STUDY DESIGN: Prospective, randomized, clinical comparative study of Dexmedetomidine and Midazolam intravenous infusion in patients undergoing Middle ear surgeries under local anaesthesia with Monitored Anaesthesia Care (MAC).

APPROVAL: Study was approved by the institutional medical ethics committee and written informed consent was obtained from all patients participating in the study.

STUDY POPULATION: 96 patients of either sex aged between 18-60 years of ASA grade I & II undergoing Middle ear surgeries under local anaesthesia with Monitored Anaesthesia Care were enrolled in the study.

STUDY GROUPS: Patients were allocated randomly by chit block method in two groups containing 46 patients each to receive either Inj. DEXMEDETOMIDINE (Group D) or Inj. MIDAZOLAM (Group M) for sedation during surgery.

GROUP D: Inj. Dexmedetomidine 1 µg/kg IV bolus over 10 minutes followed by continuous infusion @ 0.5 µg/kg/hr.

GROUP M: Inj. Midazolam 40 µg/kg IV bolus over 10 minutes followed by continuous infusion @ 20 µ/kg/hr.

PATIENT SELECTION:

INCLUSION CRITERIA:

- Age 18-60 years
- Patient of either sex
- ASA Grade I and II
- Patients undergoing Middle ear surgeries under local anaesthesia with MAC
- Patients consenting for the procedure

EXCLUSION CRITERIA:

- Pregnancy and Lactating women
- Patients with Asthma
- Patients on Beta Blocker drugs
- MI in last 6 months, AF, Heart blocks
- Deranged renal profile
- Advanced liver disease (liver enzymes twice the normal range or higher)
- History of chronic use of sedatives, narcotics and alcohol
- Known sensitivity to Lignocaine or allergy to study drugs.

RANDOMISATION: Patients were allocated randomly by chit block method in two groups containing 48 patients each i.e. Group D and Group M.

STUDY MATERIALS: Inj. Dexmedetomidine, Inj. Midazolam, Inj. Fentanyl, Inj. Propofol, Inj. Diclofenac, infusion pump and O_2 Nasal canula were used in the study.

METHODOLOGY:

- 96 patients undergoing middle ear surgery under MAC were divided in two groups containing 48 each according to chit block method to receive Dexmedetomidine (Group D) or Midazolam (Group M) infusion during surgery.
- Pre anaesthetic evaluation was done on the day before surgery and required investigations were advised.Patients were explained in detail about LA, operative procedure and sedation. Visual Analogue Scale was explained to patient during pre-operative visit.
- Patients meeting above criteria were asked to participate in study and informed consent was taken and they were advised to be nil by mouth overnight.
- **Investigations :**
  - ✓ Complete hemogram, Total leucocyte count, Differential Count, Bleeding Time, Clotting time.
  - ✓ Random blood sugar, Blood urea and Serum Creatinine.
  - ✓ Chest X-ray (when age >35 years or if necessary)
  - ✓ ECG
  - ✓ HIV, HBsAg (In accordance with universal safety precautions)
- **Preliminaries:**

✓ Written informed consent.

✓ Intravenous access with a 20 gauge I.V cannula on the contralateral upper limb under aseptic techniques.

- On the day of surgery, patient was taken to Operating room. ECG, non invasive BP and pulse oximetry were attached and baseline vitals were recorded. Inj. Glycopyrrolate 0.01-0.02 mg/kg and Inj. Ondansetron 0.15 mg/kg IV was given and IV Ringer Lactate solution at 2ml/kg/hr was started. O_2 was administered with nasal canula at 2lit/min.
- Patients in group D received Inj. Dexmedetomidine 1 µg/kg IV bolus over 10 minutes followed by continuous infusion at 0.5 µg/kg/hr.
- Patients in group M received Inj. Midazolam 40 µg/kg IV over 10 minutes followed by continuous infusion at 20 µg/kg/hr.
- Loading dose of both the drugs were calculated and diluted to 20 ml with 0.9% Normal saline and kept at constant rate of 120ml/hr given over 10 minutes.
- After the loading dose of the drug, Ramsay Sedation Score was assessed and sedation titrated to target sedation of RSS 3. Infusion was stopped when RSS was 3 or full 20 ml bolus had been given whichever was earlier. If the RSS < 3 at the end of 10 min of loading dose, patients were given Inj Propofol 100-300 mcg/kg IV bolus as a rescue sedative. The protocol of upto a maximum of 2 rescue doses was set. RSS was assessed throughout the duration of surgery and in postoperative period every 15 minutes up to 120 minutes.
- Once RSS was 3, Lidocaine 2% with adrenaline 1:200,000, 6-7 ml was given by the surgeon. The maintenance infusion was commenced at constant infusion rate for both the groups calculated according to weight of patient.
- Group D: Inj. Dexmedetomidine infusion was prepared by adding 100 mcg in 25 ml of 0.9% normal saline containing 4 µg/ml at 0.5 µg/kg/hr.

- Group M: Inj. Midazolam infusion was prepared by adding 4 mg in 25 ml of normal saline containing 0.16mg/ml at 20 µg/kg/hr.
- Intraoperative pain intensity was assessed with VAS (0-10). If VAS >3 or whenever patient complained of pain during surgery, Inj. Fentanyl @1 mcg/kg was given as rescue analgesic and additional dose of local anaesthetic 2-3 ml (not exceeding the maximum dose) was repeated by surgeon if required. The maintenance infusions were discontinued approximately 15 minutes before the end of surgery.
- Heart rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean arterial pressure(MAP), Respiratory Rate(RR), Oxygen Saturation(SpO_2) were recorded at the start of loading infusion, 5 minutes after, at the end of loading infusion and every 15 minutes thereafter till the end of surgery and postoperatively for 2 hours.
- Any time during the procedure if dosage of rescue drugs has crossed the acceptable dosage then the technique was discontinued and converted to any alternative sedative or anesthetic technique. Such incidents were noted and the subjects were withdrawn from further analysis.
- Patients were shifted to Post Anaesthesia Care Unit (PACU) after completion of surgery and were monitored for hemodynamic parameters. Pain was assessed postoperatively using Visual analog scale and if VAS >3, then Inj. Diclofenac 1.5mg/kg I.V was given.
- At the end of surgery, surgeons were asked to grade their satisfaction using Likert scale; score of 4 and 5 were taken as acceptable.

PARAMETERS MONITORED:

1. Heart Rate (HR)

2. Blood Pressure (SBP, DBP)

3. Mean Arterial Pressure (MAP)

4. Spontaneous Breathing Respiratory Rate (RR)

5. Oxygen Saturation (SpO_2).

6. Ramsay sedation score

7. Visual analog score

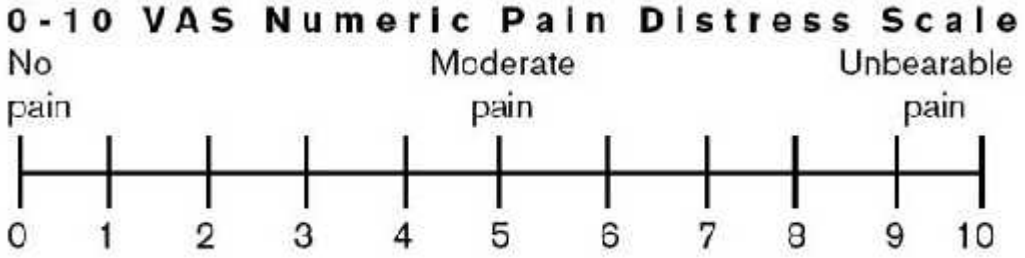
8. Surgeon satisfaction score

Ramsay Sedation Scale (RSS) for assessment of sedation.

Clinical score	Level of sedation achieved
1	Patient anxious, agitated or restless
2	Patient co-operative, oriented and tranquil
3	Patient responds to commands
4	Asleep but with brisk response to light glabellar tap or loud auditory stimulus
5	Asleep, sluggish response to light glabellar tap or loud auditory stimulus
6	Asleep, no response

FIGURE 1. Ramsey scale

VISUAL ANALOGUE SCALE for assessment of pain.



SURGEON SATISFACTION SCORE:

Very Dissatisfied (1)	Dissatisfied (2)	Neither Satisfied nor Dissatisfied (3)	Satisfied (4)	Very Satisfied (5)
○	○	○	○	○

SIDE EFFECTS:

Patients were monitored for adverse effects like dry mouth, nausea, vomiting, bradycardia, hypotension, hypertension etc both intraoperatively and postoperatively for 2 hours and treated accordingly.

Bradycardia was defined as pulse rate < 60 beats/min or < 20% of baseline heart rate and was treated with Inj. Atropine 0.01mg/kg.

Hypotension was defined as Mean Arterial Pressure < 20% of baseline level and was treated with fluid replacement and when this therapy was inadequate then I.V Ephedrine 5 mg in incremental doses was administered.

Hypertension was defined as increase in Mean Arterial Pressure > 20% of baseline and was treated using standard therapy.

Desaturation was defined as SPO_2 < 90% and was treated by increasing O_2 flow @ 6 lit/min via Hudson's Face mask or bag mask ventilation if required.

Bradypnea was defined as respiratory rate less than 8 cycles per min. and was treated by assisting or supporting the ventilation.

STATISTICAL ANALYSIS

All characteristics were summarized descriptively. For continuous variables, the summary statistics of N, mean, standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries. Chi-square (χ^2)/ Freeman-Halton Fisher exact test was employed to determine the significance of differences between groups for categorical data. The difference of the means of analysis variables between two independent groups was tested by unpaired t test.

If the p-value was < 0.05, the results were considered to be statistically significant. Data was analyzed using SPSS software v.23.0. and Microsoft office.

RESULTS

Table 1: Comparison of Mean Age between study groups

Parameters	Group D		Group M		p value
	Mean	SD	Mean	SD	
Age (years)	37.8	12.1	35.2	12.3	0.302

Range	Group D	Group M
Age (years)	18-60	18-58

Chart A: Comparison of Mean Age between study groups

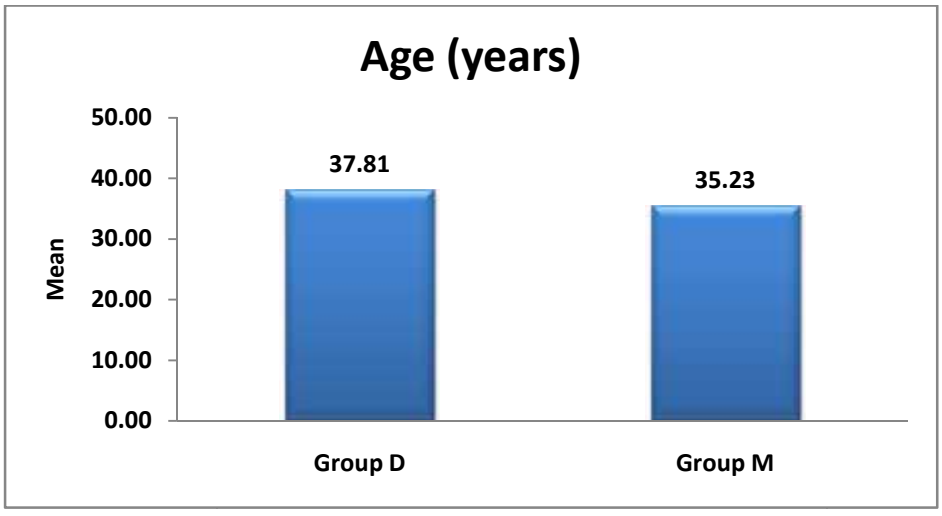


Table 1 and Chart A show mean distribution of age between the 2 study groups. There was no statistical difference between the groups.

Table 2: Comparison of Mean Weight (Kg) between study groups

Parameters	Group D		Group M		p value
	Mean	SD	Mean	SD	
Wt(Kg)	61.5	8.0	59.5	8.0	0.067

Range	Group D	Group M
Wt(Kg)	49-78	45-72

Chart B: Comparison of Mean Weight (Kg) between study groups

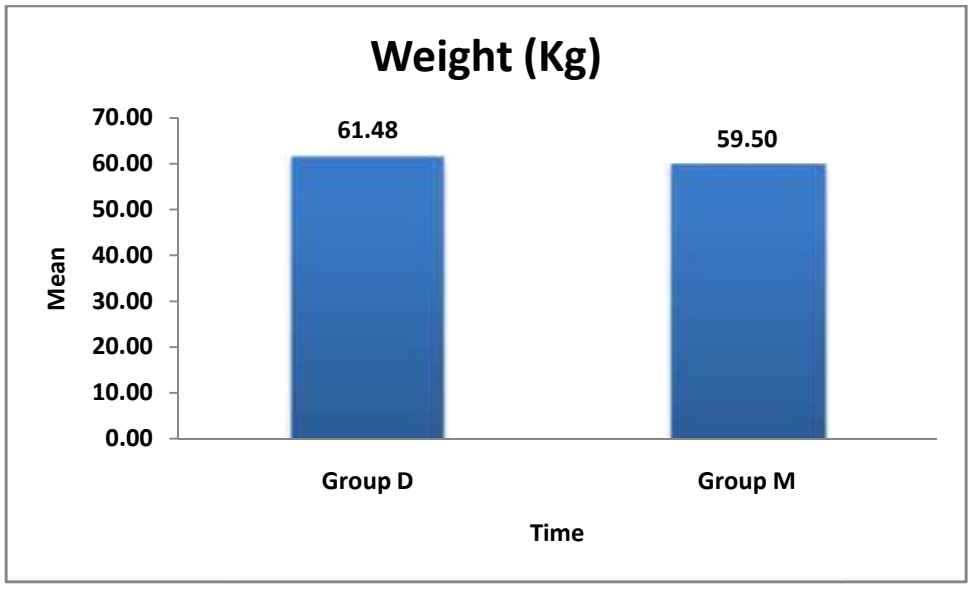


Table 2 and Chart B shows distribution of weight between 2 study groups. There is no statistical significance between both groups.

Table 3: Gender distribution between study groups

Sex	Group D		Group M		Total		p value
	N	%	N	%	N	%	
Male	29	60.4	29	60.4	58	60.4	
Female	19	39.6	19	39.6	38	39.6	-
Total	48	100.0	48	100.0	96	100.0	

Chart C: Gender distribution between study groups

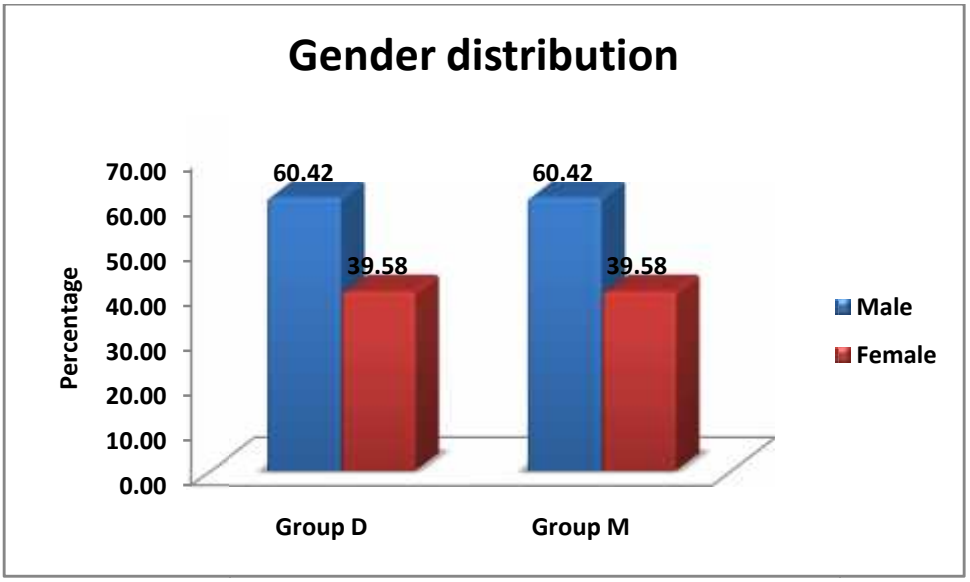


Table 3 and Chart Cshows gender distribution between study groups. There is no statistical significance.

Table 4: Distribution of Patients of ASA Grade I and II between study groups

ASA Grade	Group D		Group M		Total		p value
	N	%	N	%	N	%	
I	39	81.3	38	79.2	77	80.2	0.798
II	9	18.8	10	20.8	19	19.8	
Total	48	100.0	48	100.0	96	100.0	

Chart D: Distribution of patients of ASA Grade I and II between study groups

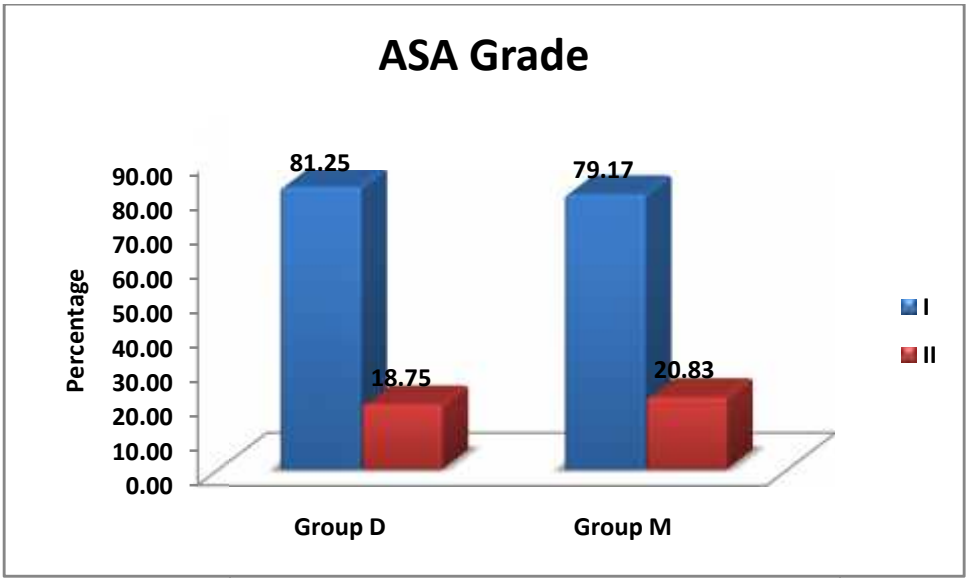


Table 4 and Chart D show distribution of patients of ASA grading I and II between study groups. The difference is not significant.

Table 5: Distribution of Mean Duration of Surgery between study groups

Parameters	Group D		Group M		p value
	Mean	SD	Mean	SD	
Duration of Surgery (minutes)	85.6	11.6	88.1	15.4	0.370

Range	Group D	Group M
Duration of Surgery (minutes)	75-120	60-120

Chart E: Distribution of Mean Duration of Surgerybetween study groups

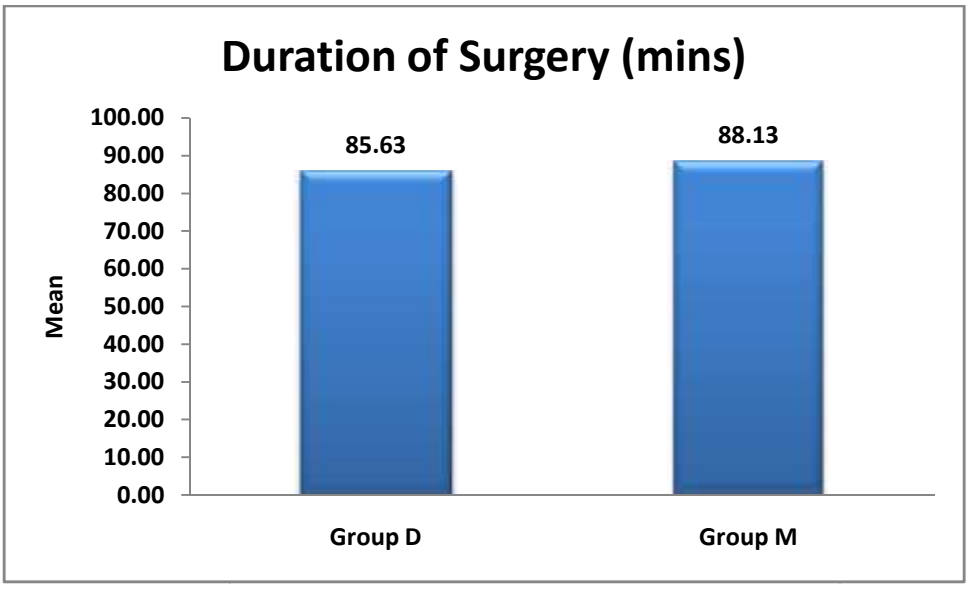


Table 5 and Chart E shows mean duration of surgery (minutes) in Group D and Group M. Both groups were comparable and there is no statistical significance.

Table 6: Change in mean Intra operative Ramsay sedation score (RSS) between study groups

Parameters	Group D		Group M		p value
	Mean	**SD**	**Mean**	**SD**	
5 MIN	1.40	0.49	1.44	0.50	0.683
10 MIN	2.85	0.46	2.85	0.36	1.000
15 MIN	3.00	0.29	2.77	0.42	**0.003***
30 MIN	3.06	0.24	2.77	0.42	**<0.001***
45 MIN	3.02	0.14	2.88	0.33	**0.007***
60 MIN	3.00	0.21	2.85	0.36	**0.016***
75 MIN	2.94	0.24	2.74	0.44	**0.01***
90 MIN	3.00	0.53	2.65	0.49	**0.015***
105 MIN	3.00	0.00	2.77	0.44	0.265
120 MIN	3.00	-	3.00	0.00	-

Note: *means significant at 5% level of significance ($p<0.05$)

Chart F: Change in mean Intraoperative RSS between study groups

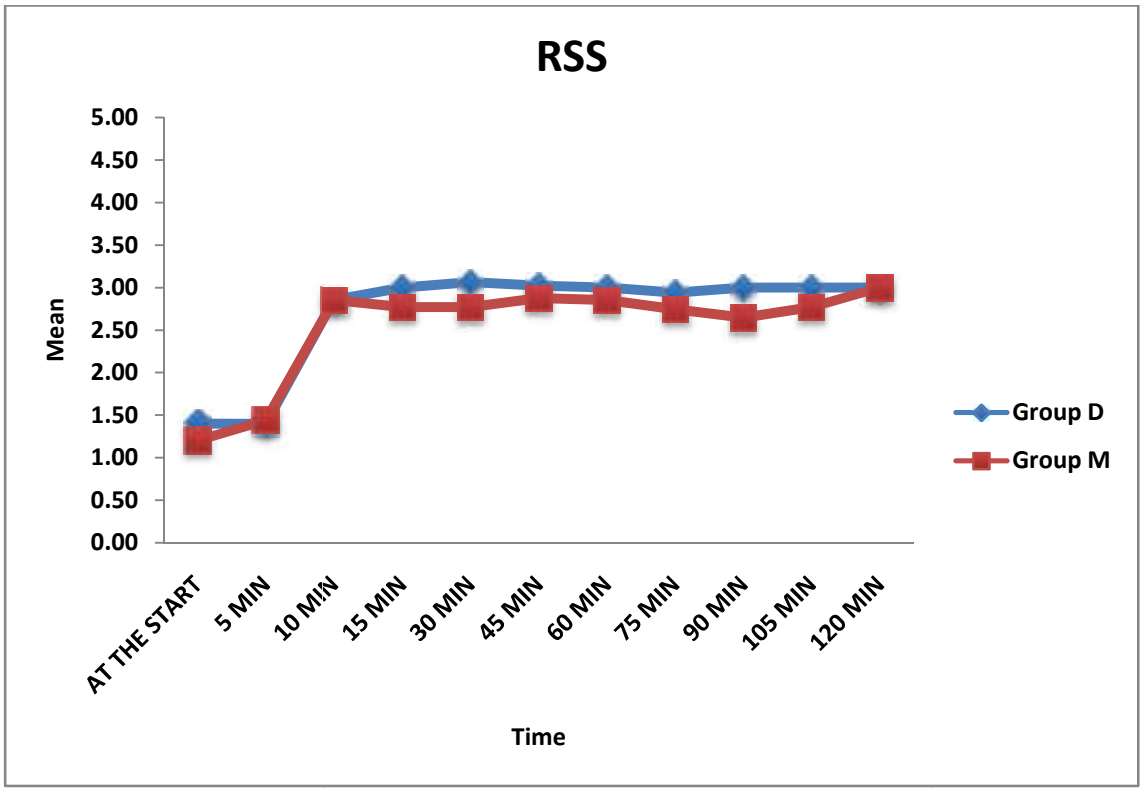


Table 6 and Chart F shows intra operative RSS among the study groups.

Data was analysed by student t test. Significant p value is shown in bold.

There was statistically significant difference in RSS between the study groups from 15 minutes of surgery up to 90 minutes.

Table 7: Change in mean Postoperative RSS between study groups

Parameters	Group D		Group M		p value
	Mean	SD	Mean	SD	
AT THE START	1.96	0.54	2.34	0.48	**<0.001***
15 MIN	1.29	0.54	1.92	0.54	**<0.001***
30 MIN	1.29	0.54	1.73	0.61	**<0.001***
45 MIN	1.29	0.54	1.52	0.50	**0.035***
60 MIN	1.29	0.54	1.35	0.48	0.553
75 MIN	1.06	0.24	1.29	0.46	**0.003***
90 MIN	1.06	0.24	1.25	0.44	0.011
105 MIN	1.06	0.24	1.25	0.44	0.011
120 MIN	1.06	0.24	1.27	0.45	**0.006***

Note: *means significant at 5% level of significance ($p<0.05$)

Chart G: Change in mean Postoperative RSS between study groups

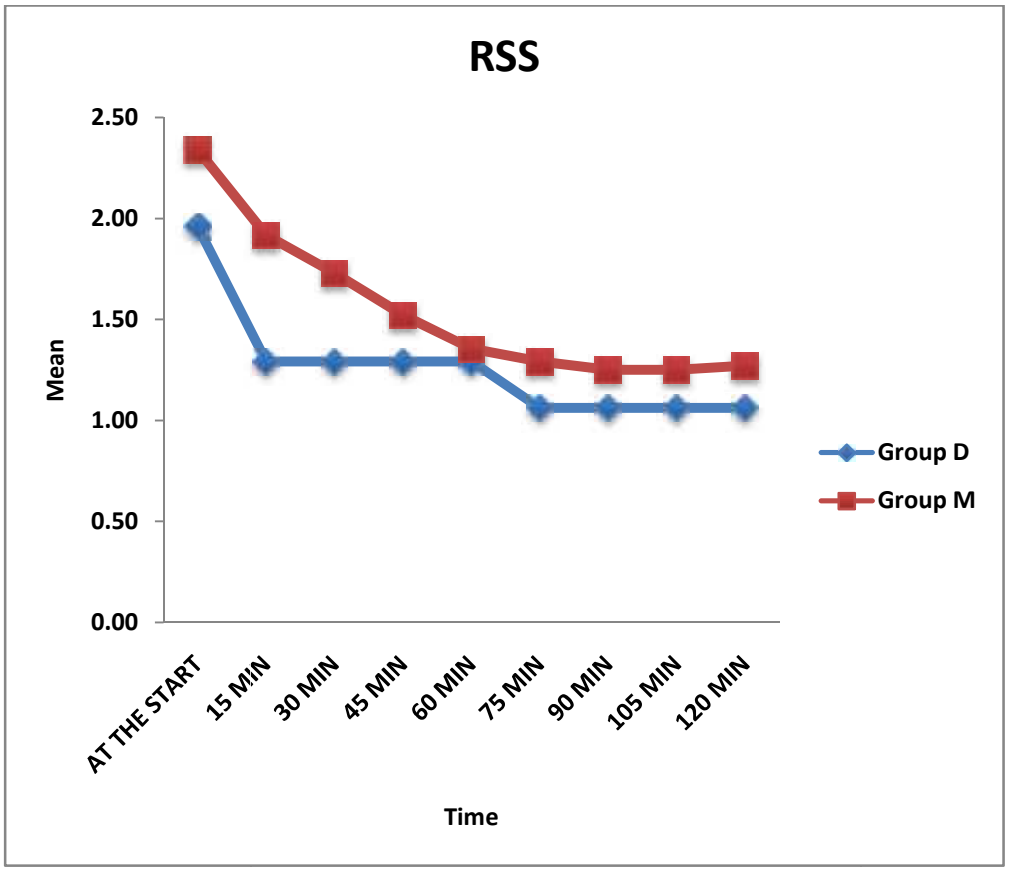


Table 7 and Chart G show RSS in both groups in postoperative period.

RSS on arrival to PACU was 1.96+0.54 in Group D and 2.34+0.48 in Group M.

The difference was statistically significant up to 45 minutes and again at 75 minutes and 120 minutes.

Table 8: Change in mean Intraoperative VAS between study groups

Parameters	Group D		Group M		p value
	Mean	**SD**	**Mean**	**SD**	
AT THE START	0.00	0.00	0.00	0.00	-
5 MIN	0.00	0.00	0.00	0.00	-
10 MIN	0.48	0.65	0.29	0.87	0.237
15 MIN	0.44	0.80	2.10	0.66	**<0.001***
30 MIN	0.52	0.90	2.02	0.56	**<0.001***
45 MIN	0.50	0.77	2.08	0.45	**<0.001***
60 MIN	0.60	1.01	2.06	0.43	**<0.001***
75 MIN	0.67	0.78	2.23	0.52	**<0.001***
90 MIN	1.41	0.73	2.29	0.46	**<0.001***
105 MIN	1.00	0.71	2.23	0.44	**<0.001***
120 MIN	1.00	-	2.75	0.50	0.052

Note: *means significant at 5% level of significance ($p<0.05$)

Chart H: Change in mean Intraoperative Visual Analog Scale (VAS) score between study groups

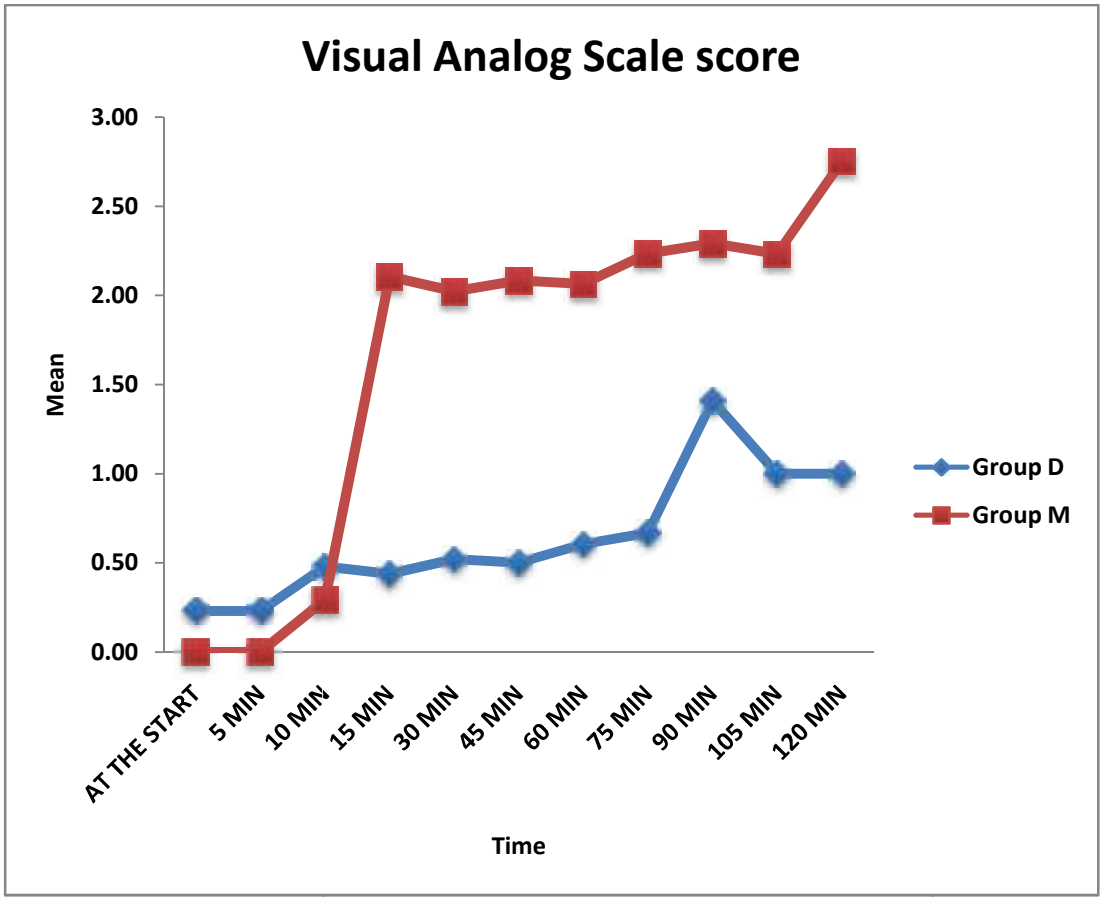


Table 8 and Chart H show Visual analog scale scores in both groups in intraoperative period.

Data was analyzed by student t test.

VAS score was higher in Group M with statistically significant difference from 15 minutes onwards throughout the duration of surgery except at 120 minutes.

Table 9: Change in mean Postoperative VAS between study groups

Parameters	Group D		Group M		p value
	Mean	SD	Mean	SD	
AT THE START	0.77	0.99	2.45	0.58	**<0.001***
15 MIN	0.92	1.03	2.67	0.72	**<0.001***
30 MIN	0.83	0.86	2.71	0.77	**<0.001***
45 MIN	0.79	0.77	2.73	0.82	**<0.001***
60 MIN	0.75	0.73	2.40	0.92	**<0.001***
75 MIN	0.40	0.64	2.46	0.94	**<0.001***
90 MIN	0.40	0.64	2.48	0.95	**<0.001***
105 MIN	0.40	0.64	2.29	0.82	**<0.001***
120 MIN	0.40	0.64	2.10	0.75	**<0.001***

Note: *means significant at 5% level of significance ($p<0.05$)

Chart I: Change in mean Postoperative VAS between study groups

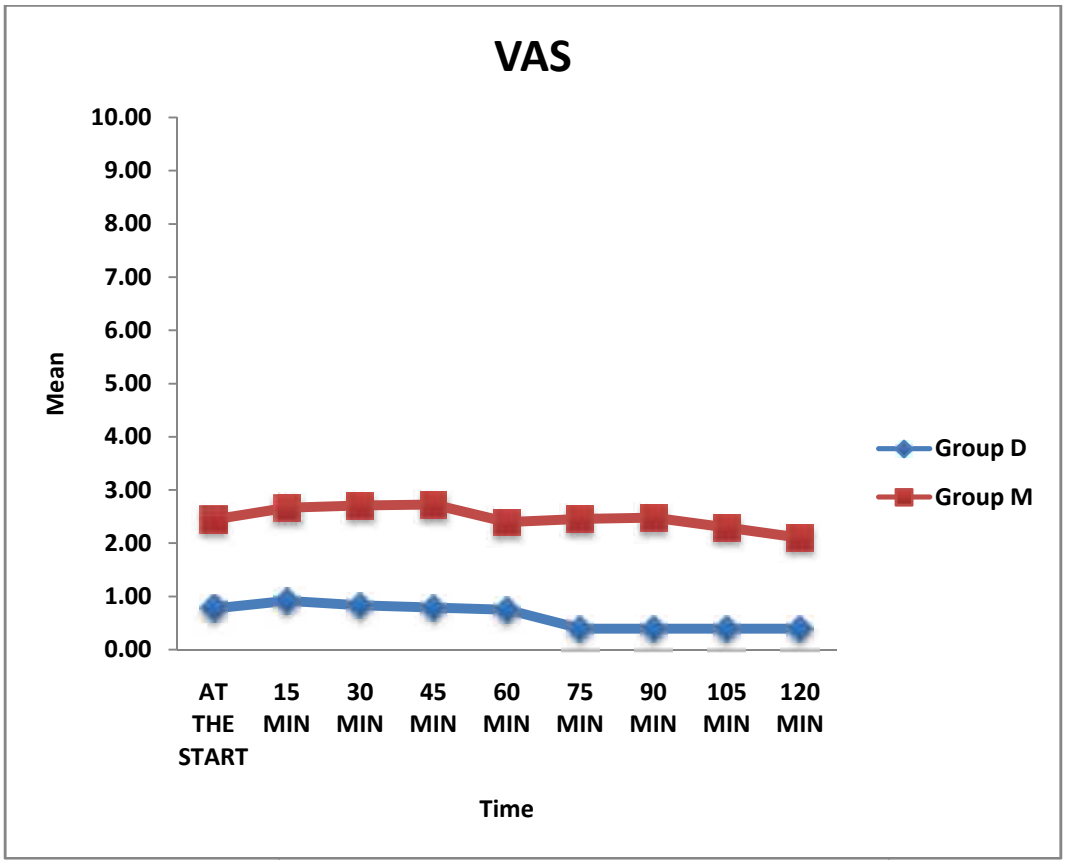


Table 9 and Chart I show mean postoperative VAS score between the 2 groups.

VAS score was significantly lower in Group D than Group M throughout the postoperative period.

Table 10: Requirement of additional drugs in study groups

Additional requirement	Group D		Group M		Total		p value
	N	%	N	%	N	%	
Additional analgesic	5	10.4	15	31.3	20	20.8	**0.012***
Additional sedation	2	4.2	5	10.4	7	7.3	0.128
Total	48	100.0	48	100.0	96	100.0	

Note: *means significant at 5% level of significance ($p<0.05$)

Chart J: Requirement of additional sedative and analgesic between study groups

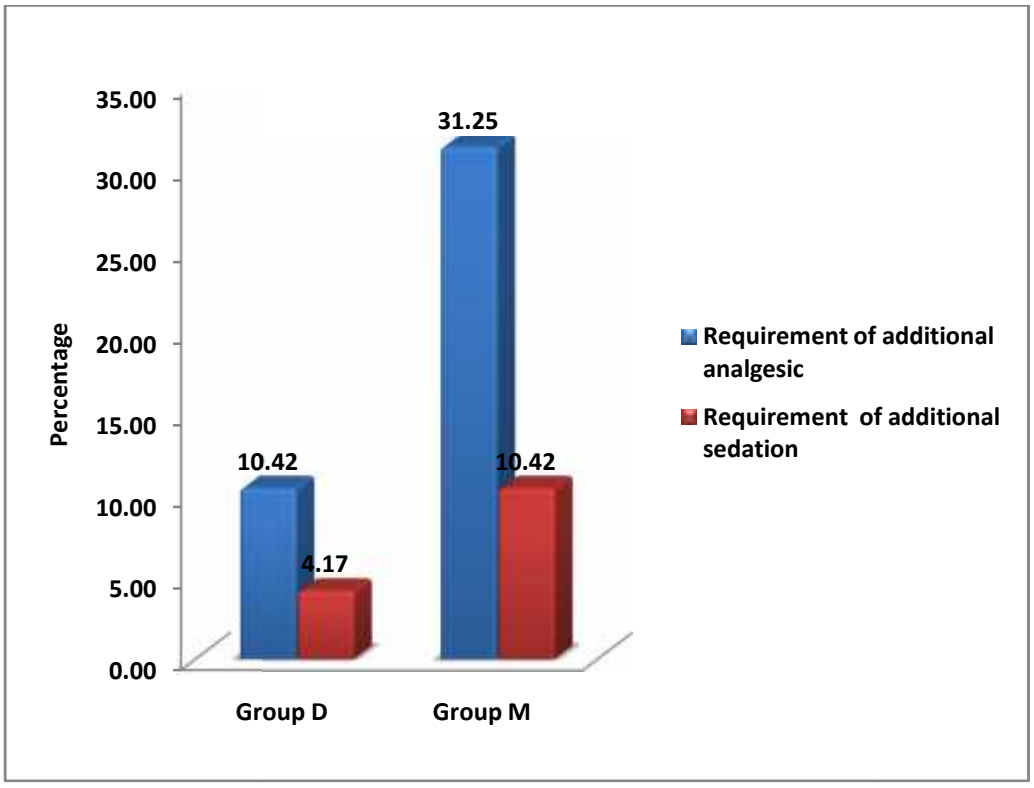


Table 10 and Chart J shows requirement of additional sedative and analgesic in two groups.

In Group D, 5 out of 48 patients required additional analgesic in comparison to 15 out of 48 patients in Group M. The difference was statistically significant with p value of **0.012.**

In Group D, 2 out of 48 patients required additional sedation in comparison to 5 out of 48 patients in Group M. The difference was not statistically significant.

Table 11: Change in mean Intraoperative Heart rate between study groups

Parameters	Group D		Group M		p value
	Mean	**SD**	**Mean**	**SD**	
AT THE START	75.17	5.77	81.04	10.46	**<0.001***
5 MIN	70.75	5.75	82.67	9.99	**<0.001***
10 MIN	67.54	5.96	81.40	9.81	**<0.001***
15 MIN	65.96	4.90	80.29	9.62	**<0.001***
30 MIN	66.52	5.14	79.35	10.73	**<0.001***
45 MIN	65.67	4.37	78.48	10.37	**<0.001***
60 MIN	65.29	3.79	78.02	10.55	**<0.001***
75 MIN	62.55	3.26	78.71	9.36	**<0.001***
90 MIN	64.40	2.19	74.54	5.24	**<0.001***
105 MIN	62.00	-	73.00	1.15	**<0.001***
120 MIN	76.17	6.57	80.88	9.77	**0.007***

Note: *means significant at 5% level of significance ($p<0.05$)

Chart K: Change in mean Intraoperative Heart rate between study groups

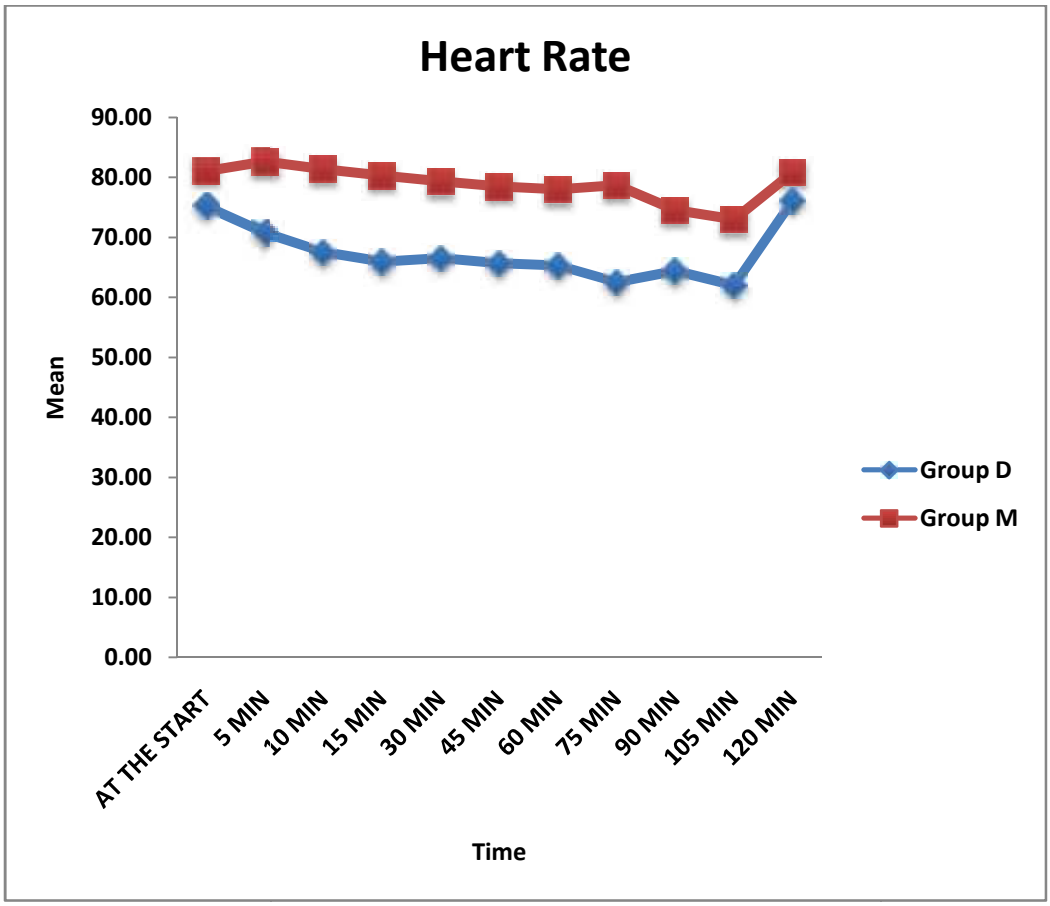


Table 11 and Chart K shows mean intraoperative Heart rate in both groups. Heart rate was lower in Group D from the start of surgery up to 105 minutes with p value of **<0.001**.

Table 12: Change in mean Postoperative Heart rate between study groups

Parameters	Group D		Group M		p value
	Mean	SD	Mean	SD	
AT THE START	68.96	4.13	78.23	7.67	**<0.001***
15 MIN	68.96	4.13	78.50	7.16	**<0.001***
30 MIN	68.96	4.13	78.52	7.19	**<0.001***
45 MIN	68.96	4.13	78.54	7.85	**<0.001***
60 MIN	70.67	4.31	78.67	7.83	**<0.001***
75 MIN	70.67	4.31	77.19	4.63	**<0.001***
90 MIN	70.67	4.31	77.31	5.03	**<0.001***
105 MIN	70.67	4.31	76.83	6.00	**<0.001***
120 MIN	66.42	4.56	77.72	8.56	**<0.001***

Note: *means significant at 5% level of significance ($p<0.05$)

Chart L: Change in mean Postoperative Heart rate between study groups

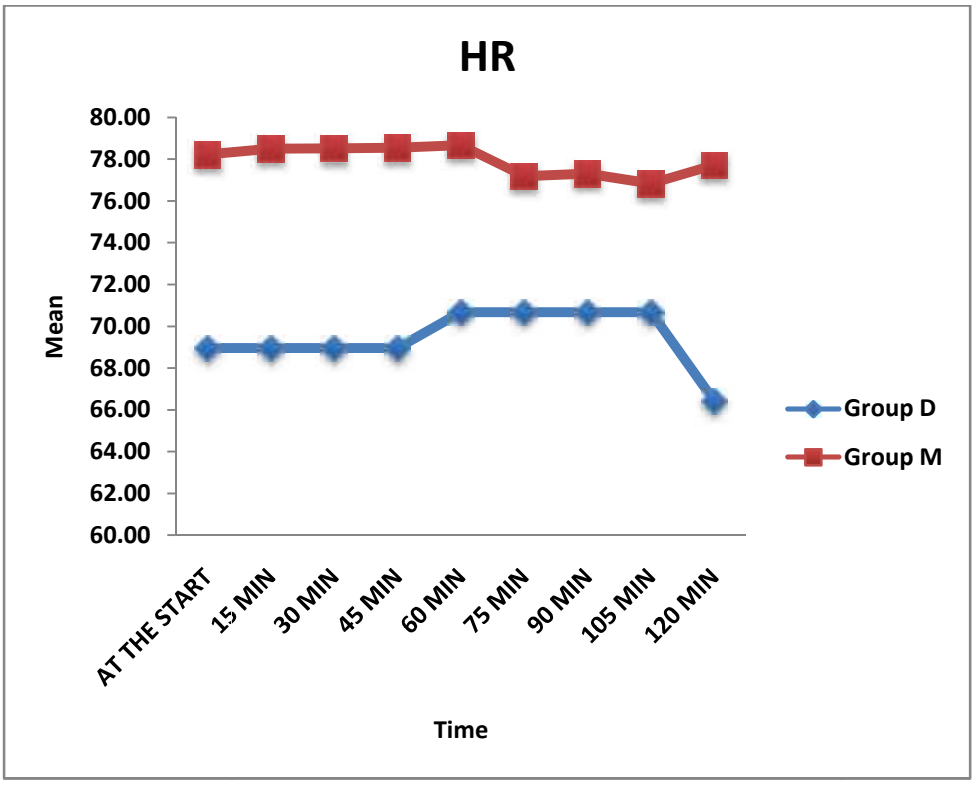


Table 12 and Chart K shows mean heart rate in the post operative period in both study groups. Data was analyzed by student t test and significant p value is shown in bold.

Heart rate was significantly lower in Group D than Group M from arrival to recovery room up to 120 minutes.

Table 13: Change in mean Intraoperative SpO_2 between study groups

Parameters	Group D		Group M		p value
	Mean	SD	Mean	SD	
AT THE START	99.48	0.50	99.00	0.51	0.061
5 MIN	99.27	0.57	99.13	0.49	0.184
10 MIN	99.44	0.50	99.31	0.69	0.312
15 MIN	99.13	0.70	99.00	0.51	0.320
30 MIN	99.35	0.48	99.00	0.98	0.052
45 MIN	98.96	0.58	98.88	0.53	0.465
60 MIN	98.92	0.50	98.96	0.46	0.671
75 MIN	99.00	0.36	98.94	0.53	0.491
90 MIN	99.00	0.00	99.06	0.36	0.405
105 MIN	99.00	0.00	98.92	0.28	0.551
120 MIN	99.00	-	99.00	0.00	-

Chart M: Change in mean Intraoperative SpO_2 between study groups

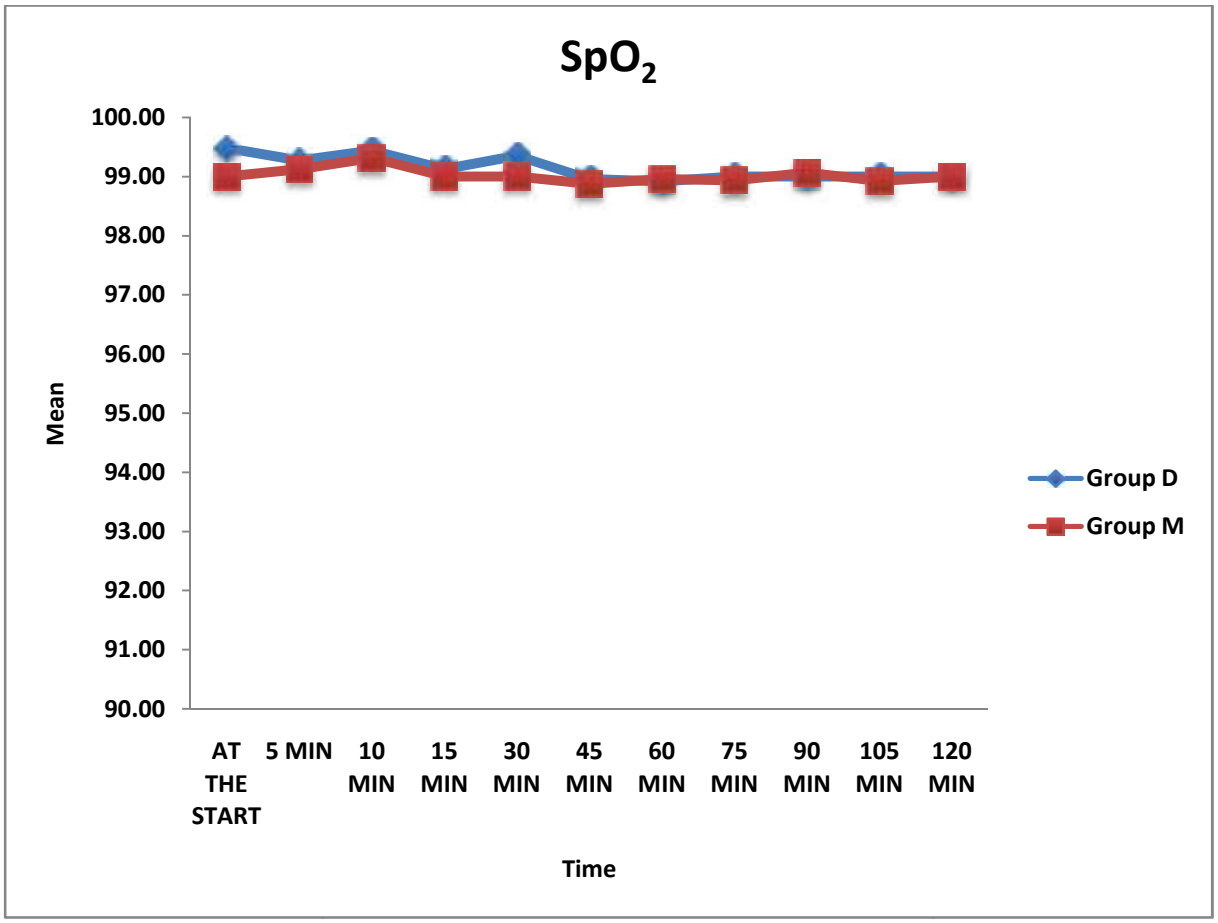


Table 13 and Chart M show mean SpO_2 in the intraoperative period among both groups.

Baseline SpO_2 in Group D was 99.48 % and in Group M was 99 %. The difference between both groups is not statistically significant.

Table 14: Change in mean Postoperative SpO_2 between study groups

Parameters	Group D		Group M		p value
	Mean	SD	Mean	SD	
AT THE START	99.06	0.52	99.11	0.43	0.656
15 MIN	99.23	0.96	98.94	0.48	0.486
30 MIN	99.23	0.86	98.94	0.48	0.057
45 MIN	99.23	0.76	98.88	0.53	0.062
60 MIN	99.23	0.55	98.98	0.44	0.056
75 MIN	99.29	0.98	98.94	0.48	0.089
90 MIN	99.29	0.46	98.88	0.39	0.071
105 MIN	99.29	0.97	98.83	0.43	0.234
120 MIN	99.29	0.67	98.83	0.43	0.063

Note: *means significant at 5% level of significance ($p<0.05$)

Chart N: Change in mean Postoperative SpO_2between study groups

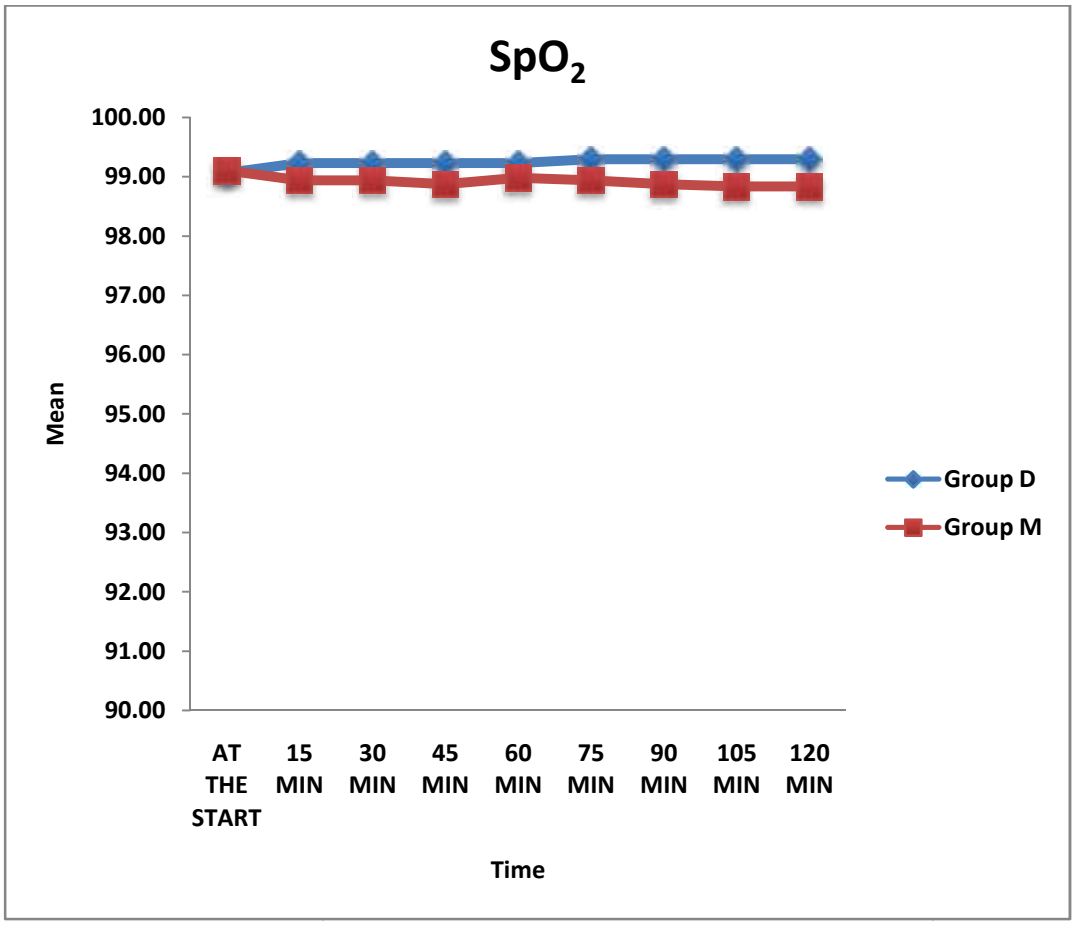


Table 14 and Chart N show mean SpO_2 in the postoperative period in both groups. Data was analyzed by student t test. There was no fall in saturation in both groups and p value is not statistically significant.

Table 15: Change in mean Intra operative Systolic Blood Pressure (SBP) between study groups

Parameters	Group D		Group M		p value
	Mean	SD	Mean	SD	
AT THE START	120.04	10.97	123.42	10.08	0.120
5 MIN	118.77	9.35	123.85	9.62	**0.01***
10 MIN	113.33	11.92	120.81	9.48	**0.001***
15 MIN	109.00	11.84	118.48	8.59	**<0.001***
30 MIN	105.29	10.01	117.06	7.73	**<0.001***
45 MIN	104.21	11.38	116.90	6.24	**<0.001***
60 MIN	102.58	8.69	117.65	6.97	**<0.001***
75 MIN	102.38	8.65	116.32	6.70	**<0.001***
90 MIN	102.09	7.67	116.23	7.11	**<0.001***
105 MIN	104.40	8.17	114.31	8.38	**0.038***
120 MIN	100.00	-	122.50	2.52	**0.004***

Note: *means significant at 5% level of significance ($p<0.05$)

Chart O: Change in mean Intra operative SBP between study groups

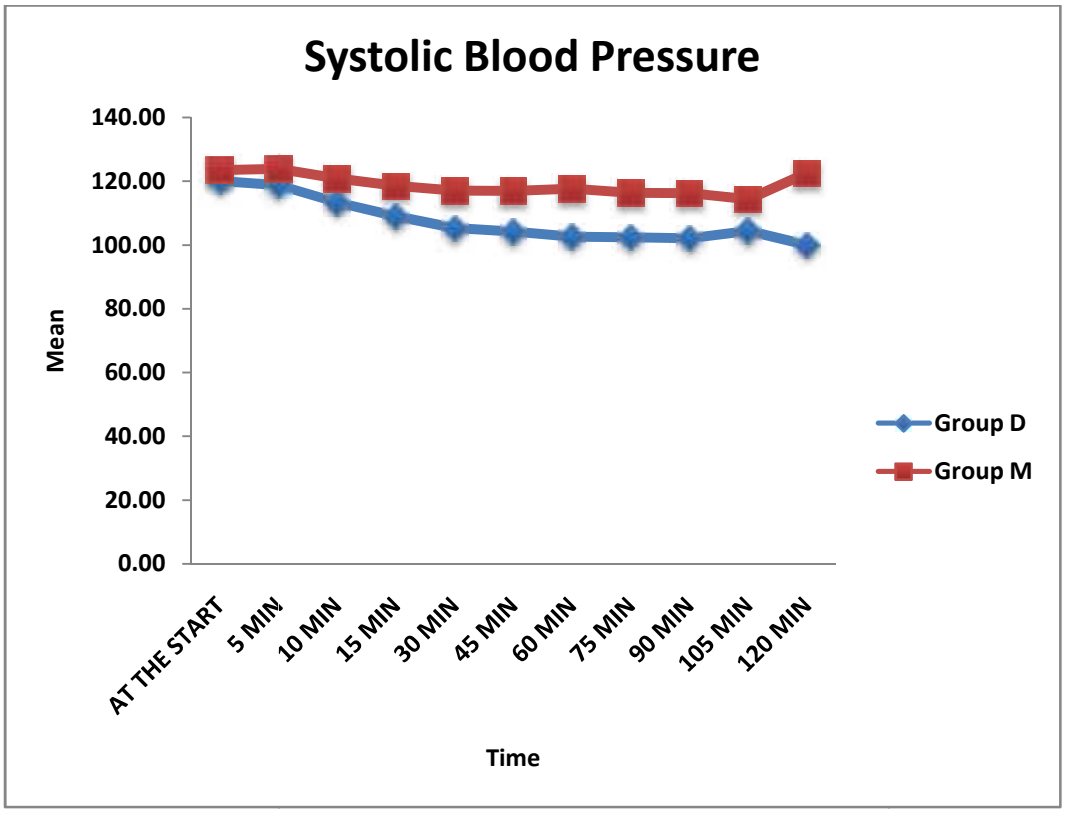


Table 15 and Figure O show mean intra operative Systolic blood pressure between study groups. Data was analyzed by student t test and significant p value is highlighted in bold.

In Group D baseline SBP was 120±10.97, which decreased to 118.7±9.35 at 5 minutes. In Group M baseline SBP was 123.42±10.08, which decreased to 123.85±9.62 at 5 minutes.

Baseline SBP was comparable in both groups. Reduction in SBP was significantly lower in Group D from 5 minutes onwards throughout duration of surgery. ($p < 0.05$)

Table 16: Change in mean Postoperative SBP between study groups

Parameters	Group D		Group M		p value
	Mean	**SD**	**Mean**	**SD**	
AT THE START	102.79	8.63	116.85	7.32	**<0.001***
15 MIN	105.42	8.02	118.96	6.65	**<0.001***
30 MIN	105.42	8.02	119.58	5.98	**<0.001***
45 MIN	105.42	8.02	119.25	6.24	**<0.001***
60 MIN	105.42	8.02	119.46	6.32	**<0.001***
75 MIN	108.96	8.47	120.13	6.52	**<0.001***
90 MIN	108.96	8.47	122.33	6.51	**<0.001***
105 MIN	108.96	8.47	122.63	6.35	**<0.001***
120 MIN	108.96	8.47	122.29	6.36	**<0.001***

Note: *means significant at 5% level of significance ($p<0.05$)

Chart P: Change in mean Postoperative SBP between study groups

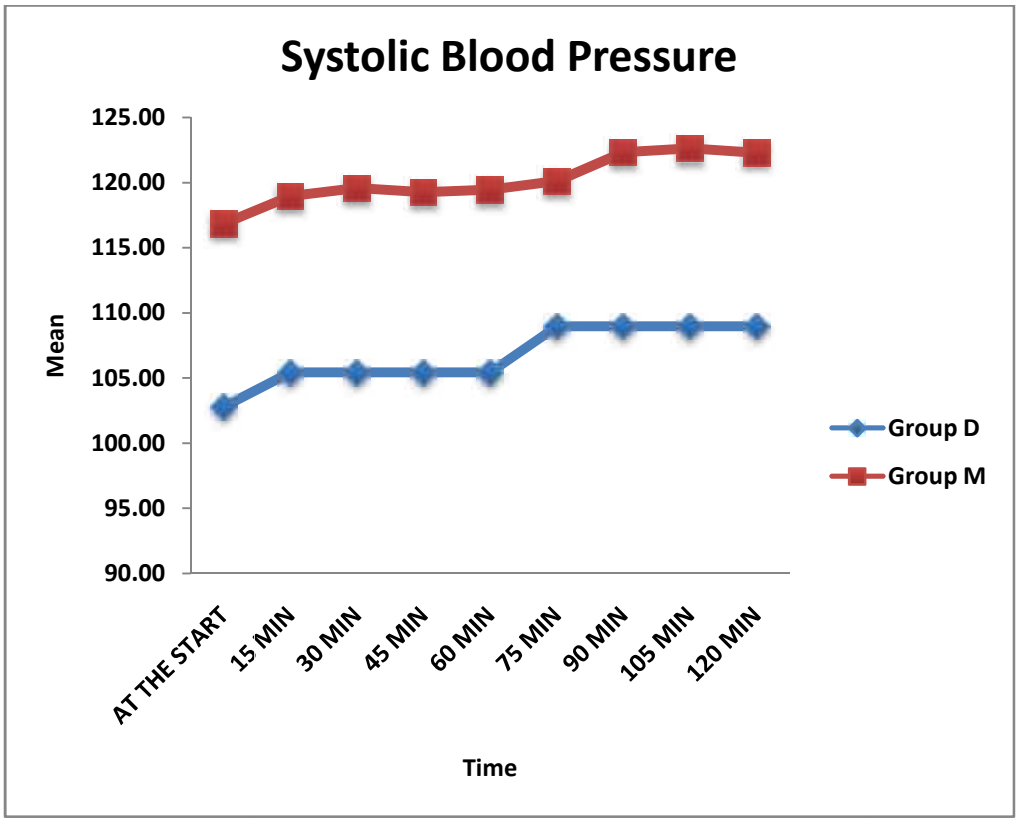


Table 16 and Chart P show mean Systolic blood pressure among both groups in post operative period.

Data was analyzed by student t test and significant p value is shown in bold.

Mean SBP was significantly lower in Group D compared to Group M. ($p < 0.001$).

Table 17: Change in mean Intra operative Diastolic Blood Pressure(DBP) between study groups

Parameters	Group D		Group M		p value
	Mean	**SD**	**Mean**	**SD**	
AT THE START	78.38	7.68	80.54	4.92	0.103
5 MIN	77.46	7.51	78.13	7.35	0.661
10 MIN	72.21	7.04	75.44	7.57	**0.033***
15 MIN	69.50	7.51	74.58	6.95	**<0.001***
30 MIN	68.25	5.90	73.35	7.36	**<0.001***
45 MIN	66.88	6.13	74.08	4.69	**<0.001***
60 MIN	65.58	5.47	74.17	5.39	**<0.001***
75 MIN	65.13	5.49	73.96	4.69	**<0.001***
90 MIN	66.36	6.07	74.10	5.58	**<0.001***
105 MIN	70.00	9.59	69.69	6.70	0.939
120 MIN	78.00	-	76.50	4.43	0.782

Note: *means significant at 5% level of significance ($p<0.05$)

Chart Q: Change in mean Intra operative Diastolic Blood Pressure between study groups

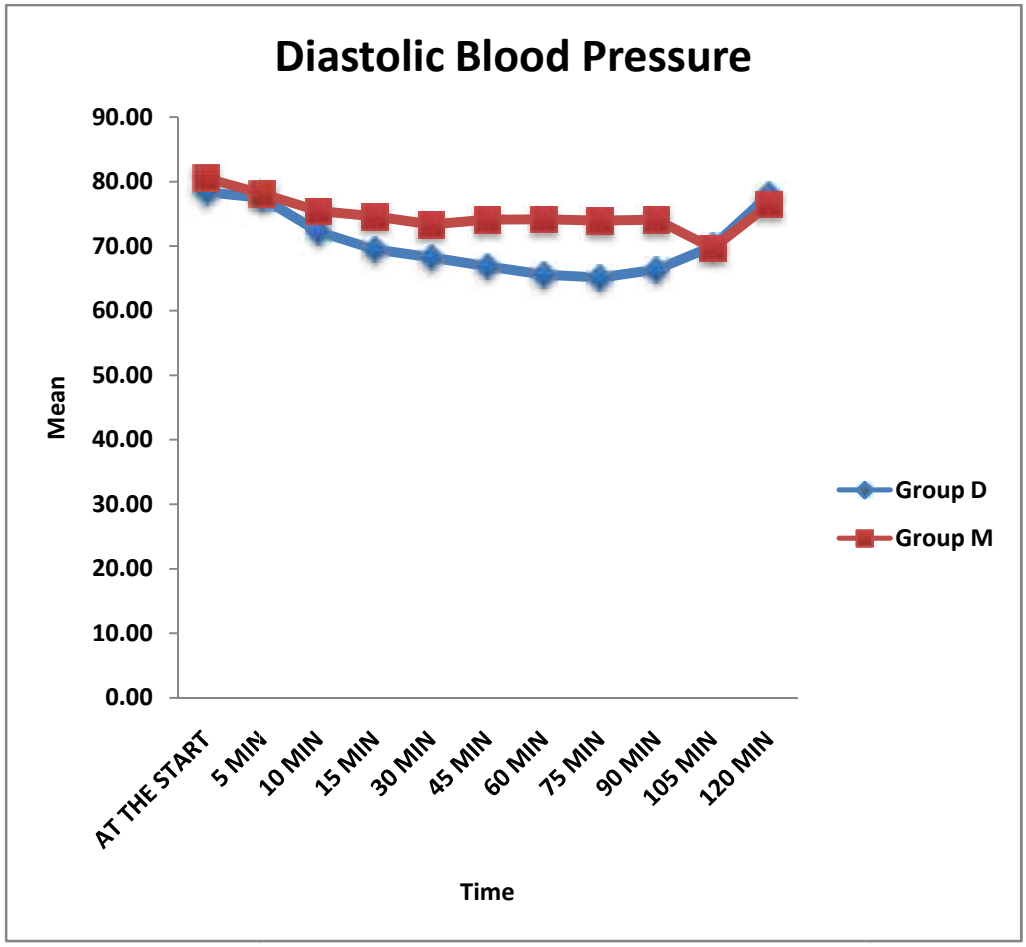


Table 17 and Chart Q show mean intra operative Diastolic blood pressure among both groups. Data was analyzed by student t test and significant p value is highlighted in bold.

Baseline Diastolic Blood pressure in Group D was 73.38±7.68 and in Group M was 73.38±4.92.

Fall in Diastolic blood pressure was more in Group D than Group M from 15 minutes of surgery up to 90 minutes of surgery with p value < 0.05.

Table 18: Change in mean Postoperative Diastolic Blood Pressure between study groups

Parameters	Group D		Group M		p value
	Mean	SD	Mean	SD	
AT THE START	66.71	5.26	73.51	5.44	**<0.001***
15 MIN	69.21	5.12	74.67	3.23	**<0.001***
30 MIN	69.21	5.12	74.79	3.32	**<0.001***
45 MIN	69.21	5.12	74.67	3.23	**<0.001***
60 MIN	69.21	5.12	75.04	3.89	**<0.001***
75 MIN	71.58	5.41	75.08	3.48	**<0.001***
90 MIN	71.58	5.41	77.00	4.62	**<0.001***
105 MIN	71.58	5.41	77.21	4.90	**<0.001***
120 MIN	71.58	5.41	77.21	4.90	**<0.001***

Note: *means significant at 5% level of significance ($p<0.05$)

Chart R: Change in mean Postoperative Diastolic Blood Pressure between study groups

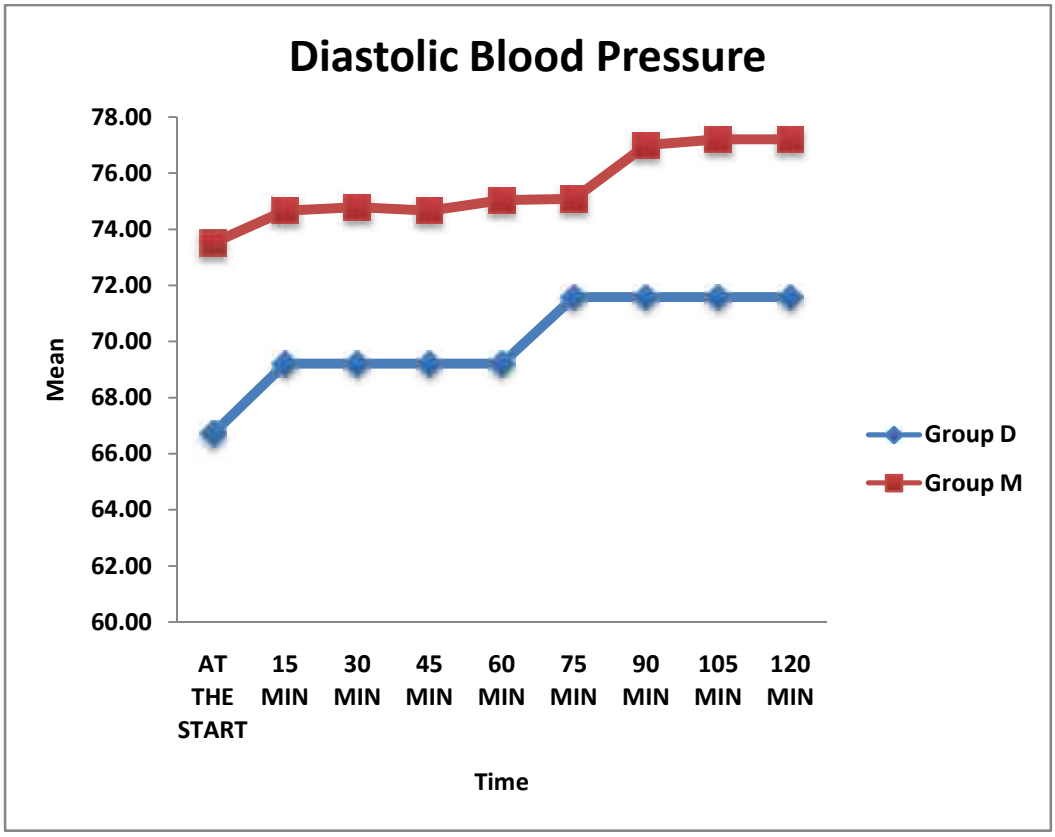


Table 18 and Chart R show mean Diastolic blood pressure in postoperative period in both groups.

Data was analyzed by student t test and significant p value is shown in bold.

Diastolic blood pressure was significantly lower in Group D compared to Group M in postoperative period with p value <0.001.

Table 19: Change in mean Intra operative Mean Arterial Pressure (MAP) between study groups

Parameters	Group D		Group M		p value
	Mean	**SD**	**Mean**	**SD**	
AT THE START	92.26	8.62	94.83	6.24	0.098
5 MIN	91.23	7.90	93.37	6.40	0.148
10 MIN	85.92	8.43	90.56	6.22	**0.003***
15 MIN	82.67	8.83	89.22	6.68	**<0.001***
30 MIN	80.60	7.05	87.92	6.82	**<0.001***
45 MIN	79.32	7.75	88.35	4.77	**<0.001***
60 MIN	77.92	6.31	88.66	5.32	**<0.001***
75 MIN	77.13	5.57	88.08	4.87	**<0.001***
90 MIN	78.27	6.44	88.10	5.53	**<0.001***
105 MIN	81.47	8.48	84.26	7.35	0.498
120 MIN	85.33	-	91.84	3.66	0.211

Note: *means significant at 5% level of significance ($p<0.05$)

Chart S: Change in mean Intra operative mean arterial pressure between study groups

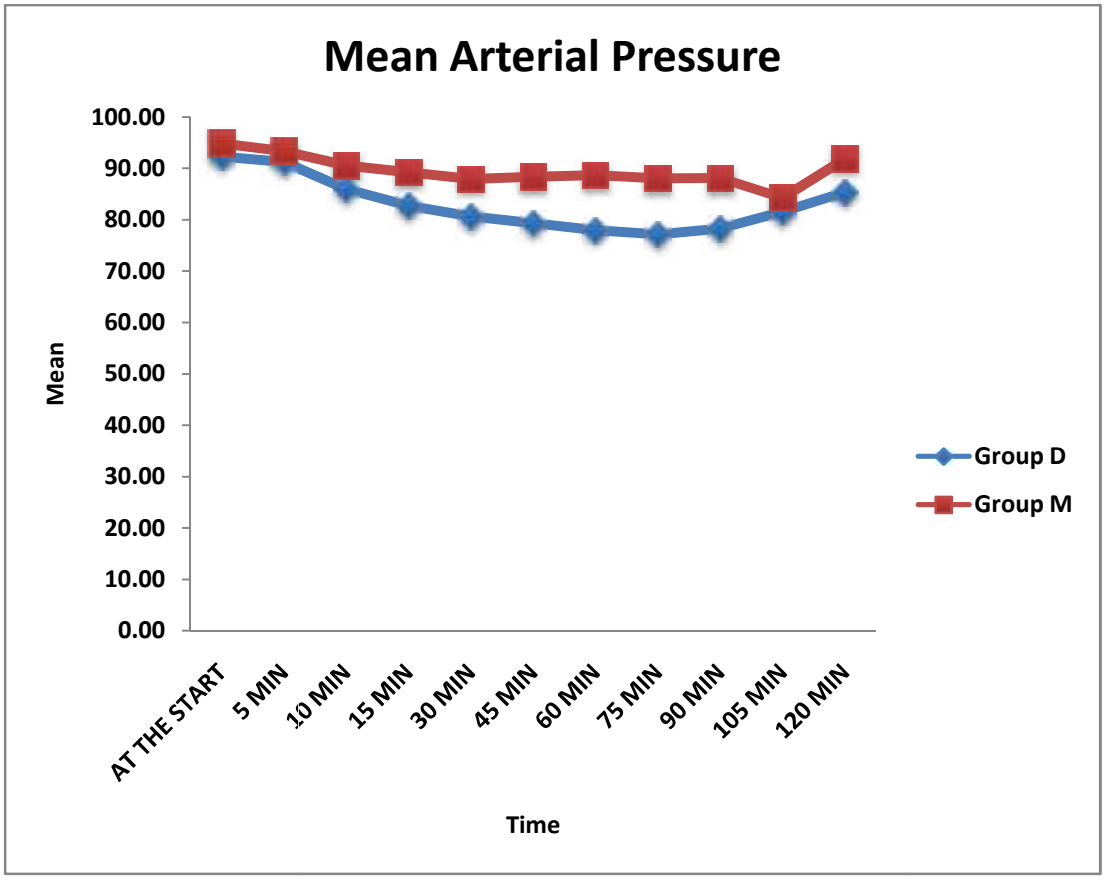


Table 19 and Chart S show mean intra operative arterial blood pressure in both groups.

Data was analyzed by student t test. Significant p value is shown in bold.

Baseline MAP was 92.26 ±8.62 in Group D compared to 94.83±6.24 in Group M. Mean arterial pressure at baseline was comparable between both groups. Mean arterial pressure decreased significantly from 10 minutes up to 90 minutes of surgery with p value <0.05.

Table 20: Change in mean Postoperative Mean arterial pressure between study groups

Parameters	Group D		Group M		p value
	Mean	**SD**	**Mean**	**SD**	
AT THE START	78.74	6.18	87.96	5.73	**<0.001***
15 MIN	81.28	5.86	89.43	3.75	**<0.001***
30 MIN	81.28	5.86	89.72	3.67	**<0.001***
45 MIN	81.28	5.86	89.53	3.66	**<0.001***
60 MIN	81.28	5.86	89.85	4.07	**<0.001***
75 MIN	84.04	6.12	90.10	3.98	**<0.001***
90 MIN	84.04	6.12	92.11	4.43	**<0.001***
105 MIN	84.04	6.12	92.35	4.53	**<0.001***
120 MIN	84.04	6.12	92.24	4.56	**<0.001***

Note: *means significant at 5% level of significance ($p<0.05$)

Figure T: Change in mean Postoperative MAP between study groups

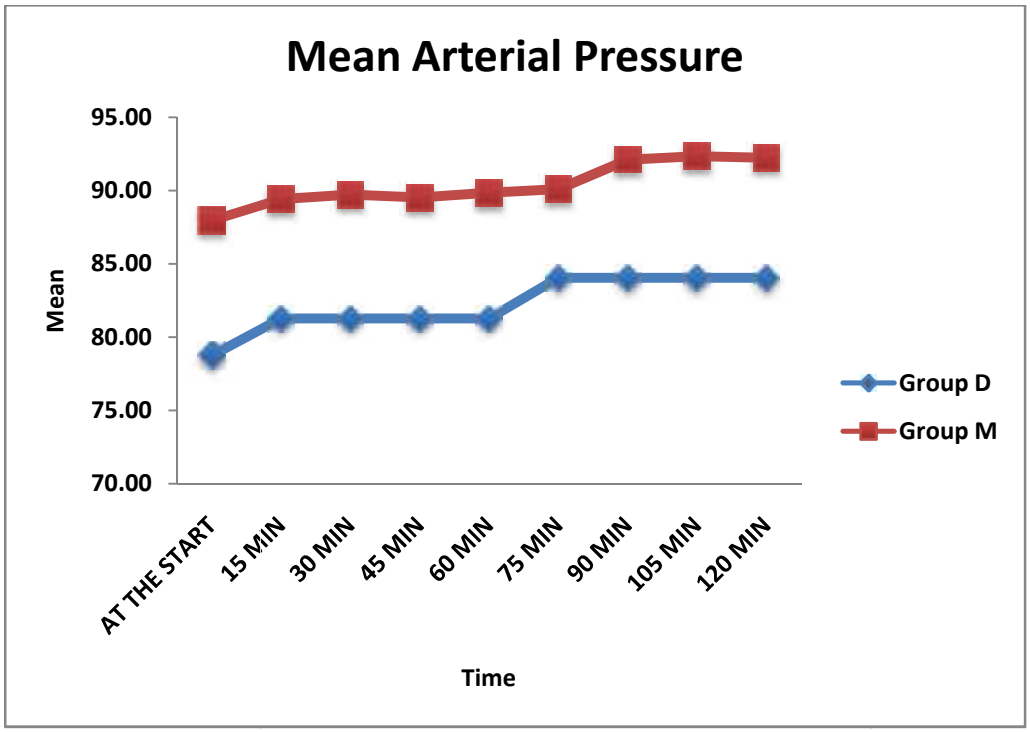


Table 20 and Chart T show mean arterial pressure in both groups in the postoperative period.

Data was analyzed with student t test and significant p value is shown in bold.

Mean arterial pressure was significantly lower in Group D compared to Group M with p value <0.05.

Table 21: Change in mean Intra operative Respiratory rate (RR) between study groups

Parameters	Group D		Group M		p value
	Mean	**SD**	**Mean**	**SD**	
AT THE START	13.60	1.48	13.46	1.52	0.074
5 MIN	13.60	1.48	13.46	1.52	0.074
10 MIN	13.50	1.34	12.69	2.17	0.065
15 MIN	13.38	1.38	12.15	1.39	0.340
30 MIN	13.42	1.41	12.25	1.30	0.231
45 MIN	13.38	1.44	12.08	1.91	0.548
60 MIN	13.38	1.44	12.00	1.70	0.698
75 MIN	13.50	1.40	11.60	1.64	**0.007***
90 MIN	12.96	1.73	11.65	1.47	0.064
105 MIN	14.18	1.59	11.15	1.08	**<0.001***
120 MIN	12.40	0.89	11.08	0.64	**0.002***

Note: *means significant at 5% level of significance ($p<0.05$)

Chart U: Change in mean Intraoperative RR between study groups

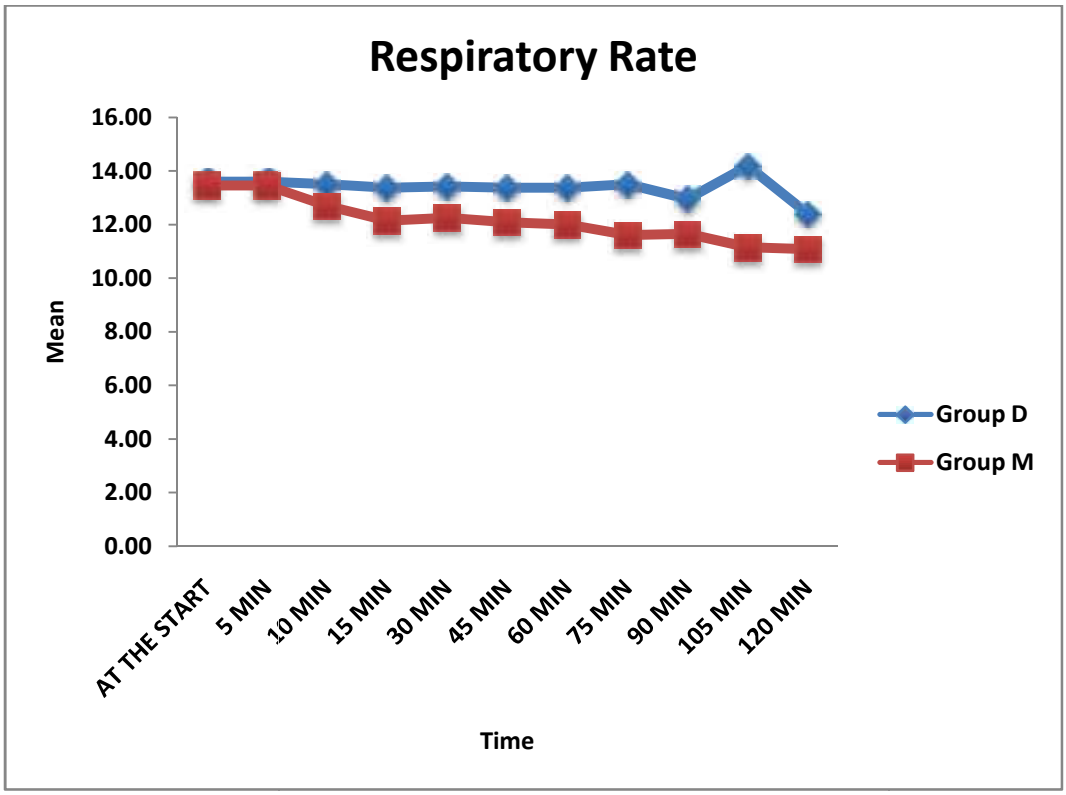


Table 21 and Chart U show mean intra operative respiratory rate among study groups.

Data was analyzed by student t test and significant p value is shown in bold.

Baseline Respiratory rate was 13.60± 1.48 in Group D and 13.46±1.52 in Group M.

Respiratory rate decreased from baseline value in Group M at 75 minutes and again at 105 and 120 minutes in comparison to Group D with p value<0.05, but respiratory rate was within normal range.

Table 22: Change in mean Postoperative RR between study groups

Parameters	Group D		Group M		p value
	Mean	**SD**	**Mean**	**SD**	
AT THE START	13.40	1.32	12.86	1.37	**0.041***
15 MIN	13.27	1.12	12.87	1.14	**0.049***
30 MIN	13.27	1.12	12.80	1.14	0.053
45 MIN	13.27	1.12	12.80	1.14	0.053
60 MIN	13.27	1.12	12.93	1.28	**0.046***
75 MIN	13.23	1.08	12.80	1.14	**0.032***
90 MIN	13.23	1.08	12.97	1.46	0.051
105 MIN	13.23	1.08	12.97	1.46	0.051
120 MIN	13.23	1.08	13.10	1.56	0.087

Note: *means significant at 5% level of significance ($p<0.05$)

Chart V: Change in mean Postoperative RR between study groups

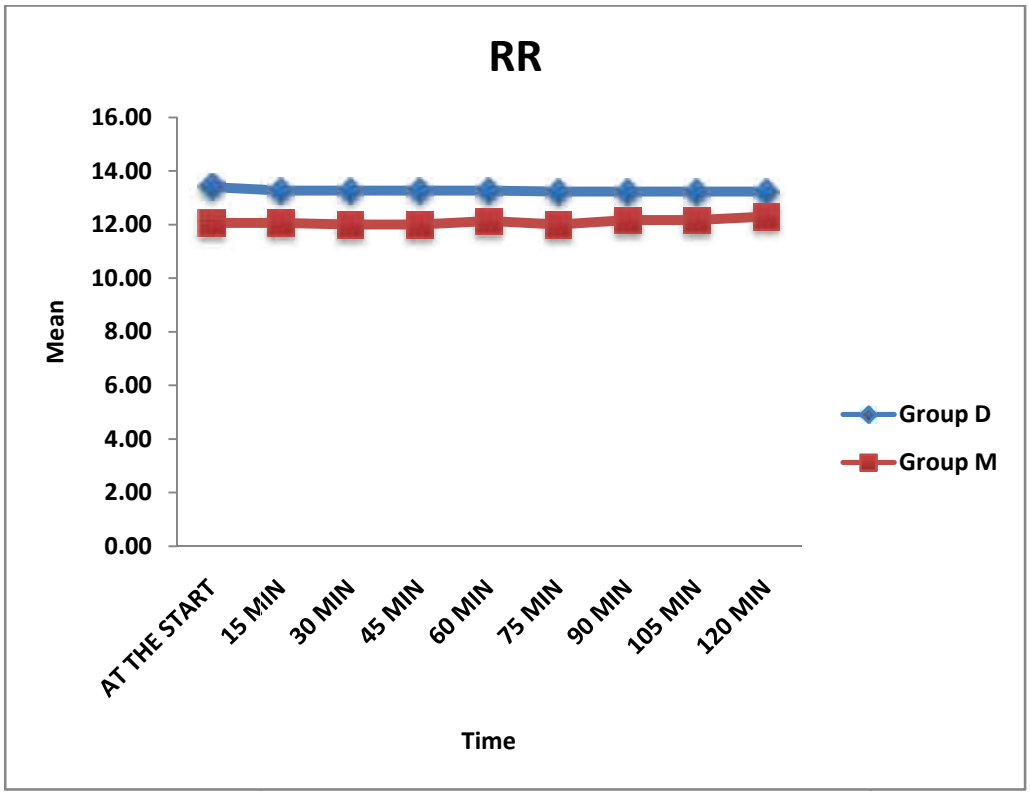


Table 22 and Chart V show mean respiratory rate in the postoperative period in both groups.

Mean Respiratory rate on arrival to post anaesthesia care unit (PACU) was 13.40 ±1.32 in Group D compared to 12.86 ± 1.37 in Group M.

Patients in Group M showed significant decrease in Respiratory rate compared to baseline value on arrival to PACU, at 15 minutes, 60 minutes and 75 minutes postoperatively, but respiratory rate was within normal range in both groups.

Table 23: Distribution of Surgeon satisfaction score between study groups

Surgeon satisfaction score (1-5)	**Group D**		**Group M**		**Total**		**p value**
	N	**%**	**N**	**%**	**N**	**%**	
3	2	4.2	9	18.8	11	11.5	**0.001***
4	15	31.3	25	52.1	40	41.7	
5	31	64.6	14	29.2	45	46.9	
Total	48	100.0	48	100.0	96	100.0	

Note: *means significant at 5% level of significance ($p<0.05$)

Chart W: Distribution of Surgeon satisfaction score between study groups

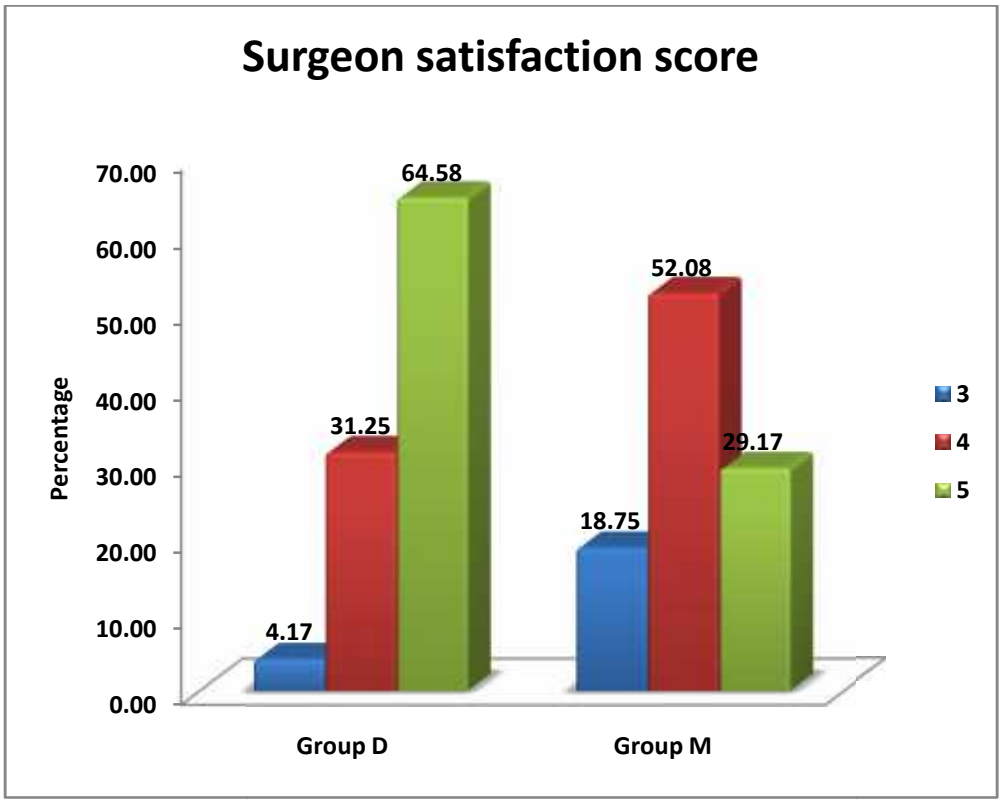


Table 23 and Chart W show Surgeon satisfaction score among both groups.

Group D had significantly higher surgeon satisfaction scores compared to Group M with p value of 0.001.

31 out of 48 surgeries (64.6 %) in Group D were rated 5 on surgeon satisfaction score compared to 14 out of 48 (29.2 %) surgeries in Group M.

Table 24: Distribution of Side effects between study groups

Side effects	Group D		Group M		Total		p value
	N	%	N	%	N	%	
Bradycardia	2	4.2	0	0.0	2	2.1	0.153
Hypotension	2	4.2	0	0.0	2	2.1	0.153
Hypertension	0	0.0	0	0.0	0	0.0	-
Desaturation	0	0.0	0	0.0	0	0.0	-
Post operative nausea vomiting (PONV)	0	0.0	0	0.0	0	0.0	-
Dryness of mouth	0	0.0	0	0.0	0	0.0	-
Total	48	100.0	48	100.0	96	100.0	

Chart X: Distribution of Side effects between study groups

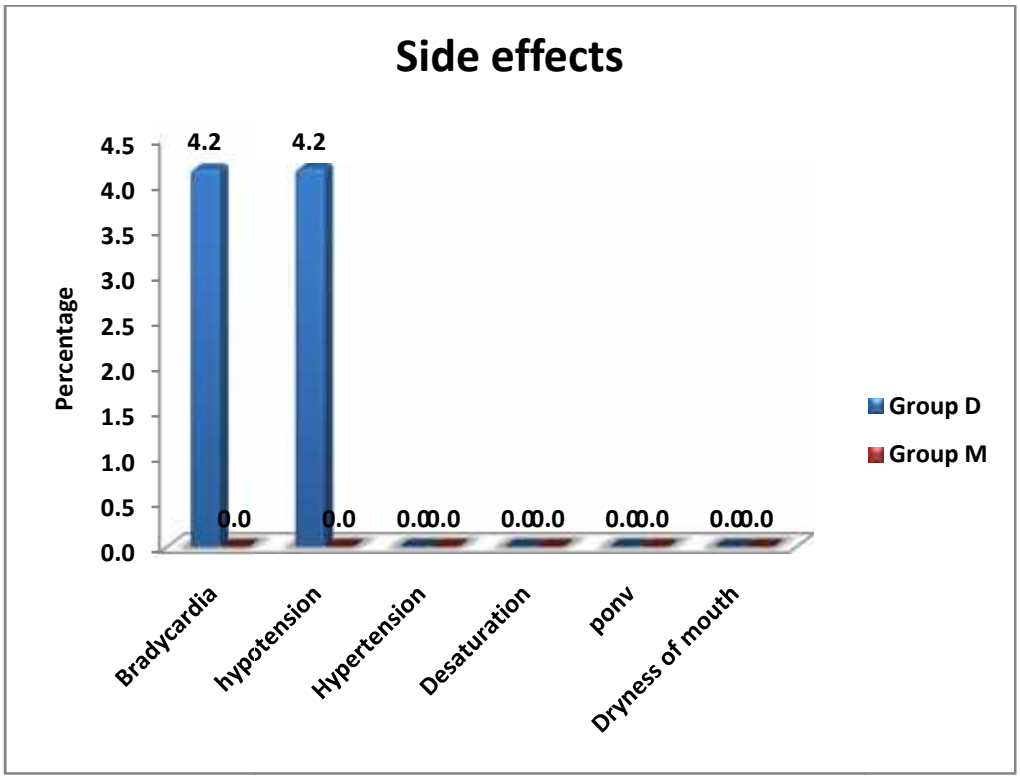


Table 23 and Chart X show side effects in both groups.

Data was analyzed by Chi square test.

2 patients in Group D had Bradycardia and Hypotension. Bradycardia was treated with Inj. Atropine 0.01 mg/kg. Hypotension was treated with IV fluids and Inj. Ephedrine 5 mg bolus. No side effects were seen in Group M. p value was not statistically significant.

DISCUSSION

Monitored anaesthesia care (MAC) may be used in various ENT surgeries which require adequate sedation and analgesia which is desirable for comfort of both the patient and surgeon. MAC involves administration of local anaesthesia with intravenous sedatives, anxiolytic and analgesic drugs with detailed monitoring of vital parameters. It has many advantages such as less bleeding, cost-effectiveness, postoperative analgesia, faster recovery and ability to test hearing intra operatively. Thus the primary objective in providing MAC is to ensure patient comfort, safety, and satisfaction during surgery[1].

The ASA defines MAC as instances in which an anaesthesiologist has been requested to provide specific anaesthesia services to a particular patient undergoing a planned procedure, in connection with which a patient receives local anaesthesia or, in some cases, no anaesthesia at all[1,2].

The standards for preoperative evaluation, intra-operative monitoring, and the continuous presence of an anaesthesiologist are no different from those for general or regional anaesthesia. Preoperative assessment includes evaluation of the patient's ability to remain immobile and cooperative. Verbal communication between the anaesthesiologist and patient is important in order to evaluate the level of sedation, reassure the patient, and provide a mechanism when the patient is required to cooperate.

A level of sedation that allows verbal communication should be optimal for the patient's comfort and safety. If the level of sedation is deepened to the extent that verbal communication is lost, most of the advantages of monitored anaesthesia care are also lost,

and the risk of this technique almost approaches to general anaesthesia with an unprotected and uncontrolled airway.

Arterial hypoxemia as a result of alveolar hypoventilation is a risk after the administration of sedatives, hypnotics, or analgesics. A patient who is receiving minimal supplemental oxygen may have acceptable oxygenation despite significant alveolar hypoventilation.

American Society of Anaesthesiologists (ASA) Standards for Basic Anaesthetic Monitoring that is applicable to all levels of anaesthesia care includes monitored anaesthesia care too. It includes pulse oximetry (SpO_2), Electrocardiography (ECG), NIBP Monitor. It is important to continually evaluate patient's response to verbal commands in order to titrate the level of sedation and to allow early detection of neurologic or cardiopulmonary dysfunction.

Several drugs have been used for sedation during surgery under local anaesthesia with monitored anaesthesia care including Propofol, benzodiazepines and opioids. However, Propofol may cause over sedation and disorientation[11], Benzodiazepines may result in confusion, particularly in elderly and opioids are associated with increased risk of respiratory depression[35]. All of these untoward effects hamper patient's cooperation during surgery and make these agents less ideal for sedation in MAC.

Use of continuous intravenous infusion of short acting sedative - hypnotic drugs has been found to be associated with fewer side effects and shorter recovery times than the traditional intermittent bolus techniques. It also provides stable level of sedation.

Midazolam is most commonly used for sedation in MAC and reported to be well tolerated by patients.

Dexmedetomidine provides dose-dependent sedation, analgesia, sympatholysis and anxiolysis without causing respiratory depression. Hypotension and bradycardia have been observed in studies done earlier with Dexmedetomidine[78, 79, 80]. These effects are known to be related to the dose, route of administration and infusion rate (in intravenous administrations) [8,43,81,82]. Reports of its use state that, alpha-2 agonist effect is observed on administration of low and moderate doses and at slow rates of infusion and alpha 1 agonism is seen at high dose and faster rate of infusion.[54]Taking this into account, we decided to use a loading dose of 1 μg/kg Dexmedetomidine, in order to avoid side effects associated with high infusion rates.

We conducted a comparative clinical study in 96 patients of ASA Grade I & II, aged between 18 - 60 yrs, undergoing middle ear surgeries to evaluate and compare the effects of intravenous infusion of Inj. Dexmedetomidine and Midazolam in terms of sedation, analgesia and hemodynamic stability intraoperatively and postoperatively. All these patients were operated under Monitored Anaesthesia Care using local infiltration with 2% Lignocaine with Adrenaline 1:200000 and sedation using either Dexmedetomidine or Midazolam infusion.

Patients were randomly divided in two groups of 48 each according to chit block method to receive either Inj. Dexmedetomidine (Group D) or Inj. Midazolam (Group M) intravenous infusion during surgery.

Group D - Inj. Dexmedetomidine 1 mcg/kg IV bolus over 10 minutes followed by continuous infusion @0.5 mcg/kg/h

Group M – Inj. Midazolam 40 mcg/kg IV bolus over 10 minutes followed by continuous infusion @20 mcg/kg/hr.

- ***DEMOGRAPHIC DATA:***

All the patients are comparable with respect to the demographic parameters: age, weight and sex. In Group D mean age was 37.8 years and in Group M it was 35.2 years. In Group D and Group M there were 29 males and 19 female patients. The mean weight in Group D was 61.5 kg and in Group M it was 59.5 kg. Group D had 39 ASA I patients and 9 ASA II patients, whereas Group M had 38 ASA I patients and 10 ASA II patients. Both groups were comparable and there was no statistically significant difference **(Table 1-4).**

Mean duration of surgery in Group D was 85.6 ± 11.6 minutes while in Group M it was 88.1 ± 15.4 minutes. The difference was not statistically significant ($p<0.05$) **(Table 5 & Chart E)**

- ***PERIOPERATIVE SEDATION:***

Turan A, Sapolyo O, Karamanlioglu B, Kurt I, Pamukcu Z (2004)[15] studied 40 patients for sedation under MAC in Septoplasty and Functional endoscopic sinus surgeries. Patients received either Dexmedetomidine 1 mcg/kg IV over 5 minutes followed by infusion at 0.4 mcg/kg/hr or Propofol at 0.8 mg/kg bolus followed by infusion at 2 mg/kg/hr. They concluded that sedation caused by Dexmedetomidine was

more profound. In our study also we found that sedation was better with Dexmedetomidine from 15 minutes of surgery up to 90 minutes. **(Table 6 & Chart F)**

Üstün Y, Gündüz M, Erdoğan Ö, Benlidayi ME.(2006)[16] compared Dexmedetomidine and Midazolam sedation in third molar removal surgery. 20 patients with impacted mandibular third molars on both sides were included in this study to receive Inj. Dexmedetomidine (Group D) 4 µg/kg/h or Midazolam (Group M) 0.4 mg/kg/hr 15 minutes before start of the first surgery and other agent was given for second surgery. They found that 65% patients showed preference for Dexmedetomidine sedation. They concluded that Dexmedetomidine sedation was more preferred by patients and is a great alternative to Midazolam.

O'Daniel TG, Shanahan PT (2006) [17] conducted a study to determine the efficacy of Dexmedetomidine as a multifunctional sedative agent for 50 patients undergoing extended superficial musculo aponeurotic system (SMAS) face lift surgery. They found that Dexmedetomidine provided adequate sedation in 42 out of 50 patients and concluded that in their population of non-intubated patients undergoing facial rejuvenation surgery, Dexmedetomidine fulfilled the properties sought in a sedative agent.

Demiraran Y, Korkut E, Tamer A, Yorulmaz I, Kocaman B, Sezen G, Akcan Y (2007)[19] compared Dexmedetomidine with Midazolam for sedation in patients undergoing Upper GI endoscopy. They concluded that Dexmedetomidine is a better alternative to Midazolam for sedation in patients undergoing upper GI endoscopy.

Kaygusuz K, Gokce G, Gursoy S, Ayan S, Mimaroglu C, Gultekin Y (2008)[22] conducted a randomised control trial to compare Inj. Dexmedetomidine and Inj. Propofol

in terms of sedation in 46 patients undergoing Extra corporeal shockwave lithotripsy (ESWL). They concluded that Dexmedetomidine is effective for sedation in ESWL compared to Propofol.

Eren G, Cukurova Z, Demir G, Hergunsel O, Kozanhan B, Emir NS (2011)[23] compared Dexmedetomidine with three different doses of Midazolam for sedation in 125 patients. They concluded that Dexmedetomidine was as effective at lower doses in comparison to Midazolam at higher doses in terms of sedation.

Candiotti KA, Bergese SD, Bokesch PM, Feldman MA, Wisemandle W, Bekker AY (2010)[24] conducted a study on Monitored Anaesthesia Care with Dexmedetomidine in 326 patients who were randomized 2:2:1 to receive Inj. Dexmedetomidine 0.5 µg/kg, Dexmedetomidine 1 µg/kg, or Normal Saline as loading dose, followed by a maintenance infusion of 0.2–1.0 µg/kg/h of Dexmedetomidine or equivalent volume of saline titrated to achieve sedation level 4 on the Observer's Assessment of Alertness/Sedation Scale [OAA/S], 15 minutes before placement of block. They concluded that Dexmedetomidine is an effective sedative for patients undergoing surgeries under MAC as it provides better patient satisfaction, less opioid requirement. This correlates with the findings of our study.

Parikh DA et al (2013)[26] compared Dexmedetomidine (1mcg/kg over 10 min followed by 0.2 mcg/kg/hr infusion) versus Midazolam-Fentanyl (0.06 mg/kg Midazolam + Fentanyl 1 mcg/kg over 10 min followed by NS infusion @ 0.2 ml/kg/hr) in 90 patients undergoing tympanoplasty. In this study rescue sedation with propofol was required for

one patient in group D and 4 patients in group M, but p value was not statistically significant.

In our study 2 out of 48 patients in Group D required additional sedation in comparison to 5 patients in Group M. **(Table 10 & Chart J)**

Koroglu A, Demirbilek S, Teksan H, Sagır O, But AK, Ersoy MO (2005)[58] studied and compared the sedative, hemodynamic and respiratory effects of Dexmedetomidine with Midazolam in children undergoing MRI examination. They found that sedation was better in group D than in group M (P<0.001) and that the onset of sedation was faster in Group D than in group M (P<0.001). This is in accordance to our study.

- ***PERIOPERATIVE ANALGESIA:***

Mc Cutcheon CA, Orme RM, Scott DA, Davies MJ, Mc Glade DP (2006)[8] compared Dexmedetomidine with Midazolam- Fentanyl for sedation in 56 patients undergoing carotid endarterectomy (CEA) under regional anaesthesia. They found that the number of patients requiring additional pain relief in the post anaesthesia care unit was significantly higher in Midazolam-Fentanyl group.

In our study 5 out of 48 patients required additional analgesic in group D compared to 15 out of 48 patients in Group M with statistically significant p value of 0.012. **(Table 10 & Chart J)**

Turan A, Sapolyo O, Karamanlioglu B, Kurt I, Pamukcu Z (2004)[15] compared Dexmedetomidine and Propofol for monitored anaesthesia care in 40 patients undergoing Septoplasty and Endoscopic sinus surgeries in terms of hemodynamic, analgesic and

sedative effects. They found that VAS, intraoperative sedation scores and additional analgesic requirement was higher in Propofol group. They concluded that Dexmedetomidine causes better postoperative analgesia and is a better alternative to Propofol in MAC.

Karaaslan K, Yilmaz F, Gulcu N, Colak C, Sereflican M, Kocoglu H (2007)[18] compared Dexmedetomidine (1 mcg/kg over 10 min followed by 0.5 mcg/kg/hr infusion) and Midazolam (40 mcg/kg for 10 min followed by 50 mcg/kg/hr infusion) as primary drugs for MAC combined with Tramadol IV bolus1.5mg/kg via PCA in endoscopic nasal surgery. They found pain and sedation scores were similar in both groups, but the amount of rescue Tramadol needed was significantly higher in group M (P = 0.001) suggesting that better analgesic effect was achieved by Dexmedetomidine.

In our study also we found that analgesia was better with Dexmedetomidine than Midazolam. In perioperative period VAS score was less in Group D than in Group M. **(Table 8 & Chart H and Table 9 & Chart I)**.

Ayoglu H, Yapakci O, Ugur MB, Uzun L, Altunkaya H, Ozer Y, Uyanik R, Cinar F, Ozkocak I (2008)[20] studied 80 patients of ASA I/II for the effectiveness of Dexmedetomidine in reducing bleeding during ENT surgeries. Patients received either Inj. Dexmedetomidine 1 mcg/kg followed by 0.7mcg/kg/hr or identical amount of saline, with Fentanyl as rescue analgesia in both groups. They concluded that Dexmedetomidine reduces intraoperative Fentanyl consumption.

Goksu S, Arik H, Demiryurek S, Mumbuc S, Oner U, Demiryurek AT (2008)[21]conducted a study to understand haemodynamic effects of perioperatively

administered Dexmedetomidine for Functional endoscopic sinus surgery under local anaesthesia in 62 patients. They concluded that Dexmedetomidine provides analgesia, adequate sedation and surgical comfort without adverse effects in patients undergoing functional endoscopic sinus surgery under local anaesthesia.

Vyas DA, Hihoriya NH, Gadhavi RA(2013)[25]conducted study on 50 patients of ASA grade I/II for MAC in ENT surgeries. They concluded that Dexmedetomidine provides better sedation, intraoperative analgesia and bloodless surgical field in comparison to Midazolam

Verma R, Gupta R, Bhatia VK, Bogra J, Agarwal SP (2014)[27] conducted a study comparing Dexmedetomidine versus Propofol for MAC in patients undergoing middle ear surgeries. They concluded that both drugs provide adequate sedation but Propofol group was associated with more requirements of rescue analgesia and poor patient and surgeon satisfaction.

Padmaja A, Varma T (2015) [29] conducted a study comparing efficacy of Midazolam versus Dexmedetomidine in 40 patients undergoing minor ENT procedures under MAC in terms of sedative properties, rescue analgesic doses needed and hemodynamics. They concluded that Midazolam and Dexmedetomidine are comparable in terms of sedation but Dexmedetomidine reduces dose of rescue analgesic making it a more favourable choice for ENT surgeries.

The findings in above studies are similar to our study, suggesting analgesic effect of Dexmedetomidine is better than Midazolam in patients undergoing surgery under local anaesthesia with MAC.

❖ ***HEMODYNAMIC PARAMETERS DURING PERIOPERATIVE PERIOD:***

Alhashemi JA(2006)[7] conducted a comparative study of Dexmedetomidine versus Midazolam for monitored anaesthesia care in 44 patients undergoing cataract surgery under peribulbar block. They found that Group D had lower MAP, PR and better patient satisfaction score in comparison to Midazolam.

Nociti JR, Serzedo PS, Zuccoloto EB, Sebben F, GonzalesRF(2003)[14] studied the effects of Dexmedetomidine on Propofol requirements and cardiovascular and respiratory stability for sedation under local anaesthesia in 40 patients scheduled for elective face, nose and breast plastic surgeries. They found that Mean blood pressure values, pulse rate, mean duration to open eyes was lower in group D and that this group also showed better bleeding control. They concluded that Dexmedetomidine-Propofol combination is safe and has the advantages of decrease in Propofol requirements, good cardiovascular stability, and excellent perioperative bleeding control without causing any depression in ventilation.

O'Daniel TG, Shanahan PT(2006) [17] conducted a study to determine the efficacy of Dexmedetomidine as a multifunctional sedative agent for patients undergoing extended superficial musculo aponeurotic system (SMAS) face lift surgery. Heart rate, Respiratory rate, postoperative emergent rates and adverse events were recorded. They found that Dexmedetomidine infusion controlled systolic blood pressure to < 120 mm Hg and provided adequate sedation in 42 out of 50 patients.

Karaaslan K, Yilmaz F, Gulcu N, Colak C, Sereflican M, Kocoglu H(2007)[18] compared Dexmedetomidine with Midazolam in combination with Tramadol patient-controlled analgesia in 70 patients undergoing Septoplasty or Endoscopic sinus surgery under MAC. They found that Hemodynamic parameters like Systolic blood pressure, Diastolic blood pressure, mean arterial pressure and heart rate were higher in Midazolam group compared to Dexmedetomidine group.

Dexmedetomidine leads to depressive effects on hemodynamic parameters at the loading dose of 1 μg/kg over 10 min, but this effect does not reach the level of severe impairment as shown by **Eren G, Cukurova Z, Demir G, Hergunsel O, Kozanhan B, Emir NS** (2011)[23].

Parikh DA, Kolli SN, Karnik HS, Lele SS, Tendolkar BA (2013)[26] found that intraoperative mean heart rate and mean arterial pressure was lower in Dexmedetomidine group than the baseline values and the corresponding values in Midazolam-Fentanyl group.

The findings in our study are similar to above mentioned studies, suggesting that Dexmedetomidine and Midazolam both produce stable haemodynamics.HR, SBP, DBP, MAP were lower in Dexmedetomidine group compared to baseline values and corresponding values in Group M, with clinical advantage over Midazolam in providing better operative field for microscopic surgery[26].**(Table 11-20 & Chart K-T)**

In our study, Dexmedetomidine-induced bradycardia was not statistically significant in comparison to Midazolam and was not clinically challenging. Similar observations

were reported by**Dyck JB, Maze M, Haack C, Vuorilehto L, Shafer SL**[84]**,** who compared intravenous and intramuscular administration of Dexmedetomidine.

- ***RESPIRATORY PARAMETERSDURING PERIOPERATIVE PERIOD:***

Hsu YW, Cortinez LI, Robertson KM, Keifer JC, Sum-Ping ST, Moretti EW, Young CC, Wright DR, MacLeod DB, Somma J (2004)[83]compared the effects of Remifentanil and Dexmedetomidine on respiratory parameters. They concluded that the hypercapneic ventilator response was unaffected with Dexmedetomidine.

Eren G, Cukurova Z, Demir G, Hergunsel O, Kozanhan B, Emir NS (2011)[23] compared Dexmedetomidine and three different doses of Midazolam in preoperative sedation. They found RR and SpO2 values were lower in Midazolam groups. In their study, the differences in respiratory rates between groups was not significant ($p > 0.05$), however, decrease in SpO_2 was significant in the group with higher dose of Midazolam 0.06mg/kg. ($p<0.01$).

The findings in our study are similar to above mentioned studies. Group M patients had significant reduction in respiratory rate compared to baseline values and compared to Group D perioperatively, but rate was within normal limits (RR >8/min) **(Table 21,22 & Chart U,V)**, suggesting that there is no respiratory depression with Dexmedetomidine. SpO2 was maintained within normal limits in both the groups.

- ***SURGEON SATISFACTION:***

Vyas DA, Hihoriya NH, Gadhavi RA(2013)[25]compared Dexmedetomidine versus Midazolam for sedation during Tympanoplasty and Modified radical mastoidectomy

under local anaesthesia in 50 patients. They found out that Surgeon's satisfaction score and patient's satisfaction score were higher in Group D. They concluded that Dexmedetomidine is a suitable alternative to Midazolam for ENT surgeries done under MAC.

Parikh DA, Kolli SN, Karnik HS, Lele SS, Tendolkar BA (2013)[26]compared Dexmedetomidine with Midazolam-Fentanyl for Tympanoplasty under local anaesthesia. They concluded that Dexmedetomidine is better than Midazolam-Fentanyl for sedation during Tympanoplasty with better surgeon and patient satisfaction.

Verma R, Gupta R, Bhatia VK, Bogra J, Agarwal SP (2014)[27] conducted a study comparing Dexmedetomidine versus Propofol for MAC in patients undergoing middle ear surgeries. They concluded that both drugs provide adequate sedation but Propofol group was associated with more requirements of rescue analgesia and poor patient and surgeon satisfaction.

Gupta K, Bansal M, Gupta PK, Pandey M N, Agarwal S (2015)[28] conducted a study on 64 patients undergoing middle ear surgery under General anaesthesia to assess better operating conditions, bloodless field and depth of anaesthesia and rapid emergence. They concluded that Dexmedetomidine infusion provides oligemic field thereby providing better visualisation with operating microscope for middle ear surgery.

In our study, 31 out of 48 surgeries (64.6 %) in Group D were rated 5 on surgeon satisfaction score compared to 14 out of 48 (29.2 %) surgeries in Group M. **(Table 23 & Chart W)**.Group D had significantly higher surgeon satisfaction scores compared to Group M with p value of 0.001.

❖ ***SIDE EFFECTS:***

Karaaslan K, Yilmaz F, Gulcu N, Colak C, Sereflican M, Kocoglu H(2007)[18] compared Dexmedetomidine with Midazolam in combination with Tramadol patient-controlled in 70 patients undergoing Septoplasty or Endoscopic sinus surgery under MAC. They found a higher, though not statistically significant, prevalence of adverse events like hypotension, bradycardia and perioperative nausea and vomiting in Group D.

Demiraran Y, Korkut E, Tamer A, Yorulmaz I, Kocaman B, Sezen G, Akcan Y (2007)[19] compared Dexmedetomidine with Midazolam for sedation in 50 patients undergoing Upper GI endoscopy. They found that the number of patients having adverse effects was higher in Midazolam group than the Dexmedetomidine group ($P<0.05$).

Goksu S, Arik H, Demiryurek S, Mumbuc S, Oner U, Demiryurek AT (2008)[21]conducted a study to understand haemodynamic effects of perioperatively administered Dexmedetomidine for Functional endoscopic sinus surgery under local anaesthesia in 62 patients. They observed that Postoperative nausea and vomiting rates were significantly lower in the Dexmedetomidine group.

In our study, 2 patients in Group D had Bradycardia and Hypotension. Bradycardia was treated with Inj. Atropine 0.01 mg/kg. Hypotension was treated with IV fluids and Inj. Ephedrine 5 mg bolus. No side effects were seen in Group M. p value was not statistically significant. **(Table 24 & Chart X)**

CONCLUSION

From our study, we conclude that Dexmedetomidine in comparison to Midazolam causes:

1. Better sedation.
2. Better intraoperative and postoperative analgesia.
3. Reduced requirement of rescue analgesics perioperatively.
4. Better hemodynamic stability.
5. Better Surgeon satisfaction.
6. No significant side effects.

Dexmedetomidine causes more profound sedation without causing any ventilatory depression, better perioperative analgesia with reduced requirement of additional analgesics. It also normalises the increases in blood pressure and heart rate caused by perioperative anxiety by virtue of its anxiolytic property. It causes better surgeon satisfaction by creating an oligemic surgical field. Dexmedetomidine is cost effective and it has no significant side effects.

Hence, we conclude that, Dexmedetomidine is a safe and attractive agent for sedation in patients undergoing Middle ear surgeries under local anaesthesia with monitored anaesthesia care as it provides a calm patient, causes better analgesia and rapid recovery.

LIMITATIONS

- Our study was done only in ASA I and II patients aged between 18-60 years.
- More studies are needed to focus on the effects of Dexmedetomidine in debilitated, geriatric and pediatric patients.

SUMMARY

BACKGROUND: Monitored Anaesthesia Care (MAC) involves administration of local anaesthesia with intravenous sedatives, anxiolytic and analgesic drugs with detailed monitoring of vital parameters. It has many advantages such as less bleeding, cost-effectiveness, postoperative analgesia, faster recovery and ability to test hearing intraoperatively.

In our study, we used intravenous infusion of Dexmedetomidine and Midazolam to evaluate and compare the effects of each drug with respect to sedation, analgesia and hemodynamic stability intraoperatively and postoperatively.

METHODOLOGY: We conducted a study on 96 patients undergoing middle ear surgery under MAC. Patients were divided in two groups containing 48 each according to chit block method to receive Dexmedetomidine (Group D) or Midazolam (Group M) infusion during surgery.

- Pre anaesthetic evaluation was done on the day before surgery and required investigations were advised. Patients were explained in detail about LA, operative procedure and sedation. Visual Analogue Scale was explained to patient during pre-operative visit.
- Patients meeting above criteria were asked to participate in study and informed consent was taken and they were advised to be nil by mouth overnight.
- On the day of surgery, patient was taken to Operating room. ECG, non invasive BP and pulse oximetry were attached and baseline vitals were recorded. Inj. Glycopyrrolate 0.01-0.02 mg/kg and Inj. Ondansetron 0.15 mg/kg IV was given

and IV Ringer Lactate solution @ 2ml/kg/hr was started. O_2 was administered with nasal canula @ 2lit/min.

- Patients in group D received Inj. Dexmedetomidine 1 µg/kg IV bolus over 10 minutes followed by continuous infusion at 0.5 µg/kg/hr.
- Patients in group M received Inj. Midazolam 40 µg/kg IV over 10 minutes followed by continuous infusion at 20 µg/kg/hr.
- Loading dose of both the drugs were calculated and diluted to 20 ml with 0.9% Normal saline and kept at constant rate of 120ml/hr given over 10 minutes.
- After the loading dose of the drug, Ramsay Sedation Score was assessed and sedation titrated to target sedation of RSS 3. Infusion was stopped when RSS was 3 or full 20 ml bolus had been given whichever was earlier. If the RSS < 3 at the end of 10 min of loading dose, patients were given Inj. Propofol 100-300 mcg/kg IV bolus as a rescue sedative. RSS was assessed throughout the duration of surgery and in postoperative period every 15 minutes till 120 minutes.
- Once RSS was 3, Lidocaine 2% with adrenaline 1:200,000, 6-7 ml was given by the surgeon. The maintenance infusion was commenced at constant infusion rate for both the groups calculated according to weight of patient.
- Intraoperative pain intensity was assessed with VAS (0-10). If VAS >3 or whenever patient complained of pain during surgery, Inj. Fentanyl @1 mcg/kg was given as rescue analgesic.
- Heart rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean arterial pressure(MAP), Respiratory Rate(RR), Oxygen Saturation(SpO_2) were recorded at the start of loading infusion, 5 minutes after, at the end of

loading infusion and every 15minutes thereafter till the end of surgery and postoperatively for 2 hours.

- Patients were shifted to Post Anaesthesia Care Unit (PACU) after completion of surgery and were monitored for hemodynamic parameters. Pain was assessed postoperatively using Visual analog scale and if VAS >3, then Inj. Diclofenac 1.5mg/kg I.V was given.
- At the end of surgery, surgeons were asked to grade their satisfaction using Likert scale; score of 4 and 5 were taken as acceptable.

RESULTS*:* In our study, we observed that

1. Sedation with Dexmedetomidine was more profound compared to Midazolam.
2. Analgesic effects of Dexmedetomidine were better than Midazolam.
3. Fall in Heart Rate was significantly more in Group D compared to baseline value and compared to Group M
4. Systolic Blood Pressure and Diastolic Blood Pressure were maintained within normal limits in both the groups but the fall in SBP and DBP was significantly more in Group D than in Group M.
5. Mean arterial pressure was within normal limits in both the groups but fall in MAP was significantly more in Group D than Group M.
6. Oxygen saturation and Respiratory rate were maintained within normal limits in both the groups.
7. Better Surgeon satisfaction scores were seen with Dexmedetomidine.
8. No significant side effects were noted in both the groups.

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ANNEXURE I

B.L.D.E.UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR – 586103
INSTITUTIONAL ETHICAL COMMITTEE

No/58/2015
20/11/15

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 17/11/2015 *at* 03 pm *scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.*

Title "A Comparative Study of dexmedetomidine versus midazolam for monitored Anaesthesia care in middle ear Surgeries"

Name of P.G. Student : Dr. Ramya. K.
Dept of Anaesthesiology

Name of Guide/Co-investigator : Dr. Vijaykumar T. K.
Professor of Anaesthesiology

DR.TEJASWINI VALLABHA
CHAIRMAN

CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,BIJAPUR-586103.

Following documents were placed before E.C. for Scrutinization:
1)Copy of Synopsis/Research Project
2)Copy of informed consent form.
3)Any other relevant documents.

ANNEXURE II

INFORMED CONSENT FORM

TITLE OF THE PROJECT: **"A COMPARATIVE STUDY OF DEXMEDETOMIDINE VERSUS MIDAZOLAM FOR MONITORED ANAESTHESIA CARE IN MIDDLE EAR SURGERIES"**

PRINCIPAL INVESTIGATOR : **Dr. RAMYA K**,

Department of Anaesthesiology,

Email: dr.ramyakota@gmail.com

PG GUIDE :**Dr. VIJAY KUMAR T.K**,

Professor,

Department of Anaesthesiology,

B.L.D.E University's

Shri B.M. Patil Medical College,

Hospital & Research Centre,

Vijayapur, Karnataka.

I have been informed that this study is **"A COMPARATIVE STUDY OF DEXMEDETOMIDINE VERSUS MIDAZOLAM FOR MONITORED ANAESTHESIA CARE IN MIDDLE EAR SURGERIES"**. I have been explained about this study in the language which I understand. I have been explained about the reason for doing this study and selecting me/my ward as a subject for this study. I have been told that my participation in the above study is voluntary and I am aware that I can opt out of the study at any time without having to give any reasons for doing so. I am also informed that my refusal to participate in this study will not affect my treatment by any means.

I agree to participate in the above study and cooperate fully. I agree to follow the Doctor's instructions about my treatment to the best of my ability.

CONFIDENTIALITY:

I understand that medical information produced by this study will become a part of this Hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. Information of a sensitive, personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code key connecting name to numbers will be kept in a separate secure location.

If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audio tapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time and Dr. Ramya K is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.

If during this study, or later, I wish to discuss my participation or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me and that a copy of this consent form will be given to me for my careful reading.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that Dr. Ramya K will terminate my participation in this study at any time after she has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me/ my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided. I understand that by my agreement to participate in this study, I am not waiving any of my legal rights. I have been explained about the purpose of this research, the procedures required and the possible risks and benefits, in my own language. I have been explained all the above in detail and I understand the same. Therefore I agree to give my consent to participate as a subject in this research project.

Patient's Signature: Witness Signature

Name: Name:

Date: Date:

Dr. VIJAYKUMAR T.K **Dr. RAMYA K.**

(Guide) (Investigator)

ANNEXURE III

PROFORMA

STUDY: **"A COMPARATIVE STUDY OF DEXMEDETOMIDINE VERSUS MIDAZOLAM FOR MONITORED ANAESTHESIA CARE IN MIDDLE EAR SURGERIES"**

Serial No. Group [D] Group [M]

Name of the patient: I.P. No. :

Age: Sex: Weight:

Date of Admission: Date of Surgery:

Diagnosis:

Proposed Surgery:

PRE ANESTHETIC EVALUATION

Chief complaints:

Past History:

a) Presence of any co-morbid condition - Diabetes/ Hypertension/ Ischemic heart disease/ Cerebrovascular accident / Asthma/ Epilepsy/ Bleeding disorder/ Drug allergy/ any other .

b) Drug Therapy

c) H/o previous anaesthetic exposure:

Family History:

General Physical Examination:

- General condition :
- Pallor / Icterus / Cyanosis / Clubbing / Lympadenopathy / Pedal edema.
- Temperature:
- Pulse rate:
- Respiratory rate:
- Blood Pressure :

Mallampati grade:

Systemic Examination:

- Cardiovascular system
- Respiratory system
- Central nervous system
- Others

Investigations:

- Hb% :
- Total Leucocyte count :
- Differential count :
- Platelet count :
- Bleeding time/ Clotting time :
- Random Blood sugar :
- Urine routine:
- ECG :
- Chest X ray:
- Blood Urea:
- Serum Creatinine:
- Any other :

ASA Grade:

ANAESTHESIA PROTOCOL:

Anaesthetic Technique: Local anaesthesia with Monitored anaesthesia care.

- Premedication :

  Inj. Glycopyrolate 0.01-0.02 mg/kg IV [ ]

  Inj Ondansetron 0.15 mg/kg IV [ ]

- O_2 supplementation with nasal cannula at the rate of 2 lit/min [ ]
- Loading dose of study drug

  Group D:

  Inj. Dexmedetomidine 1 mcg/kg in 20 ml of 0.9% NS at the rate of 120ml/hr IV bolus over 10 minutes. [ ]

  Group M:

  Inj. Midazolam 40 mcg/kg in 20 ml of 0.9% NS at the rate of 120ml/hr IV bolus over 10 minutes. [ ]

- Ramsay Sedation Score assessment at 10 minutes after loading dose :

Score > 3 [ ]

If Score< 3 : Inj Propofol 100-300 mcg/kg IV [ ]

- Local infiltration with Inj. Lidocaine 2% with Adrenaline 1:200000,

6-8 mg/ kg by the surgeon. [ ]

- Maintenance infusion of study drug :

  Group D:

  Inj. Dexmedetomidine 100 mcg in 25 ml of 0.9% NS (4 mcg/ml) at the rate of 0.5 mcg/kg/hr. [ ]

  Group M : Inj. Midazolam 4 mg in 25 ml of 0.9 % NS (0.16 mg/ml) at the rate of 20 mcg/kg/hr. [ ]

- Intraoperative Rescue analgesia (Inj. Fentanyl 1 mcg/kg IV) [ ]
- Post-operative rescue analgesia (Inj. Diclofenac 1.5 mg/kg IV) [ ]

INTRA OPERATIVE MONITORING:

TIME	PR	SBP	DBP	MAP	RR	SpO_2	RESCUE ANALGESIA	RESCUE SEDATION
BASELINE								
AT THE START OF LOADING DOSE								
AFTER 5 MINUTES								
AT THE END OF INFUSION- 10 minutes								

Ramsay Sedation Score at the end of infusion:

TIME	PR	SBP	DBP	MAP	RR	SpO_2	RESCUE ANALGESIA	RESCUE SEDATION
15 MINUTES								
30 MINUTES								
45 MINUTES								
60 MINUTES								
75 MINUTES								
90 MINUTES								
105 MINUTES								
120 MINUTES								

POST OPERATIVE MONITORING:

TIME	PR	BP	RR	SpO_2	VAS	RESCUE ANALGESIA
15 MINUTES						
30 MINUTES						
45 MINUTES						
60 MINUTES						
75 MINUTES						
90 MINUTES						
105 MINUTES						
120 MINUTES						

SURGEON SATISFACTION SCORE:

Very Dissatisfied (1)	Dissatisfied (2)	Neither Satisfied nor Dissatisfied (3)	Satisfied (4)	Very Satisfied (5)
○	○	○	○	○

MASTER CHART - DEXMEDETOMIDINE

Sr No	Group	Age (years)	Sex	Wt(Kg)	ASA Grade	Diagnosis	Surgery	Duration of Surgery (mins)	AT THE START						5 MIN									10 MIN									15 MIN									30 MIN								
									HR	SpO2	SBP	DBP	MAP	RR	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication
1	D	51	F	60	II	Rt. CSOM	Rt. Tympanoplasty	75	72	100	120	80	93.3333	12	70	99	120	78	92	12	2	0		64	99	110	70	83.3333	12	3	0		64	98	110	68	82	12	3	0		64	100	100	66	77.3333	12	3	0	
2	D	30	F	55	I	Rt. CSOM	Rt. Tympanoplasty	75	88	100	110	70	83.3333	14	88	100	110	70	83.3333	14	1	0		80	99	104	66	78.6667	14	2	2		78	99	104	66	78.6667	14	2	3	Inj.Propofol	72	100	100	66	77.3333	12	4	0	
3	D	30	F	55	I	Rt. CSOM	Rt. Tympanoplasty	75	74	100	110	72	84.6667	12	72	99	110	68	82	12	1	0		66	99	104	66	78.6667	12	2	0		66	99	100	60	73.3333	12	3	1		66	100	100	60	73.3333	12	3	1	
4	D	20	M	50	I	Lt. CSOM	Lt. Tympanoplasty	75	74	99	124	80	94.6667	12	74	100	120	80	93.3333	12	2	0		68	100	114	68	83.3333	12	3	0		64	100	110	70	83.3333	12	3	0		64	99	104	70	81.3333	12	3	0	
5	D	60	M	70	II	Lt. CSOM	Lt. Tympanoplasty	90	72	100	140	90	106.667	16	72	100	140	90	106.667	14	1	0		66	99	120	80	93.3333	14	3	0		60	100	110	70	83.3333	16	3	0		64	99	110	70	83.3333	16	3	0	
6	D	23	M	50	I	Lt. CSOM	Lt. Tympanoplasty	90	80	99	120	78	92	16	78	99	120	78	92	16	1	1		74	100	116	72	86.6667	16	3	1		70	98	110	70	83.3333	16	3	0		66	99	104	68	80	16	3	0	
7	D	60	M	50	II	Lt. CSOM	Lt. Tympanoplasty	90	72	100	140	90	106.667	16	72	100	140	90	106.667	14	1	0		66	99	120	80	93.3333	14	3	0		60	100	110	70	83.3333	16	3	0		64	99	110	70	83.3333	16	3	0	
8	D	35	M	60	I	Rt. CSOM	Rt. Tympanoplasty	90	88	100	110	78	88.6667	14	84	98	110	76	87.3333	14	2	1		80	99	104	70	81.3333	12	3	1		68	100	100	70	80	14	3	1		66	100	100	66	77.3333	14	3	4	Inj. Fentanyl
9	D	20	M	71	I	Lt. CSOM	Lt. Tympanoplasty	90	80	99	120	78	92	16	78	99	120	78	92	16	1	1		74	100	116	72	86.6667	16	3	1		70	98	110	70	83.3333	16	3	0		66	99	104	68	80	16	3	0	
10	D	47	M	67	II	Lt. CSOM	Lt. Tympanoplasty	90	72	100	140	90	106.667	16	72	100	140	90	106.667	14	1	0		66	99	120	80	93.3333	14	3	0		60	100	110	70	83.3333	16	3	0		64	99	110	70	83.3333	16	3	0	
11	D	45	M	72	II	Lt. CSOM	Lt. Tympanoplasty	75	72	100	120	80	93.3333	12	70	99	120	78	92	12	2	0		64	99	110	70	83.3333	12	3	0		64	98	110	68	82	12	3	0		64	100	100	66	77.3333	12	3	0	
12	D	24	F	50	I	Rt. CSOM	Rt. Tympanoplasty	90	72	99	110	70	83.3333	14	74	99	110	70	83.3333	14	1	1		70	99	110	70	83.3333	14	3	1		64	100	104	70	81.3333	14	3	0		64	100	100	68	78.6667	14	3	0	
13	D	45	M	65	II	Lt. CSOM	Lt. Tympanoplasty	75	72	100	120	80	93.3333	12	70	99	120	78	92	12	2	0		64	99	110	70	83.3333	12	3	0		64	98	110	68	82	12	3	0		64	100	100	66	77.3333	12	3	0	
14	D	26	F	62	I	Rt. CSOM	Rt. Tympanoplasty	90	74	99	118	78	91.3333	14	74	100	116	78	90.6667	14	2	0		72	99	114	70	84.6667	14	3	0		66	99	110	66	80.6667	14	3	0		64	99	104	64	77.3333	14	3	2	
15	D	23	M	55	I	Rt. CSOM	Rt. Tympanoplasty	75	74	99	124	80	94.6667	12	74	100	120	80	93.3333	12	2	0		68	100	114	68	83.3333	12	3	0		64	100	110	70	83.3333	12	3	0		64	99	104	70	81.3333	12	3	0	
16	D	30	F	60	I	Rt. CSOM	Rt. Tympanoplasty	75	80	99	118	70	86	14	80	100	118	70	86	14	1	0		74	100	110	70	83.3333	14	3	1		70	99	110	70	83.3333	14	3	0		66	99	110	70	83.3333	14	3	0	
17	D	47	M	67	I	Lt. CSOM	Lt. Tympanoplasty	105	58	99	100	65	76.6667	12	60	99	102	68	79.3333	12	1	0		59	99	94	65	74.6667	12	3	0		60	99	80	50	60	12	3	0	Inj. Ephedrin	70	99	90	58	68.6667	12	3	0	
18	D	56	F	60	I	Lt. CSOM	Lt. Tympanoplasty	75	72	100	110	70	83.3333	12	70	100	110	72	84.6667	12	2	1		66	100	102	66	78	12	3	0		61	100	100	64	76	12	3	1		58	100	98	64	75.3333	12	3	1	Inj. Atropine
19	D	25	F	54	I	Lt. CSOM	Lt. Tympanoplasty	90	72	99	110	70	83.3333	14	74	99	110	70	83.3333	14	1	1		70	99	110	70	83.3333	14	3	1		64	100	104	70	81.3333	14	3	0		64	100	100	68	78.6667	14	3	0	
20	D	48	M	68	II	Lt. CSOM	Lt. Tympanoplasty	75	86	99	148	92	110.667	14	80	99	135	84	101	14	2	0		84	99	158	92	114	14	3	0		84	99	148	90	109.333	13	3	0		83	99	140	88	105.333	14	3	0	
21	D	41	M	60	I	Lt. CSOM	Lt. Tympanoplasty	120	86	99	130	90	103.333	16	80	99	124	90	101.333	16	1	0		76	99	124	90	101.333	16	4	0		70	99	120	80	93.3333	14	4	2		66	99	110	78	88.6667	14	3	1	
22	D	30	M	60	I	Rt. CSOM	Rt. Tympanoplasty	75	72	100	120	78	92	12	72	98	120	80	93.3333	12	1	0		68	99	110	70	83.3333	12	3	1		64	98	110	70	83.3333	12	3	1		64	100	102	68	79.3333	12	3	1	
23	D	45	F	55	I	Lt. CSOM	Lt. Tympanoplasty	75	74	99	124	80	94.6667	12	74	100	120	80	93.3333	12	2	0		68	100	114	68	83.3333	12	3	0		64	100	110	70	83.3333	12	3	0		64	99	104	70	81.3333	12	3	0	
24	D	32	F	68	I	Lt. CSOM	Lt. Tympanoplasty	75	88	100	110	70	83.3333	14	88	100	110	70	83.3333	14	1	0		80	99	104	66	78.6667	14	2	2		78	99	104	66	78.6667	14	2	3	Inj.Propofol	72	100	100	66	77.3333	12	4	3	
25	D	35	F	60	I	Lt. CSOM	Lt. Tympanoplasty	75	74	100	110	72	84.6667	12	72	99	110	68	82	12	1	0		66	99	104	66	78.6667	12	2	0		66	99	100	60	73.3333	12	3	1		66	100	100	60	73.3333	12	3	1	
26	D	21	M	50	I	Lt. CSOM	Lt. Tympanoplasty	90	80	99	120	78	92	16	78	99	120	78	92	16	1	1		74	100	116	72	86.6667	16	3	1		70	98	110	70	83.3333	16	3	0		66	99	104	68	80	16	3	0	
27	D	27	M	60	I	Rt. CSOM	Rt. Tympanoplasty	90	74	100	118	74	88.6667	15	74	98	116	72	86.6667	14	2	0		70	100	110	70	83.3333	14	3	0		66	99	110	70	83.3333	14	3	0		66	99	104	66	78.6667	14	3	0	
28	D	38	M	65	I	Lt. CSOM	Lt. Tympanoplasty	90	72	100	110	70	83.3333	16	72	99	110	70	83.3333	16	1	0		70	99	110	70	83.3333	16	3	0		66	98	102	68	79.3333	14	3	0		64	100	100	68	78.6667	14	3	0	
29	D	33	F	60	I	Lt. CSOM	Lt. Tympanoplasty	90	74	99	130	90	103.333	12	74	99	130	90	103.333	12	2	0		70	100	120	80	93.3333	12	3	1		72	99	120	80	93.3333	12	3	0		64	99	110	76	87.3333	12	3	1	
30	D	18	F	60	I	Lt. CSOM	Lt. Tympanoplasty	75	80	100	120	80	93.3333	12	82	99	118	78	91.3333	12	2	0		72	100	110	70	83.3333	12	4	0		72	100	110	70	83.3333	12	4	0		68	99	104	66	78.6667	12	4	0	
31	D	44	M	70	I	Rt. CSOM	Rt. Tympanoplasty	90	80	100	120	80	93.3333	14	78	99	118	78	91.3333	14	1	0		70	99	110	72	84.6667	14	3	1		68	99	104	64	77.3333	14	3	1		62	99	100	64	76	14	3	1	
32	D	24	M	50	I	Rt. CSOM	Rt. Tympanoplasty	90	80	99	120	78	92	16	78	99	120	78	92	16	1	1		74	100	116	72	86.6667	16	3	1		70	98	110	70	83.3333	16	3	0		66	99	104	68	80	16	3	0	
33	D	44	M	65	I	Lt. Otosclerosis	Lt. Stapedectomy	105	78	100	110	70	83.3333	14	78	100	110	70	83.3333	14	1	0		76	99	110	68	82	14	3	0		70	99	104	66	78.6667	14	3	0		66	100	100	64	76	14	3	0	
34	D	55	F	60	I	Lt. CSOM	Lt. Tympanoplasty	90	70	100	130	88	102	14	70	99	130	90	103.333	14	1	1		66	100	124	82	96	14	2	0		62	100	120	80	93.3333	14	3	0		60	99	118	68	84.6667	14	3	0	
35	D	48	M	68	I	Lt. CSOM	Lt. Tympanoplasty	105	88	99	120	80	93.3333	14	88	99	120	78	92	14	1	0		78	99	116	76	89.3333	14	3	0		72	99	110	70	83.3333	14	3	0		66	99	110	70	83.3333	14	3	0	
36	D	56	M	70	I	Lt. CSOM	Lt. Tympanoplasty	90	74	99	130	90	103.333	12	74	99	130	90	103.333	12	2	0		70	100	120	80	93.3333	12	3	1		72	99	120	80	93.3333	12	3	0		64	99	110	76	87.3333	12	3	1	
37	D	49	M	70	I	Rt. CSOM	Rt. Tympanoplasty	75	72	100	110	72	84.6667	14	72	99	110	70	83.3333	14	1	0		70	100	104	68	80	14	2	0		68	99	100	70	80	14	3	0		66	99	96	66	76	14	3	0	
38	D	55	M	65	I	Lt. CSOM	Lt. Tympanoplasty	90	70	100	130	88	102	14	70	99	130	90	103.333	14	1	1		66	100	124	82	96	14	2	0		62	100	120	80	93.3333	14	3	0		60	99	118	68	84.6667	14	3	0	
39	D	45	F	49	I	Lt. CSOM	Lt. Tympanoplasty	75	78	99	110	74	86	13	74	99	110	70	83.3333	14	2	0		70	100	104	64	77.3333	12	2	2		66	99	100	64	76	12	3	2		66	100	100	66	77.3333	12	3	2	
40	D	49	M	65	I	Rt. CSOM	Rt. Tympanoplasty	105	80	99	118	78	91.3333	14	80	100	118	70	86	14	1	0		76	99	110	68	82	14	3	0		68	99	108	68	81.3333	14	3	0		66	99	100	66	77.3333	14	3	0	
41	D	40	M	66	I	Lt. Otosclerosis	Lt. Stapedectomy	105	58	99	100	65	76.6667	12	60	99	102	68	79.3333	12	1	0		59	99	94	65	74.6667	12	3	0		60	99	80	50	60	12	3	0	Inj. Ephedrin	70	99	90	58	68.6667	12	3	0	
42	D	26	F	55	I	Rt. CSOM	Rt. Tympanoplasty	75	78	99	110	74	86	13	74	99	110	70	83.3333	14	2	0		70	100	104	64	77.3333	12	2	2		66	99	100	64	76	12	3	2		66	100	100	66	77.3333	12	3	2	
43	D	19	M	60	I	Lt. CSOM	Lt. Tympanoplasty	75	74	99	124	80	94.6667	12	74	100	120	80	93.3333	12	2	0		68	100	114	68	83.3333	12	3	0		64	100	110	70	83.3333	12	3	0		64	99	104	70	81.3333	12	3	0	
44	D	45	M	78	I	Lt. CSOM	Lt. Tympanoplasty	90	80	100	120	80	93.3333	14	78	99	118	78	91.3333	14	1	0		70	99	110	72	84.6667	14	3	1		68	99	104	64	77.3333	14	3	1		62	99	100	64	76	14	3	1	
45	D	41	M	78	II	Lt. CSOM	Lt. Tympanoplasty	75	86	99	148	92	110.667	14	80	99	135	84	101	14	2	0		84	99	158	92	114	14	3	0		84	99	148	90	109.333	13	3	0		83	99	140	88	105.333	14	3	0	
46	D	45	F	78	II	Rt. CSOM	Rt. Tympanoplasty	105	80	99	130	90	103.333	12	78	99	123	90	101	12	1	0		80	99	128	80	96	12	3	1		82	99	128	78	94.6667	12	3	1		78	99	130	78	95.3333	12	3	2	
47	D	30	F	55	I	Lt. CSOM	Lt. Tympanoplasty	75	80	99	118	70	86	14	80	100	118	70	86	14	1	0		74	100	110	70	83.3333	14	3	1		70	99	110	70	83.3333	14	3	0		66	99	110	70	83.3333	14	3	0	
48	D	35	F	50	I	Lt. CSOM	Lt. Tympanoplasty	75	72	100	110	70	83.3333	12	70	100	110	72	84.6667	12	2	1		66	100	102	66	78	12	3	0		61	100	100	64	76	12	3	1		58	100	98	64	75.3333	12	3	1	Inj. Atropine

MASTER CHART - DEXMEDETOMIDINE

45 MIN									60 MIN								75 MIN								90 MIN								105 MIN								120 MIN							
HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication
62	99	100	66	77.3333	12	3	0		64	98	98	60	72.6667	12	3	0		62	99	98	60	72.6667	12	3	0																														
70	99	100	62	74.6667	12	3	0		68	99	100	60	73.3333	14	3	0		68	99	100	60	73.3333	14	3	0																														
66	99	98	64	75.3333	12	3	0		64	99	98	64	75.3333	12	3	0		68	99	100	60	73.3333	12	2	1																														
64	99	100	66	77.3333	12	3	0		64	99	100	66	77.3333	12	3	0		68	99	100	64	76	11	3	0																														
66	99	110	70	83.3333	16	3	0		62	99	104	66	78.6667	16	3	0		62	98	108	68	81.3333	16	3	0		64	99	110	72	84.667	16	4	1																														
66	98	100	66	77.3333	16	3	0		66	99	100	66	77.3333	16	3	0		66	99	100	66	77.3333	16	3	0		60	99	96	60	72	16	3	1																														
66	99	110	70	83.3333	16	3	0		62	99	104	66	78.6667	16	3	0		62	98	108	68	81.3333	16	3	0		64	99	110	72	84.667	16	4	1																														
66	99	100	64	76	14	3	2		64	98	100	68	78.6667	14	3	2		66	99	100	60	73.3333	14	3	1		62	99	100	68	78.667	14	3	1																														
66	98	100	66	77.3333	16	3	0		66	99	100	66	77.3333	16	3	0		66	99	100	66	77.3333	16	3	0		60	99	96	60	72	16	3	1																														
66	99	110	70	83.3333	16	3	0		62	99	104	66	78.6667	16	3	0		62	98	108	68	81.3333	16	3	0		64	99	110	72	84.667	16	4	1																														
62	99	100	66	77.3333	12	3	0		64	98	98	60	72.6667	12	3	0		62	99	98	60	72.6667	12	3	0																														
64	100	100	64	76	14	3	0		62	99	98	66	76.6667	14	3	0		62	99	98	66	76.6667	14	3	0		60	99	90	60	70	14	3	3																														
62	99	100	66	77.3333	12	3	0		64	98	98	60	72.6667	12	3	0		62	99	98	60	72.6667	12	3	0																														
68	99	100	66	77.3333	14	3	2		66	99	100	64	76	14	3	2		66	99	100	64	76	14	3	2		66	99	98	60	72.667	14	3	2																														
64	99	100	66	77.3333	12	3	0		64	99	100	66	77.3333	12	3	0		68	99	100	64	76	11	3	0																														
66	99	110	70	83.3333	14	3	0		66	99	104	66	78.6667	14	3	0		68	99	108	68	81.3333	12	3	0																														
72	99	92	58	69.3333	12	3	0		68	99	90	56	67.3333	12	3	0		64	99	90	56	67.333	12	3	1																														
76	100	98	64	75.3333	12	3	1		74	98	100	64	76	12	3	1		70	99	96	60	72	12	3	2																														
64	100	100	64	76	14	3	0		62	99	98	66	76.6667	14	3	0		62	99	98	66	76.6667	14	3	0		60	99	90	60	70	14	3	3																														
84	99	148	88	108	14	3	2		80	99	132	80	97.3333	14	3	2		76	99	130	74	92.666	12	3	2																														
66	99	106	76	86	14	3	2		64	99	106	80	88.6667	14	3	2		64	99	104	78	86.6667	14	3	1		64	99	108	74	85.3333	14	3	2		62	99	100	78	85.3333	14	3	1		62	99	100	78	85.3333	14	3	1	
66	100	100	64	76	12	3	1		66	99	100	64	76	12	3	1		68	99	90	60	70	10	3	1																														
64	99	100	66	77.3333	12	3	0		64	99	100	66	77.3333	12	3	0		68	99	100	64	76	11	3	0																														
70	99	100	62	74.6667	12	3	1	Inj. Fentanyl	68	99	100	60	73.3333	14	3	0		68	99	100	60	73.3333	14	3	0																														
66	99	98	64	75.3333	12	3	0		64	99	98	64	75.3333	12	3	0		68	99	100	60	73.3333	12	2	1																														
66	98	100	66	77.3333	16	3	0		66	99	100	66	77.3333	16	3	0		66	99	100	66	77.3333	16	3	0		60	99	96	60	72	16	3	1																														
66	99	104	68	80	14	3	0		66	99	104	66	78.6667	14	3	0		66	99	104	66	78.6667	14	3	0		62	99	104	66	78.667	12	3	1																														
64	99	98	64	75.3333	14	3	0		64	99	98	66	76.6667	14	3	0		64	100	98	66	76.6667	14	3	0		68	99	100	68	78.667	14	2	1																														
64	100	110	70	83.3333	12	3	1		64	98	110	70	83.3333	12	3	1		64	99	110	70	83.3333	12	3	1		60	99	102	70	80.667	11	3	2																														
68	99	100	66	77.3333	12	4	0		64	99	104	66	78.6667	12	4	0		62	100	104	66	78.667	12	3	1																														
62	99	100	62	74.6667	14	3	1		62	99	100	60	73.3333	14	3	1		62	99	98	60	72.6667	12	3	2																														
66	98	100	66	77.3333	16	3	0		66	99	100	66	77.3333	16	3	0		66	99	100	66	77.3333	16	3	0		60	99	96	60	72	16	3	1																														
66	98	100	64	76	14	3	0		66	99	96	60	72	14	3	0		66	99	98	60	72.6667	14	3	0		65	99	94	60	71.3333	14	3	0		64	99	98	60	72.667	12	3	0												
60	98	110	64	79.3333	14	3	0		60	100	108	66	80	14	3	0		60	99	110	68	82	14	3	0		58	99	110	68	82	14	2	1																														
65	99	110	70	83.3333	14	3	0		64	99	110	72	84.6667	14	3	2		64	99	108	76	86.6667	14	3	2		65	99	106	72	83.3333	14	3	2		64	99	106	72	83.333	12	3	2												
64	100	110	70	83.3333	12	3	1		64	98	110	70	83.3333	12	3	1		64	99	110	70	83.3333	12	3	1		60	99	102	70	80.667	11	3	2																														
64	99	90	60	70	14	3	0		64	99	90	60	70	14	3	0		60	100	90	60	70	12	2	1																														
60	98	110	64	79.3333	14	3	0		60	100	108	66	80	14	3	0		60	99	110	68	82	14	3	0		58	99	110	68	82	14	2	1																														
62	98	100	66	77.3333	12	3	2		66	100	100	64	76	12	3	2		60	99	98	66	76.6667	10	3	1																														
64	99	100	64	76	14	3	0		62	99	100	64	76	14	3	1		64	99	98	68	78	14	3	1		66	99	98	60	72.6667	14	3	1		64	99	100	60	73.333	12	3	1												
72	99	92	58	69.3333	12	3	0		68	99	90	56	67.3333	12	3	0		64	99	90	56	67.333	12	3	1																														
62	98	100	66	77.3333	12	3	2		66	100	100	64	76	12	3	2		60	99	98	66	76.6667	10	3	1																														
64	99	100	66	77.3333	12	3	0		64	99	100	66	77.3333	12	3	0		68	99	100	64	76	11	3	0																														
62	99	100	62	74.6667	14	3	1		62	99	100	60	73.3333	14	3	1		62	99	98	60	72.6667	12	3	2																														
84	99	148	88	108	14	3	2		80	99	132	80	97.3333	14	3	2		76	99	130	74	92.666	12	3	2																														
74	99	132	84	100	12	3	2		76	99	130	80	96.6667	14	2	5	Inj.Fentanyl	72	99	126	82		12	3	2		70	99	120	80	93.3333	12	3	2		68	99	118	80	92.666	12	3	1										
66	99	110	70	83.3333	14	3	0		66	99	104	66	78.6667	14	3	0		68	99	108	68	81.3333	12	3	0																														
76	100	98	64	75.3333	12	3	1		74	98	100	64	76	12	3	1		70	99	96	60	72	12	3	2																														

MASTER CHART - DEXMEDETOMIDINE

IN RECOVERY AT ARRIVAL									15 MIN									30 MIN									45 MIN									60 MIN								
HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional medication
64	99	100	64	76	12	2	0		68	99	100	68	78.6667	12	1	0		68	99	100	68	78.6667	12	1	0		68	99	100	68	78.6667	12	1	0		68	99	100	68	78.6667	12	1	0	
70	99	100	64	76	14	2	2		70	99	104	64	77.3333	14	2	1		70	99	104	64	77.3333	14	2	1		70	99	104	64	77.3333	14	2	1		70	99	104	64	77.3333	14	2	1	
68	99	96	66	76	12	2	0		72	100	100	68	78.6667	12	1	1		72	100	100	68	78.6667	12	1	1		72	100	100	68	78.6667	12	1	1		72	100	100	68	78.6667	12	1	1	
68	100	100	66	77.3333	12	2	0		72	100	104	70	81.3333	12	1	0		72	100	104	70	81.3333	12	1	0		72	100	104	70	81.3333	12	1	0		72	100	104	70	81.3333	12	1	0	
66	98	110	70	83.3333	15	1	0		68	98	110	72	84.6667	15	1	0		68	98	110	72	84.6667	15	1	0		68	98	110	72	84.6667	15	1	0		68	98	110	72	84.6667	15	1	0	
66	99	100	68	78.6667	16	2	0		70	99	104	70	81.3333	14	1	0		70	99	104	70	81.3333	14	1	0		70	99	104	70	81.3333	14	1	0		70	99	104	70	81.3333	14	1	0	
66	98	110	70	83.3333	15	1	0		68	98	110	72	84.6667	15	1	0		68	98	110	72	84.6667	15	1	0		68	98	110	72	84.6667	15	1	0		68	98	110	72	84.6667	15	1	0	
66	99	100	68	78.6667	14	2	0		68	99	104	68	80	14	1	1		68	99	104	68	80	14	1	1		68	99	104	68	80	14	1	1		68	99	104	68	80	14	1	1	
66	99	100	68	78.6667	16	2	0		70	99	104	70	81.3333	14	1	0		70	99	104	70	81.3333	14	1	0		70	99	104	70	81.3333	14	1	0		70	99	104	70	81.3333	14	1	0	
66	98	110	70	83.3333	15	1	0		68	98	110	72	84.6667	15	1	0		68	98	110	72	84.6667	15	1	0		68	98	110	72	84.6667	15	1	0		68	98	110	72	84.6667	15	1	0	
64	99	100	64	76	12	2	0		68	99	100	68	78.6667	12	1	0		68	99	100	68	78.6667	12	1	0		68	99	100	68	78.6667	12	1	0		68	99	100	68	78.6667	12	1	0	
62	99	100	60	73.3333	14	1	0		66	99	104	66	78.6667	15	1	1		66	99	104	66	78.6667	15	1	1		66	99	104	66	78.6667	15	1	1		66	99	104	66	78.6667	15	1	1	
64	99	100	64	76	12	2	0		68	99	100	68	78.6667	12	1	0		68	99	100	68	78.6667	12	1	0		68	99	100	68	78.6667	12	1	0		68	99	100	68	78.6667	12	1	0	
66	99	104	66	78.6667	14	2	2		70	99	104	68	80	14	1	3		70	99	104	68	80	14	1	1		70	99	104	68	80	14	1	1		70	99	104	68	80	14	1	1	
68	100	100	66	77.3333	12	2	0		72	100	104	70	81.3333	12	1	0		72	100	104	70	81.3333	12	1	0		72	100	104	70	81.3333	12	1	0		72	100	104	70	81.3333	12	1	0	
70	100	104	68	80	14	1	2		70	100	110	72	84.6667	14	1	2		70	100	110	72	84.6667	14	1	2		70	100	110	72	84.6667	14	1	2		70	100	110	72	84.6667	14	1	2	
58	98	90	60	70	12	3	0		56	99	90	58	68.6667	12	2	1		56	99	90	58	68.6667	12	2	1		56	99	90	58	68.6667	12	2	1		56	99	90	58	68.6667	12	2	1	
74	99	100	64	76	12	2	1		70	100	100	64	76	12	1	1		70	100	100	64	76	12	1	1		70	100	100	64	76	12	1	1		70	100	100	64	76	12	1	1	
62	99	100	60	73.3333	14	1	0		66	99	104	66	78.6667	15	1	1		66	99	104	66	78.6667	15	1	1		66	99	104	66	78.6667	15	1	1		66	99	104	66	78.6667	15	1	1	
80	99	130	80	96.6667	14	3	2		80	99	126	80	95.3333	14	3	2		80	99	126	80	95.3333	14	3	2		80	99	126	80	95.3333	14	3	2		80	99	126	80	95.3333	14	3	2	
64	99	100	60	73.3333	14	2	2		66	99	102	78	86	14	2	2		66	99	102	78	86	14	2	2		66	99	102	78	86	14	2	2		66	99	102	78	86	14	2	2	
66	100	104	68	80	12	2	0		72	100	108	70	82.6667	12	1	1		72	100	108	70	82.6667	12	1	1		72	100	108	70	82.6667	12	1	1		72	100	108	70	82.6667	12	1	1	
68	100	100	66	77.3333	12	2	3		72	100	104	70	81.3333	12	1	4	Inj. Diclofenac	72	100	104	70	81.3333	12	1	3		72	100	104	70	81.3333	12	1	2		72	100	104	70	81.3333	12	1	1	
70	99	100	64	76	14	2	2		70	99	104	64	77.3333	14	2	1		70	99	104	64	77.3333	14	2	1		70	99	104	64	77.3333	14	2	1		70	99	104	64	77.3333	14	2	1	
68	99	96	66	76	12	2	0		72	100	100	68	78.6667	12	1	1		72	100	100	68	78.6667	12	1	1		72	100	100	68	78.6667	12	1	1		72	100	100	68	78.6667	12	1	1	
66	99	100	68	78.6667	16	2	0		70	99	104	70	81.3333	14	1	0		70	99	104	70	81.3333	14	1	0		70	99	104	70	81.3333	14	1	0		70	99	104	70	81.3333	14	1	0	
66	99	100	70	80	14	2	0		70	100	108	70	82.6667	14	1	0		70	100	108	70	82.6667	14	1	0		70	100	108	70	82.6667	14	1	0		70	100	108	70	82.6667	14	1	0	
68	100	104	70	81.3333	14	1	0		72	99	108	70	82.6667	14	1	0		72	99	108	70	82.6667	14	1	0		72	99	108	70	82.6667	14	1	0		72	99	108	70	82.6667	14	1	0	
64	99	110	70	83.3333	12	2	2		70	99	118	74	88.6667	12	1	1		70	99	118	74	88.6667	12	1	1		70	99	118	74	88.6667	12	1	1		70	99	118	74	88.6667	12	1	1	
66	99	104	66	78.6667	12	2	0		68	99	108	66	80	12	2	0		68	99	108	66	80	12	2	0		68	99	108	66	80	12	2	0		68	99	108	66	80	12	2	0	
62	99	100	60	73.3333	14	2	1		68	99	100	64	76	14	1	1		68	99	100	64	76	14	1	1		68	99	100	64	76	14	1	1		68	99	100	64	76	14	1	1	
66	99	100	68	78.6667	16	2	0		70	99	104	70	81.3333	14	1	0		70	99	104	70	81.3333	14	1	0		70	99	104	70	81.3333	14	1	0		70	99	104	70	81.3333	14	1	0	
64	99	90	60	70	14	3	0		66	99	90	60	70	14	2	0		66	99	90	60	70	14	2	0		66	99	90	60	70	14	2	0		66	99	90	60	70	14	2	0	
60	99	108	70	82.6667	14	2	0		64	100	110	70	83.3333	14	1	0		64	100	110	70	83.3333	14	1	0		64	100	110	70	83.3333	14	1	0		64	100	110	70	83.3333	14	1	0	
62	99	104	72	82.6667	14	2	2		64	99	104	74	84	14	1	2		64	99	104	74	84	14	1	2		64	99	104	74	84	14	1	2		64	99	104	74	84	14	1	2	
64	99	110	70	83.3333	12	2	2		70	99	118	74	88.6667	12	1	1		70	99	118	74	88.6667	12	1	1		70	99	118	74	88.6667	12	1	1		70	99	118	74	88.6667	12	1	1	
66	99	90	60	70	14	2	0		70	99	96	64	74.6667	14	1	0		70	99	96	64	74.6667	14	1	0		70	99	96	64	74.6667	14	1	0		70	99	96	64	74.6667	14	1	0	
60	99	108	70	82.6667	14	2	0		64	100	110	70	83.3333	14	1	0		64	100	110	70	83.3333	14	1	0		64	100	110	70	83.3333	14	1	0		64	100	110	70	83.3333	14	1	0	
66	99	100	68	78.6667	12	2	2		70	99	108	74	85.3333	12	2	2		70	99	108	74	85.3333	12	2	2		70	99	108	74	85.3333	12	2	2		70	99	108	74	85.3333	12	2	2	
66	99	98	60	72.6667	14	3	0		66	99	98	64	75.3333	14	2	1		66	99	98	64	75.3333	14	2	1		66	99	98	64	75.3333	14	2	1		66	99	98	64	75.3333	14	2	1	
58	98	90	60	70	12	3	0		56	99	90	58	68.6667	12	2	1		56	99	90	58	68.6667	12	2	1		56	99	90	58	68.6667	12	2	1		56	99	90	58	68.6667	12	2	1	
66	99	100	68	78.6667	12	2	2		70	99	108	74	85.3333	12	2	2		70	99	108	74	85.3333	12	2	2		70	99	108	74	85.3333	12	2	2		70	99	108	74	85.3333	12	2	2	
68	100	100	66	77.3333	12	2	3		72	100	104	70	81.3333	12	1	4	Inj. Diclofenac	72	100	104	70	81.3333	12	1	3		72	100	104	70	81.3333	12	1	2		72	100	104	70	81.3333	12	1	1	
62	99	100	60	73.3333	14	2	1		68	99	100	64	76	14	1	1		68	99	100	64	76	14	1	1		68	99	100	64	76	14	1	1		68	99	100	64	76	14	1	1	
80	99	130	80	96.6667	14	3	2		80	99	126	80	95.3333	14	3	2		80	99	126	80	95.3333	14	3	2		80	99	126	80	95.3333	14	3	2		80	99	126	80	95.3333	14	3	2	
74	99	130	84	99.3333	12	2	1		70	99	128	82	97.3333	12	1	0		70	99	128	82	97.3333	12	1	0		70	99	128	82	97.3333	12	1	0		70	99	128	82	97.3333	12	1	0	
70	100	104	68	80	14	1	2		70	100	110	72	84.6667	14	1	2		70	100	110	72	84.6667	14	1	2		70	100	110	72	84.6667	14	1	2		70	100	110	72	84.6667	14	1	2	
74	99	100	64	76	12	2	1		70	100	100	64	76	12	1	1		70	100	100	64	76	12	1	1		70	100	100	64	76	12	1	1		70	100	100	64	76	12	1	1	

MASTER CHART - DEXMEDETOMIDINE

75 MIN									90 MIN								105 MIN								120 MIN								Requirement of additional analgesic	Time of additional analgesic(min)	Requirement of additional sedation	Time of Additional sedation (min)	Side effects						Surgeon satisfaction score (1-5)
HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional medication					Bradycardia	Hypotension	Hypertension	Desaturation	PONV	Dryness of mouth	
70	99	104	70	81.3333	12	1	0		70	99	104	70	81.3333	12	1	0		70	99	104	70	81.3333	12	1	0		70	99	104	70	81.3333	12	1	0		N		N		N	N	N		N	N	5
74	99	108	68	81.3333	14	1	0		74	99	108	68	81.3333	14	1	0		74	99	108	68	81.3333	14	1	0		74	99	108	68	81.3333	14	1	0		N		Y	15 MIN	N	N	N		N	N	3
72	99	100	70	80	12	1	0		72	99	100	70	80	12	1	0		72	99	100	70	80	12	1	0		72	99	100	70	80	12	1	0		N		N		N	N	N		N	N	5
72	100	104	70	81.3333	12	1	0		72	100	104	70	81.3333	12	1	0		72	100	104	70	81.3333	12	1	0		72	100	104	70	81.3333	12	1	0		N		N		N	N	N		N	N	4
72	99	118	76	90	15	1	0		72	99	118	76	90	15	1	0		72	99	118	76	90	15	1	0		72	99	118	76	90	15	1	0		N		N		N	N	N		N	N	4
70	99	108	70	82.6667	14	1	0		70	99	108	70	82.6667	14	1	0		70	99	108	70	82.6667	14	1	0		70	99	108	70	82.6667	14	1	0		N		N		N	N	N		N	N	5
72	99	118	76	90	15	1	0		72	99	118	76	90	15	1	0		72	99	118	76	90	15	1	0		72	99	118	76	90	15	1	0		N		N		N	N	N		N	N	4
70	99	104	68	80	14	1	0		70	99	104	68	80	14	1	0		70	99	104	68	80	14	1	0		70	99	104	68	80	14	1	0		Y	30 MINS	N		N	N	N		N	N	4
70	99	108	70	82.6667	14	1	0		70	99	108	70	82.6667	14	1	0		70	99	108	70	82.6667	14	1	0		70	99	108	70	82.6667	14	1	0		N		N		N	N	N		N	N	5
72	99	118	76	90	15	1	0		72	99	118	76	90	15	1	0		72	99	118	76	90	15	1	0		72	99	118	76	90	15	1	0		N		N		N	N	N		N	N	4
70	99	104	70	81.3333	12	1	0		70	99	104	70	81.3333	12	1	0		70	99	104	70	81.3333	12	1	0		70	99	104	70	81.3333	12	1	0		N		N		N	N	N		N	N	5
70	100	110	70	83.3333	14	1	0		70	100	110	70	83.3333	14	1	0		70	100	110	70	83.3333	14	1	0		70	100	110	70	83.3333	14	1	0		N		N		N	N	N		N	N	5
70	99	104	70	81.3333	12	1	0		70	99	104	70	81.3333	12	1	0		70	99	104	70	81.3333	12	1	0		70	99	104	70	81.3333	12	1	0		N		N		N	N	N		N	N	5
74	99	110	72	84.6667	14	1	1		74	99	110	72	84.6667	14	1	1		74	99	110	72	84.6667	14	1	1		74	99	110	72	84.6667	14	1	1		N		N		N	N	N		N	N	4
72	100	104	70	81.3333	12	1	0		72	100	104	70	81.3333	12	1	0		72	100	104	70	81.3333	12	1	0		72	100	104	70	81.3333	12	1	0		N		N		N	N	N		N	N	4
74	100	120	78	92	14	1	0		74	100	120	78	92	14	1	0		74	100	120	78	92	14	1	0		74	100	120	78	92	14	1	0		N		N		N	N	N		N	N	4
58	99	90	60	70	12	1	0		58	99	90	60	70	12	1	0		58	99	90	60	70	12	1	0		58	99	90	60	70	12	1	0		N		N		N	Y	N		N	N	5
70	100	108	70	82.6667	12	1	1		70	100	108	70	82.6667	12	1	1		70	100	108	70	82.6667	12	1	1		70	100	108	70	82.6667	12	1	1		N		N		Y	N	N		N	N	5
70	100	110	70	83.3333	14	1	0		70	100	110	70	83.3333	14	1	0		70	100	110	70	83.3333	14	1	0		70	100	110	70	83.3333	14	1	0		N		N		N	N	N		N	N	5
82	99	128	80	96	14	2	0		82	99	128	80	96	14	2	0		82	99	128	80	96	14	2	0		82	99	128	80	96	14	2	0		N		N		N	N	N		N	N	5
64	99	102	78	86	14	1	2		64	99	102	78	86	14	1	2		64	99	102	78	86	14	1	2		64	99	102	78	86	14	1	2		N		N		N	N	N		N	N	5
72	99	110	70	83.3333	12	1	1		72	99	110	70	83.3333	12	1	1		72	99	110	70	83.3333	12	1	1		72	99	110	70	83.3333	12	1	1		N		N		N	N	N		N	N	5
72	100	104	70	81.3333	12	1	1		72	100	104	70	81.3333	12	1	1		72	100	104	70	81.3333	12	1	1		72	100	104	70	81.3333	12	1	1		Y	Postoperatively at 15 MINS	N		N	N	N		N	N	4
74	99	108	68	81.3333	14	1	0		74	99	108	68	81.3333	14	1	0		74	99	108	68	81.3333	14	1	0		74	99	108	68	81.3333	14	1	0		Y	45 MINS	Y	15 MIN	N	N	N		N	N	3
72	99	100	70	80	12	1	0		72	99	100	70	80	12	1	0		72	99	100	70	80	12	1	0		72	99	100	70	80	12	1	0		N		N		N	N	N		N	N	5
70	99	108	70	82.6667	14	1	0		70	99	108	70	82.6667	14	1	0		70	99	108	70	82.6667	14	1	0		70	99	108	70	82.6667	14	1	0		N		N		N	N	N		N	N	5
74	99	114	78	90	14	1	0		74	99	114	78	90	14	1	0		74	99	114	78	90	14	1	0		74	99	114	78	90	14	1	0		N		N		N	N	N		N	N	5
72	99	110	70	83.3333	14	1	0		72	99	110	70	83.3333	14	1	0		72	99	110	70	83.3333	14	1	0		72	99	110	70	83.3333	14	1	0		N		N		N	N	N		N	N	5
70	99	118	74	88.6667	12	1	1		70	99	118	74	88.6667	12	1	1		70	99	118	74	88.6667	12	1	1		70	99	118	74	88.6667	12	1	1		N		N		N	N	N		N	N	4
70	99	110	70	83.3333	12	1	0		70	99	110	70	83.3333	12	1	0		70	99	110	70	83.3333	12	1	0		70	99	110	70	83.3333	12	1	0		N		N		N	N	N		N	N	5
72	99	106	70	82	14	1	1		72	99	106	70	82	14	1	1		72	99	106	70	82	14	1	1		72	99	106	70	82	14	1	1		N		N		N	N	N		N	N	5
70	99	108	70	82.6667	14	1	0		70	99	108	70	82.6667	14	1	0		70	99	108	70	82.6667	14	1	0		70	99	108	70	82.6667	14	1	0		N		N		N	N	N		N	N	5
64	99	98	60	72.6667	14	1	0		64	99	98	60	72.6667	14	1	0		64	99	98	60	72.6667	14	1	0		64	99	98	60	72.6667	14	1	0		N		N		N	N	N		N	N	5
68	100	116	70	85.3333	14	1	0		68	100	116	70	85.3333	14	1	0		68	100	116	70	85.3333	14	1	0		68	100	116	70	85.3333	14	1	0		N		N		N	N	N		N	N	5
64	99	104	74	84	14	2	2		64	99	104	74	84	14	2	2		64	99	104	74	84	14	2	2		64	99	104	74	84	14	2	2		N		N		N	N	N		N	N	4
70	99	118	74	88.6667	12	1	1		70	99	118	74	88.6667	12	1	1		70	99	118	74	88.6667	12	1	1		70	99	118	74	88.6667	12	1	1		N		N		N	N	N		N	N	4
72	99	100	68	78.6667	14	1	0		72	99	100	68	78.6667	14	1	0		72	99	100	68	78.6667	14	1	0		72	99	100	68	78.6667	14	1	0		N		N		N	N	N		N	N	5
68	100	116	70	85.3333	14	1	0		68	100	116	70	85.3333	14	1	0		68	100	116	70	85.3333	14	1	0		68	100	116	70	85.3333	14	1	0		N		N		N	N	N		N	N	5
74	100	110	78	88.6667	12	1	2		74	100	110	78	88.6667	12	1	2		74	100	110	78	88.6667	12	1	2		74	100	110	78	88.6667	12	1	2		N		N		N	N	N		N	N	5
66	99	98	64	75.3333	14	1	0		66	99	98	64	75.3333	14	1	0		66	99	98	64	75.3333	14	1	0		66	99	98	64	75.3333	14	1	0		N		N		N	N	N		N	N	5
58	99	90	60	70	12	1	0		58	99	90	60	70	12	1	0		58	99	90	60	70	12	1	0		58	99	90	60	70	12	1	0		N		N		N	Y	N		N	N	5
74	100	110	78	88.6667	12	1	2		74	100	110	78	88.6667	12	1	2		74	100	110	78	88.6667	12	1	2		74	100	110	78	88.6667	12	1	2		N		N		N	N	N		N	N	5
72	100	104	70	81.3333	12	1	1		72	100	104	70	81.3333	12	1	1		72	100	104	70	81.3333	12	1	1		72	100	104	70	81.3333	12	1	1		Y	Postoperatively at 15 MINS	N		N	N	N		N	N	4
72	99	106	70	82	14	1	1		72	99	106	70	82	14	1	1		72	99	106	70	82	14	1	1		72	99	106	70	82	14	1	1		N		N		N	N	N		N	N	5
82	99	128	80	96	14	2	0		82	99	128	80	96	14	2	0		82	99	128	80	96	14	2	0		82	99	128	80	96	14	2	0		N		N		N	N	N		N	N	5
68	99	128	90	102.667	12	1	1		68	99	128	90	102.667	12	1	1		68	99	128	90	102.667	12	1	1		68	99	128	90	102.667	12	1	1		Y	60 MIN	N		N	N	N		N	N	4
74	100	120	78	92	14	1	0		74	100	120	78	92	14	1	0		74	100	120	78	92	14	1	0		74	100	120	78	92	14	1	0		N		N		N	N	N		N	N	4
70	100	108	70	82.6667	12	1	1		70	100	108	70	82.6667	12	1	1		70	100	108	70	82.6667	12	1	1		70	100	108	70	82.6667	12	1	1		N		N		Y	N	N		N	N	5

MASTER CHART - MIDAZOLAM

Sr No	Group	Age (Years)	Sex	Wt(Kg)	ASA Grade	Diagnosis	Surgery	Duration of Surgery (mins)	At start of infusion (0 min)						5 MIN									10 MIN									15 MIN									30MIN								
									HR	SpO2	SBP	DBP	MAP	RR	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication
1	M	35	M	55	I	Rt.CSOM	Rt.Tympanoplasty	75	78	99	120	80	93.3333	12	78	99	120	80	93.3333	12	1	0		74	99	118	70	86	12	3	2		72	99	118	78	91.3333	12	2	4	Inj.Fentanyl	74	99	118	78	91.3333	12	2	1	
2	M	45	F	60	II	Rt.CSOM	Rt.Tympanoplasty	105	70	98	117	79	91.6667	14	71	99	129	80	96.3333	14	2	0		73	99	102	72	82	14	3	0		70	100	103	66	78.3333	14	3	2		70	100	109	63	78.3333	14	3	2	
3	M	18	M	56	I	Lt.CSOM	Lt.Tympanoplasty	75	68	98	116	74	88	16	70	99	116	75	88.6667	13	2	0		69	99	110	70	83.3333	13	3	3		67	98	112	71	84.6667	12	2	2	Inj.Propofol	65	99	115	63	80.3333	14	3	4	Inj.Fentanyl
4	M	21	F	50	I	Lt.CSOM	Lt.Tympanoplasty	75	78	99	118	78	91.3333	16	74	99	116	75	88.6667	12	1	0		77	100	116	75	88.6667	12	3	0		74	99	113	78	89.6667	12	3	2		76	98	116	82	93.3333	12	3	2	
5	M	18	F	45	I	Rt.CSOM	Rt.Tympanoplasty	75	88	99	116	76	89.3333	14	85	99	118	76	90	16	1	0		85	99	118	76	90	16	2	3		88	99	118	76	90	16	2	3		90	99	116	74	88	16	2	3	
6	M	38	F	50	I	Lt.CSOM	Lt.Tympanoplasty	90	80	99	144	86	105.333	16	75	99	140	82	101.333	16	1	0		102	98	138	80	99.3333	14	3	0		106	99	134	82	99.3333	14	3	3		104	99	134	82	99.3333	16	2	2	
7	M	38	F	60	I	Rt.CSOM	Rt.Tympanoplasty	90	80	99	144	86	105.333	16	75	99	140	82	101.333	16	1	0		102	98	138	80	99.3333	14	3	0		106	99	134	82	99.3333	14	3	3		104	99	134	82	99.3333	16	2	2	
8	M	19	F	47	I	Lt.otosclerosis	Lt.Stapedectomy	75	88	99	116	76	89.3333	14	85	99	118	76	90	16	1	0		85	99	118	76	90	16	2	3		88	99	118	76	90	16	2	3		90	99	116	74	88	16	2	3	
9	M	24	M	55	I	Rt.CSOM	Rt.Tympanoplasty	90	88	99	122	80	94	14	84	99	122	80	94	12	1	0		84	100	124	80	94.6667	12	3	0		86	99	116	74	88	14	3	1		82	99	114	74	87.3333	12	3	2	
10	M	25	F	50	I	Lt.Otosclerosis	Lt. Stapedectomy	75	72	99	120	80	93.3333	16	89	100	134	60	84.6667	15	2	0		96	100	130	54	79.3333	12	3	0		88	99	120	60	80	14	3	2		84	100	110	60	76.6667	12	3	2	
11	M	42	F	52	II	Lt.CSOM	Lt.Tympanoplasty	90	74	99	138	88	104.667	14	76	99	130	80	96.6667	13	2	0		74	99	125	78	93.6667	14	3	0		73	99	126	74	91.3333	16	3	2		75	99	115	69	84.3333	16	3	2	
12	M	38	F	50	I	Rt.CSOM	Rt.Tympanoplasty	75	99	99	120	84	96	14	96	98	117	90	99	19	1	0		98	98	110	82	91.3333	14	3	0		89	99	112	70	84	14	3	2		92	99	116	70	85.3333	14	3	2	
13	M	25	F	50	I	Rt.CSOM	Rt.Tympanoplasty	60	92	100	118	81	93.3333	14	108	100	119	74	89	14	2	0		96	100	119	70	86.3333	12	3	0		85	100	109	68	81.6667	12	3	2		87	100	109	68	81.6667	10	3	2	
14	M	56	M	68	II	Lt.CSOM	Lt.Tympanoplasty	120	82	99	142	88	106	15	80	99	140	84	102.667	12	1	0		80	99	134	81	98.6667	13	2	0		78	99	130	80	96.6667	13	3	1		77	99	130	82	98	13	3	2	
15	M	24	M	58	I	Rt.CSOM	Rt.Tympanoplasty	75	72	99	120	80	93.3333	16	89	100	134	60	84.6667	15	2	0		96	100	130	54	79.3333	12	3	0		88	99	120	60	80	14	3	2		84	100	110	60	76.6667	12	3	2	
16	M	50	M	60	I	Lt.CSOM	Lt.Tympanoplasty	75	120	100	130	80	96.6667	15	124	100	130	80	96.6667	15	1	0		110	100	132	82	98.6667	14	3	0		104	99	124	78	93.3333	14	3	1		100	98	128	78	94.6667	13	3	2	
17	M	34	M	62	I	Lt.CSOM	Lt.Tympanoplasty	75	80	99	124	82	96	14	80	99	120	80	93.3333	14	1	0		80	100	116	78	90.6667	14	3	0		78	99	118	74	88.6667	14	3	3		72	99	110	78	88.6667	14	3	1	
18	M	22	M	65	I	Rt.CSOM	Rt.TympaNplasty	90	88	99	122	80	94	14	84	99	122	80	94	12	1	0		84	100	124	80	94.6667	12	2	0	Inj. Propofol	86	99	116	74	88	14	3	1		82	99	114	74	87.3333	12	3	2	
19	M	56	M	72	I	Lt.CSOM	Lt.Tympanoplasty	75	84	99	130	80	96.667	16	85	99	131	82	98.3333	13	2	0		80	99	130	74	92.6667	16	3	0		78	99	128	78	94.6667	13	3	2		77	99	126	74	91.3333	13	3	2	
20	M	33	M	62	I	Lt.CSOM	Lt.Tympanoplasty	90	75	100	93	63	73	12	70	100	97	52	67	12	2	0		79	100	108	60	76	12	3	0		81	99	100	52	68	12	3	2		80	100	100	52	68	12	3	2	
21	M	45	M	65	I	Lt.CSOM	Lt.Tympanoplasty	75	72	99	120	80	93.3333	16	89	100	134	60	84.6667	15	2	0		96	100	130	54	79.3333	12	3	0		88	99	120	60	80	14	3	2		84	100	110	60	76.6667	12	3	2	
22	M	45	M	65	I	Lt.otosclerosis	Lt. Stapedectomy	75	80	99	124	82	96	14	80	99	120	80	93.3333	14	1	0		80	100	116	78	90.6667	14	3	0		78	99	118	74	88.6667	14	3	3		72	99	110	78	88.6667	14	3	1	
23	M	46	F	47	II	Lt. Otosclerosis	Lt.Stapedectomy	120	78	98	132	92	105.333	14	73	98	139	84	102.333	14	1	0		70	99	130	80	96.6667	14	3	0		71	97	130	80	96.6667	14	3	2		70	98	124	78	93.3333	14	3	2	
24	M	36	M	64	I	Rt.CSOM	Rt.TympaNplasty	105	98	100	120	84	96	14	95	100	116	90	98.6667	21	2	0		88	99	118	82	94	14	3	0		94	99	120	84	96	14	3	3		94	99	117	66	83	18	3	2	
25	M	50	F	55	I	Rt.CSOM	Rt.Tympanoplasty	75	84	99	130	80	96.667	16	85	99	131	82	98.3333	13	2	0		80	99	130	74	92.6667	16	3	0		78	99	128	78	94.6667	13	3	2		77	99	126	74	91.3333	13	3	2	
26	M	31	M	61	I	Rt.CSOM	Rt.Tympanoplasty	75	80	99	124	82	96	14	80	99	120	80	93.3333	14	1	0		80	100	116	78	90.6667	14	3	0		78	99	118	74	88.6667	14	3	3		72	99	110	78	88.6667	14	3	1	
27	M	50	M	65	I	Rt.CSOM	Lt.Tympanoplasty	90	86	100	120	84	96	14	88	100	120	84	96	14	2	0		82	100	120	88	98.6667	15	3	0		80	99	118	80	92.6667	14	3	2		76	99	118	82	94	12	3	2	
28	M	30	M	58	I	Rt.CSOM	Rt.Tympanoplasty	75	74	99	126	82	96.6667	15	78	99	120	75	90	12	1	0		74	98	118	70	86	12	3	0		77	99	116	75	88.6667	13	2	2	Inj. Propofol	74	99	115	72	86.3333	12	3	2	
29	M	42	M	65	I	Rt.CSOM	Rt.Tympanoplasty	90	80	99	144	86	105.333	16	75	99	140	82	101.333	16	1	0		102	98	138	80	99.3333	14	3	0		106	99	134	82	99.3333	14	3	3		104	99	134	82	99.3333	16	2	2	
30	M	46	M	58	II	Rt.Otosclerosis	Rt. Stapedectomy	120	82	99	142	88	106	15	80	99	140	84	102.667	12	1	0		80	99	134	81	98.6667	13	2	0		78	99	130	80	96.6667	13	3	1		77	99	130	82	98	13	3	2	
31	M	33	F	50	I	Lt.CSOM	Lt.Tympanoplasty	90	70	100	110	70	83.3333	16	72	100	108	72	84	16	2	0		72	99	106	70	82	14	3	0		74	100	100	74	82.6667	16	2	2		73	98	102	74	83.3333	14	2	2	
32	M	55	M	65	II	Lt.CSOM	Lt.Tympanoplasty	90	78	99	130	80	96.6667	14	74	99	130	80	96.6667	14	1	0		78	100	128	78	94.6667	14	3	0		80	99	124	74	90.6667	14	3	2		80	99	120	74	89.3333	12	3	2	
33	M	20	M	50	I	Lt.CSOM	Lt.Tympanoplasty	75	78	99	118	78	91.3333	16	74	99	116	75	88.6667	12	1	0		77	100	116	75	88.6667	12	3	0		74	99	113	78	89.6667	12	2	2	Inj. Propofol	76	98	116	82	93.3333	12	3	2	
34	M	48	M	50	II	Rt.CSOM	Rt.Tympanoplasty	105	70	98	117	79	91.6667	14	71	99	129	80	96.3333	14	2	0		73	99	102	72	82	14	3	0		70	100	103	66	78.3333	14	3	2		70	100	109	63	78.3333	14	3	2	
35	M	18	M	48	I	Rt.CSOM	Rt.Tympanoplasty	75	78	99	118	78	91.3333	16	74	99	116	75	88.6667	12	1	0		77	100	116	75	88.6667	12	3	0		74	99	113	78	89.6667	12	3	2		76	98	116	82	93.3333	12	3	2	
36	M	39	F	50	I	Rt.CSOM	Rt.Tympanoplasty	75	99	99	120	84	96	14	96	98	117	90	99	19	1	0		98	98	110	82	91.3333	14	3	0		89	99	112	70	84	14	3	2		92	99	116	70	85.3333	14	3	2	
37	M	21	F	55	I	Rt.CSOM	Rt.Tympanoplasty	90	88	99	122	80	94	14	84	99	122	80	94	12	1	0		84	100	124	80	94.6667	12	3	0		86	99	116	74	88	14	3	1		82	99	114	74	87.3333	12	3	2	
38	M	18	F	45	I	Lt.CSOM	Lt.Tympanoplasty	75	88	99	116	76	89.3333	14	85	99	118	76	90	16	1	0		85	99	118	76	90	16	2	3		88	99	118	76	90	16	2	3		90	99	116	74	88	16	2	4	Inj. Fentanyl
39	M	18	F	45	I	Lt.CSOM	Lt.Tympanoplasty	105	89	98	122	75	90.6667	16	88	99	116	74	88	13	2	0		82	99	112	71	84.6667	13	3	0		80	99	114	76	88.6667	12	3	2		80	99	112	71	84.6667	11	3	2	
40	M	40	M	70	I	Lt.CSOM	Lt.Tympanoplasty	105	72	99	110	80	90	20	70	99	110	80	90	18	2	0		82	100	120	86	97.3333	16	3	0		80	99	124	86	98.6667	16	2	2		73	98	120	80	93.3333	18	2	2	
41	M	35	M	70	I	Lt.CSOM	Lt.Tympanoplasty	105	72	99	110	80	90	20	70	99	110	80	90	18	2	0		82	100	120	86	97.3333	16	3	0		80	99	124	86	98.6667	16	2	2		73	98	120	80	93.3333	18	2	2	
42	M	27	F	51	I	Rt.CSOM	Rt.Tympanoplasty	120	78	99	120	80	93.3333	16	77	99	120	80	93.3333	13	2	0		74	99	116	80	92	14	2	0	Inj. Propofol	78	98	116	80	92	12	2	2		78	99	120	78	92	13	3	2	
43	M	26	M	54	I	Rt.CSOM	Rt.Tympanoplasty	105	78	99	120	84	96	16	78	99	120	82	94.6667	12	1	0		74	100	118	80	92.6667	12	3	0		74	99	114	80	91.3333	12	3	1		74	99	116	80	92	12	2	1	
44	M	45	M	72	I	Lt.CSOM	Lt.Tympanoplasty	75	84	99	130	80	96.667	16	85	99	131	82	98.3333	13	2	0		80	99	130	74	92.6667	16	3	0		78	99	128	78	94.6667	13	3	2		77	99	126	74	91.3333	13	3	2	
45	M	45	M	69	II	Lt.CSOM	Lt.Tympanoplasty	90	74	99	138	88	104.667	14	76	99	130	80	96.6667	13	2	0		74	99	125	78	93.6667	14	3	0		73	99	126	74	91.3333	16	3	2		75	99	115	69	84.3333	16	3	2	
46	M	18	M	53	I	Lt.CSOM	Lt.Tympanoplasty	105	68	99	124	74	90.6667	14	70	99	120	75	90	12	1	0		69	99	118	71	86.6667	12	3	0		66	98	114	72	86	12	3	2		70	99	118	70	86	12	3	2	
47	M	58	M	68	II	Rt.CSOM	Rt.Tympanoplasty	90	78	99	130	80	96.6667	14	74	99	130	80	96.6667	14	1	0		78	100	128	78	94.6667	14	3	0		80	99	124	74	90.6667	14	3	2		80	99	120	74	89.3333	12	3	2	
48	M	45	F	65	II	Lt.CSOM	Lt.Tympanoplasty	105	70	98	117	79	91.6667	14	71	99	129	80	96.3333	14	2	0		73	99	102	72	82	14	3	0		70	100	103	66	78.3333	14	3	2		70	100	109	63	78.3333	14	3	2	

MASTER CHART - MIDAZOLAM

45 MIN									60 MIN									75 MIN									90 MIN									105 MIN									120 MIN								
HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional medication
74	99	114	76	88.6667	12	3	1		74	99	116	74	88	12	3	1		72	99	120	82	94.67	12	3	2																															
68	100	114	71	85.3333	14	3	2		70	100	119	68	85	14	3	2		75	98	108	67	80.6667	14	3	2		75	100	105	66	79	14	3	2		74	99	105	60	73.67	12	3	2											
65	99	114	63	80	13	3	2		68	99	112	69	83.3333	12	3	2		70	100	114	72	86	13	3	2		68	99	114	72	86	12	3	3																			
75	98	116	75	88.6667	15	3	2		72	98	116	74	88	12	3	2		70	99	116	74	88	12	3	3																															
88	99	116	74	88	16	3	2		88	99	115	75	88.3333	13	3	2		84	99	112	75	87.3333	13	3	2		80	99	112	75	87.33	12	3	2																			
110	98	134	82	99.3333	14	3	2		108	99	132	80	97.3333	16	3	2		110	99	130	80	96.6667	14	2	2		104	99	126	80	95.33	12	2	2																			
110	98	134	82	99.3333	14	3	2		108	99	132	80	97.3333	16	3	2		110	99	130	80	96.6667	14	2	2		104	99	126	80	95.33	12	2	2																			
88	99	116	74	88	16	3	2		88	99	115	75	88.3333	13	3	2		84	99	112	75	87.3333	13	3	2		80	99	112	75	87.33	12	3	2																			
80	99	118	80	92.6667	13	2	4	Inj. Fentanyl	80	99	120	82	94.6667	12	3	2		80	99	118	78	91.3333	13	3	2		76	99	118	78	91.33	12	3	2																			
77	99	110	70	83.3333	12	3	2		70	99	110	70	83.3333	12	2	2		72	99	110	70	83.33	12	2	3																															
76	99	116	72	86.6667	13	3	2		74	99	126	75	92	13	3	2		70	99	120	72	88	12	3	1																															
90	99	112	70	84	14	2	2		88	99	110	70	83.3333	14	2	2		86	99	110	70	83.33	12	2	3																															
85	100	110	70	83.3333	10	2	2		82	99	110	72	84.6667	12	2	2																																					
78	99	124	78	93.3333	12	3	2		80	99	123	82	95.6667	11	3	2		78	98	124	79	94	12	3	2		77	99	125	76	92.3333	12	3	2		78	99	124	75	91.33333333	12	3	2		74	99	122	78	92.67	12	3	3	
77	99	110	70	83.3333	12	3	2		70	99	110	70	83.3333	12	2	2		72	99	110	70	83.33	12	2	3																															
100	99	120	74	89.3333	13	3	2		94	99	120	70	86.6667	14	3	2		90	99	120	70	86.6667	14	3	3																															
70	99	110	74	86	12	3	2		70	99	110	74	86	14	3	2		68	99	110	74	86	14	3	3																															
80	99	118	80	92.6667	13	2	4	Inj. Fentanyl	80	99	120	82	94.6667	12	3	2		80	99	118	78	91.3333	13	3	2		76	99	118	78	91.33	12	3	2																			
78	99	122	73	89.3333	13	3	2		76	99	123	70	87.6667	12	3	2		79	100	122	70	87.3333	13	3	2		74	99	120	72	88	12	2	3																			
78	99	106	58	74	18	3	2		79	99	101	58	72.3333	12	3	2		79	98	101	60	73.6667	12	3	2		74	99	101	60	73.67	12	3	3																			
77	99	110	70	83.3333	12	3	2		70	99	110	70	83.3333	12	2	2		72	99	110	70	83.33	12	2	3																															
70	99	110	74	86	12	3	2		70	99	110	74	86	14	3	2		68	99	110	74	86	14	3	3																															
71	98	120	78	92	12	3	2		74	98	130	80	96.6667	14	3	4	Inj. Fentanyl	70	99	120	80	93.3333	14	3	2		70	99	120	70	86.6667	14	3	3		70	98	126	73	90.66666667	14	3	2		72	99	120	70	86.67	12	3	2	
88	99	114	70	84.6667	14	3	2		93	99	110	74	86	14	2	2		88	99	122	70	87.3333	14	2	2		89	99	117	66	83	14	2	2		84	99	117	66	83	12	2	2											
78	99	122	73	89.3333	13	3	2		76	99	123	70	87.6667	12	3	2		79	100	122	70	87.3333	13	3	2		74	99	120	72	88	12	2	3																			
70	99	110	74	86	12	3	2		70	99	110	74	86	14	3	2		68	99	110	74	86	14	3	3																															
74	99	118	70	86	12	3	2		74	99	114	70	84.6667	12	3	2		74	99	112	70	84	12	3	2		74	99	112	70	84	12	3	3																			
71	99	116	74	88	13	3	2		70	99	112	71	84.6667	12	3	2		66	99	110	70	83.3333	12	3	3																															
110	98	134	82	99.3333	14	3	2		108	99	132	80	97.3333	16	3	2		110	99	130	80	96.6667	14	2	2		104	99	126	80	95.33	12	2	2																			
78	99	124	78	93.3333	12	3	2		80	99	123	82	95.6667	11	3	2		78	98	124	79	94	12	3	2		77	99	125	76	92.3333	12	3	2		78	99	124	75	91.33333333	12	3	2		74	99	122	78	92.67	12	3	3	
78	99	110	74	86	12	3	2		80	100	112	76	88	14	3	2		81	100	116	76	89.3333	12	2	2		80	99	114	74	86	11	3	2																			
80	99	124	78	93.3333	14	3	2		78	99	124	80	94.6667	14	3	2		80	99	126	80	95.3333	16	3	2		78	99	124	80	94.67	14	2	3																			
75	98	116	75	88.6667	15	3	2		72	98	116	74	88	12	3	2		70	99	116	74	88	12	3	3																															
68	100	114	71	85.3333	14	3	2		70	100	119	68	85	14	3	2		75	98	108	67	80.6667	14	3	2		75	100	105	66	79	14	3	2		74	99	105	60	73.67	12	3	2											
75	98	116	75	88.6667	15	3	2		72	98	116	74	88	12	3	2		70	99	116	74	88	12	3	3																															
90	99	112	70	84	14	2	2		88	99	110	70	83.3333	14	2	2		86	99	110	70	83.33	12	2	3																															
80	99	118	80	92.6667	13	2	3		80	99	120	82	94.6667	12	3	4	Inj. Fentanyl	80	99	118	78	91.3333	13	3	2		76	99	118	78	91.33	12	3	2																			
88	99	116	74	88	16	3	2		88	99	115	75	88.3333	13	3	2		84	99	112	75	87.3333	13	3	2		80	99	112	75	87.33	12	3	2																			
78	99	116	74	88	13	3	2		76	99	110	68	82	11	3	2		74	99	108	74	85.3333	12	3	2		76	99	108	71	83.3333	12	3	2		78	99	104	70	81.33	11	3	2											
67	98	114	80	91.3333	18	3	2		67	98	120	84	96	18	3	2		65	98	114	80	91.3333	18	2	2		72	99	110	82	91.3333	15	2	2		70	99	110	70	83.33	12	2	3											
67	98	114	80	91.3333	18	3	2		67	98	120	84	96	18	3	2		65	98	114	80	91.3333	18	2	2		72	99	110	82	91.3333	15	2	2		70	99	110	70	83.33	12	2	3											
77	99	121	78	92.3333	13	3	2		81	99	123	74	90.3333	11	3	2		80	99	120	74	89.3333	12	3	2		78	98	122	78	92.6667	12	3	2		75	99	124	80	94.66666667	12	3	2		72	99	126	80	95.33	12	3	3	
82	99	118	74	88.6667	12	3	2		80	99	121	74	89.6667	12	3	2		82	99	120	76	90.6667	12	3	2		82	99	120	78	92	12	3	2		80	99	118	78	91.33	12	3	2											
78	99	122	73	89.3333	13	3	2		76	99	123	70	87.6667	12	3	2		79	100	122	70	87.3333	13	3	2		74	99	120	72	88	12	2	3																			
76	99	116	72	86.6667	13	3	2		74	99	126	75	92	13	3	2		70	99	120	72	88	12	3	1																															
68	98	114	70	84.6667	12	3	2		66	99	115	69	84.3333	12	3	2		69	99	118	76	90	12	3	2		68	99	114	69	84	13	3	2		64	99	114	69	84	12	3	3											
80	99	124	78	93.3333	14	3	2		78	99	124	80	94.6667	14	3	2		80	99	126	80	95.3333	16	3	2		78	99	124	80	94.67	14	2	3																			
68	100	114	71	85.3333	14	3	2		70	100	119	68	85	14	3	2		75	98	108	67	80.6667	14	3	2		75	100	105	66	79	14	3	2		74	99	105	60	73.67	12	3	2											

MASTER CHART - MIDAZOLAM

In Recovery At Arrival									15 MIN								30 MIN								45 MIN								60 MIN							
HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication
74	99	114	74	87.3333	12	2	3		74	99	110	70	83.3333	12	1	2		74	99	110	70	83.3333	12	1	2		74	99	110	70	83.3333	12	1	2		74	99	110	70	83.3333	12	1	2	
68	100	103	63	76.3333	14	2	2		66	100	106	72	83.3333	14	1	2		72	100	110	72	84.6667	14	1	3		72	100	106	72	83.3333	14	1	4	Inj. Diclofenac	66	100	106	72	83.3333	16	1	2	
70	99	113	74	87	16	3	2		70	99	113	74	87	15	2	3		70	99	113	74	87	15	1	3		70	99	113	74	87	15	2	3		70	99	113	74	87	15	1	3	
75	99	116	75	88.6667	12	3	2		78	99	119	74	89	12	2	3		78	99	119	74	89	12	2	1		78	99	119	74	89	12	2	1		78	99	119	74	89	12	1	1	
78	99	114	74	87.3333	16	2	3		80	99	112	72	85.3333	14	2	2		75	99	112	72	85.3333	13	2	3		75	99	112	72	85.3333	13	1	3		75	99	112	72	85.3333	13	1	1	
102	99	130	80	96.6667	14	2	3		98	99	128	76	93.3333	16	2	4		98	99	128	76	93.3333	16	2	4		98	99	128	76	93.3333	16	2	4		98	99	128	76	93.3333	16	2	4	
102	99	130	80	96.6667	14	2	3		98	99	128	76	93.3333	16	2	4		98	99	128	76	93.3333	16	2	4		98	99	128	76	93.3333	16	2	4		98	99	128	76	93.3333	16	2	4	
78	99	114	74	87.3333	16	2	3		80	99	112	72	85.3333	14	2	2		75	99	112	72	85.3333	13	2	3		75	99	112	72	85.3333	13	1	3		75	99	112	72	85.3333	13	1	1	
80	99	117	76	89.6667	14	2	2		78	99	116	78	90.6667	13	2	3		80	99	120	78	92	13	1	3		81	98	120	76	90.6667	13	1	3		80	99	120	78	92	13	1	3	
68	99	116	72	86.6667	14	2	3		72	99	124	78	93.3333	14	2	3		72	99	124	78	93.3333	14	2	3		72	99	124	78	93.3333	14	2	3		72	99	124	78	93.3333	14	2	3	
72	99	124	70	88	13	3	2		74	99	126	72	90	13	3	2		74	99	126	72	90	13	3	2		74	99	126	72	90	13	2	2		74	99	126	72	90	13	1	2	
82	99	110	70	83.3333	16	2	2		86	98	118	72	87.3333	16	1	3		86	98	118	72	87.3333	16	1	3		86	98	118	72	87.3333	16	1	3		86	98	118	72	87.3333	16	1	3	
82	100	110	70	83.3333	14	2	2		80	100	110	70	83.3333	14	2	2		80	100	110	70	83.3333	14	2	2		80	100	110	70	83.3333	14	2	2		80	100	110	70	83.3333	14	2	2	
80	99	126	82	96.6667	13	3	2		84	98	126	76	92.6667	13	2	1		84	98	126	76	92.6667	13	2	2		84	98	126	76	92.6667	13	2	1		84	99	126	76	92.6667	13	2	1	
68	99	116	72	86.6667	14	2	3		72	99	124	78	93.3333	14	2	3		72	99	124	78	93.3333	14	2	3		72	99	124	78	93.3333	14	2	3		72	99	124	78	93.3333	14	2	3	
92	99	120	72	88	14	2	3		90	99	120	76	90.6667	14	2	3		90	99	120	76	90.6667	14	1	3		88	99	120	76	90.6667	14	1	3		92	99	122	76	91.3333	14	1	3	
70	99	110	74	86	12	2	2		74	99	110	74	86	14	2	3		74	99	112	74	86.6667	14	1	3		72	99	114	74	87.3333	14	1	3		74	99	114	74	87.3333	14	1	3	
80	99	117	76	89.6667	14	2	2		78	99	116	78	90.6667	13	2	3		80	99	120	78	92	13	1	4	Inj. Diclofenac	81	98	120	76	90.6667	13	1	3		80	99	120	78	92	13	1	3	
78	99	122	74	90	13	3	2		76	99	122	70	87.3333	13	2	3		76	99	122	70	87.3333	13	2	3		76	99	122	70	87.3333	13	2	3		76	99	122	70	87.3333	13	2	3	
74	98	101	54	69.6667	12	3	3		82	98	120	78	92	14	2	4	Inj Diclofenac	82	98	120	78	92	14	2	3		82	98	120	78	92	14	2	3		82	98	120	78	92	14	2	3	
68	99	116	72	86.6667	14	2	3		72	99	124	78	93.3333	14	2	3		72	99	124	78	93.3333	14	2	3		72	99	124	78	93.3333	14	2	3		72	99	124	78	93.3333	14	2	3	
70	99	110	74	86	12	2	2		74	99	110	74	86	14	2	3		74	99	112	74	86.6667	14	1	3		72	99	114	74	87.3333	14	1	3		74	99	114	74	87.3333	14	1	3	
72	99	128	78	94.6667	12	3	3		74	98	132	78	96	13	2	3		74	98	132	78	96	13	2	3		74	98	132	78	96	13	2	3		74	98	132	78	96	13	1	3	
89	99	120	84	96	14	2	2		88	99	124	80	94.6667	14	1	3		88	99	124	80	94.6667	14	1	3		88	99	124	80	94.6667	14	1	3		88	99	124	80	94.6667	14	1	3	
78	99	122	74	90	13	3	2		76	99	122	70	87.3333	13	2	3		76	99	122	70	87.3333	13	2	3		76	99	122	70	87.3333	13	2	3		76	99	122	70	87.3333	13	2	3	
70	99	110	74	86	12	2	2		74	99	110	74	86	14	2	3		74	99	112	74	86.6667	14	1	3		72	99	114	74	87.3333	14	1	3		74	99	114	74	87.3333	14	1	3	
									70	99	120	74	89.3333	12	2	3		74	99	120	80	93.3333	12	3	3		80	99	120	80	93.3333	12	1	3		80	99	120	80	93.3333	12	1	3	
70	99	116	74	88	15	3	2		72	99	124	80	94.6667	12	3	2		72	99	124	80	94.6667	12	3	2		72	99	124	80	94.6667	12	2	3		72	99	124	80	94.6667	12	2	1	
102	99	130	80	96.6667	14	2	3		98	99	128	76	93.3333	16	2	4		98	99	128	76	93.3333	16	2	4		98	99	128	76	93.3333	16	2	4		98	99	128	76	93.3333	16	2	4	
80	99	126	82	96.6667	13	3	2		84	98	126	76	92.6667	13	2	1		84	98	126	76	92.6667	13	2	2		84	98	126	76	92.6667	13	2	1		84	99	126	76	92.6667	13	2	1	
84	100	114	70	84.6667	12	2	3		86	99	120	70	86.6667	15	1	4		86	99	120	70	86.6667	15	1	4		86	99	120	70	86.6667	15	1	4		86	99	120	70	86.6667	15	1	4	
80	100	124	78	93.3333	14	2	3		80	99	124	80	94.6667	14	2	3		80	99	124	80	94.6667	14	2	3		80	99	120	80	93.3333	14	1	3		86	99	124	86	98.6667	14	1	2	
75	99	116	75	88.6667	12	3	2		78	99	119	74	89	12	2	3		78	99	119	74	89	12	2	1		78	99	119	74	89	12	2	1		78	99	119	74	89	12	1	1	
68	100	103	63	76.3333	14	2	2		66	100	106	72	83.3333	14	1	2		72	100	110	72	84.6667	14	1	2		72	100	106	72	83.3333	14	1	4	Inj. Diclofenac	66	100	106	72	83.3333	16	1	2	
75	99	116	75	88.6667	12	3	2		78	99	119	74	89	12	2	3		78	99	119	74	89	12	2	1		78	99	119	74	89	12	2	1		78	99	119	74	89	12	1	1	
82	99	110	70	83.3333	16	2	2		86	98	118	72	87.3333	16	1	3		86	98	118	72	87.3333	16	1	3		86	98	118	72	87.3333	16	1	3		86	98	118	72	87.3333	16	1	3	
80	99	117	76	89.6667	14	2	2		78	99	116	78	90.6667	13	2	3		80	99	120	78	92	13	1	3		81	98	120	76	90.6667	13	1	3		80	99	120	78	92	13	1	3	
78	99	114	74	87.3333	16	2	3		80	99	112	72	85.3333	14	2	2		75	99	112	72	85.3333	13	2	3		75	99	112	72	85.3333	13	1	3		75	99	112	72	85.3333	13	1	1	
75	99	106	69	81.3333	12	3	2		78	99	112	74	86.6667	12	3	2		78	99	112	74	86.6667	12	2	2		78	99	112	74	86.6667	12	2	2		78	99	112	74	86.6667	12	1	2	
78	99	118	72	87.3333	16	2	4		72	99	118	72	87.3333	14	2	2		72	99	118	72	87.3333	14	2	2		72	99	118	72	87.3333	14	2	2		72	99	118	72	87.3333	14	2	2	
78	99	118	72	87.3333	16	2	4		72	99	118	72	87.3333	14	2	2		72	99	118	72	87.3333	14	2	2		72	99	118	72	87.3333	14	2	2		72	99	118	72	87.3333	14	2	2	
80	98	124	78	93.3333	14	2	3		84	98	128	80	96	14	2	2		84	98	128	80	96	14	2	2		84	98	128	80	96	14	1	3		84	98	128	80	96	14	1	1	
82	99	120	80	93.3333	12	2	2		80	99	122	74	90	12	1	2		80	99	122	74	90	12	1	2		80	99	120	74	89.3333	12	1	2		80	99	120	74	89.3333	12	1	2	
78	99	122	74	90	13	3	2		76	99	122	70	87.3333	13	2	3		76	99	122	70	87.3333	13	2	3		76	99	122	70	87.3333	13	2	3		76	99	122	70	87.3333	13	2	3	
72	99	124	70	88	13	3	2		74	99	126	72	90	13	3	2		74	99	126	72	90	13	3	2		74	99	126	72	90	13	2	2		74	99	126	72	90	13	1	2	
68	99	118	70	86	12	3	2		69	99	120	80	93.3333	13	3	2		69	99	120	80	93.3333	13	2	2		69	99	120	80	93.3333	13	2	2		69	99	120	80	93.3333	13	2	3	
80	100	124	78	93.3333	14	2	3		80	99	124	80	94.6667	14	2	3		80	99	124	80	94.6667	14	2	3		80	99	120	80	93.3333	14	1	3		86	99	124	86	98.6667	14	1	2	
68	100	103	63	76.3333	14	2	2		66	100	106	72	83.3333	14	1	2		72	100	110	72	84.6667	14	1	4	Inj. Diclofenac	72	100	106	72	83.3333	14	1	3		66	100	106	72	83.3333	16	1	2	

MASTER CHART - MIDAZOLAM

75 MIN									90 MIN									105 MIN									120 MIN									Additional analgesic requirement Y/N	Time of Additional analgesic (min)	Additional sedation requirement Y/N	Time of additional sedation requirement (min)	Side effects							Surgeon Satisfication Score (1-5)
HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication	HR	SpO2	SBP	DBP	MAP	RR	RSS	VAS	Additional Medication					Bradycardia	Hypotension	Hypertension	Desaturation	PONV	Dryness of mouth	
74	99	110	70	83.3333	12	1	2		74	99	110	78	88.6667	12	1	1		74	99	110	78	88.6667	12	1	1		74	99	110	78	88.6667	12	1	1		Y	15 MINS	N		N	N	N	N	N	N	3
66	100	106	72	83.3333	14	1	1		70	99	134	85	101.333	14	1	3		70	99	134	85	101.333	14	1	3		61	99	134	85	101.333	14	2	3		Y	Postoperatively at 30 MINS	N		N	N	N	N	N	N	4
70	99	113	74	87	15	1	3		72	99	116	69	84.6667	15	1	3		72	99	116	69	84.6667	15	1	2		72	99	116	69	84.6667	15	1	3		Y	30 MIN	Y	15 MIN	N	N	N	N	N	N	4
78	99	119	74	89	12	1	3		73	99	116	78	90.6667	14	1	1		73	99	116	78	90.6667	14	1	2		73	99	116	78	90.6667	16	1	2		N		N		N	N	N	N	N	N	4
75	99	112	72	85.3333	13	1	1		75	99	115	74	87.6667	12	1	1		75	99	115	74	87.6667	12	1	1		75	99	115	74	87.6667	12	1	1		N		N		N	N	N	N	N	N	5
98	99	128	76	93.3333	16	2	4		80	98	130	78	95.3333	16	2	3		80	98	130	78	95.3333	16	2	3		80	98	130	78	95.3333	16	2	3		N		N		N	N	N	N	N	N	4
98	99	128	76	93.3333	16	2	4		80	98	130	78	95.3333	16	2	3		80	98	130	78	95.3333	16	2	3		80	98	130	78	95.3333	16	2	3		N		N		N	N	N	N	N	N	4
75	99	112	72	85.3333	13	1	1		75	99	115	74	87.6667	12	1	1		75	99	115	74	87.6667	12	1	1		75	99	115	74	87.6667	12	1	1		N		N		N	N	N	N	N	N	5
82	99	122	78	92.6667	13	1	3		80	99	120	80	93.3333	13	1	3		80	99	120	80	93.3333	13	1	2		80	99	120	80	93.3333	13	1	2		Y	45 MIN	N	10 MIN	N	N	N	N	N	N	4
72	99	124	78	93.3333	14	2	4	Inj. Diclofenac	80	99	122	80	94	14	2	4		80	99	122	80	94	14	2	3		80	99	122	80	94	14	2	2		Y	Postoperative at 75 MINS	N		N	N	N	N	N	N	3
74	99	126	72	90	13	1	2		76	99	128	72	90.6667	15	1	2		76	99	128	72	90.6667	15	1	2		76	99	128	72	90.6667	15	1	2		N		N		N	N	N	N	N	N	4
86	98	118	72	87.3333	16	1	3		78	99	124	76	92	16	1	3		78	99	124	76	92	16	1	3		78	99	124	76	92	16	1	3		N		N		N	N	N	N	N	N	5
80	100	110	70	83.3333	14	2	2		85	100	120	80	93.3333	14	2	2		85	100	120	80	93.3333	14	2	2		85	100	120	80	93.3333	14	2	2		N		N		N	N	N	N	N	N	4
84	98	130	80	96.6667	13	1	1		80	99	130	80	96.6667	12	1	1		78	98	128	86	100	12	1	1		78	98	128	86	100	12	1	1		N		N		N	N	N	N	N	N	4
72	99	124	78	93.3333	14	2	3		80	99	122	80	94	14	2	4	Diclofenac 75	80	99	122	80	94	14	2	3		80	99	122	80	94	14	2	2		Y	Postoperative at 90 MINS	N		N	N	N	N	N	N	3
90	99	128	76	93.3333	14	1	3		92	99	124	78	93.3333	14	1	3		96	99	124	78	93.3333	14	1	3		94	99	124	78	93.3333	14	1	3		N		N		N	N	N	N	N	N	3
74	99	118	76	90	14	1	3		72	99	118	74	88.6667	12	1	3		72	99	124	74	90.6667	12	1	2		74	99	120	74	89.3333	12	1	1		N		N		N	N	N	N	N	N	4
82	99	122	78	92.6667	13	1	3		80	99	120	80	93.3333	13	1	3		80	99	120	80	93.3333	13	1	2		80	99	120	80	93.3333	13	1	2		Y	IIN and Postoperative at 30 N	Y	10 MIN	N	N	N	N	N	N	4
76	99	122	70	87.3333	13	2	3		79	99	126	71	89.3333	15	2	3		79	99	126	71	89.3333	15	2	2		79	99	126	71	89.3333	15	1	2		N		N		N	N	N	N	N	N	5
82	98	120	78	92	14	2	2		72	98	106	60	75.3333	12	1	3		72	98	106	60	75.3333	12	1	3		72	98	106	60	75.3333	12	1	3		Y	Postoperative at 15 MINS	N		N	N	N	N	N	N	3
72	99	124	78	93.3333	14	2	3		80	99	122	80	94	14	2	4	Diclofenac 75	80	99	122	80	94	14	2	3		80	99	122	80	94	14	2	2		Y	Postoperative at 90 MINS	N		N	N	N	N	N	N	3
74	99	118	76	90	14	1	3		72	99	118	74	88.6667	12	1	3		72	99	124	74	90.6667	12	1	2		74	99	120	74	89.3333	12	1	1		N		N		N	N	N	N	N	N	4
74	98	132	78	96	13	1	3		73	98	138	77	97.3333	11	1	3		73	98	138	77	97.3333	11	1	3		73	98	138	77	97.3333	11	1	3		Y	60 MIN	N		N	N	N	N	N	N	4
88	99	124	80	94.6667	14	1	3		78	98	122	75	90.6667	14	1	4	Inj.Diclofenac	78	98	122	75	90.6667	14	1	3		78	98	122	75	90.6667	14	1	2		Y	Postoperative at 90 MINS	N		N	N	N	N	N	N	3
76	99	122	70	87.3333	13	2	3		79	99	126	71	89.3333	15	2	3		79	99	126	71	89.3333	15	2	2		79	99	126	71	89.3333	15	1	2		N		N		N	N	N	N	N	N	5
74	99	118	76	90	14	1	3		72	99	118	74	88.6667	12	1	3		72	99	124	74	90.6667	12	1	2		74	99	120	74	89.3333	12	1	1		N		N		N	N	N	N	N	N	4
82	99	120	80	93.3333	12	1	3		82	99	124	82	96	14	1	3		80	99	120	80	93.3333	14	1	3		80	99	120	80	93.3333	14	1	3		N		N		N	N	N	N	N	N	4
72	99	124	80	94.6667	12	1	1		73	98	124	72	89.3333	13	1	1		73	98	124	72	89.3333	13	1	1		73	98	124	72	89.3333	13	1	1		N		Y	15 MIN	N	N	N	N	N	N	5
98	99	128	76	93.3333	16	2	4		80	98	130	78	95.3333	16	2	3		80	98	130	78	95.3333	16	2	3		80	98	130	78	95.3333	16	2	3		N		N		N	N	N	N	N	N	4
84	98	130	80	96.6667	13	1	1		80	99	130	80	96.6667	12	1	1		78	98	128	86	100	12	1	1		78	98	128	86	100	12	1	1		N		N		N	N	N	N	N	N	4
86	99	120	70	86.6667	15	1	4		88	99	120	76	90.6667	16	1	2		88	99	120	76	90.6667	16	1	2		88	99	120	76	90.6667	16	1	2		N		N		N	N	N	N	N	N	4
86	99	124	80	94.6667	14	1	2		80	99	122	80	94	14	1	3		84	99	124	80	94.6667	14	1	3		84	99	122	80	94	14	1	3		N		N		N	N	N	N	N	N	5
78	99	119	74	89	12	1	3		73	99	116	78	90.6667	14	1	1		73	99	116	78	90.6667	14	1	2		73	99	116	78	90.6667	16	1	2		N		Y	15 MINS	N	N	N	N	N	N	4
66	100	106	72	83.3333	14	1	1		70	99	134	85	101.333	14	1	3		70	99	134	85	101.333	14	1	3		61	99	134	85	101.333	14	2	3		Y	Postoperative at 45 MINS	N		N	N	N	N	N	N	4
78	99	119	74	89	12	1	3		73	99	116	78	90.6667	14	1	1		73	99	116	78	90.6667	14	1	2		73	99	116	78	90.6667	16	1	2		N		N		N	N	N	N	N	N	4
86	98	118	72	87.3333	16	1	3		78	99	124	76	92	16	1	3		78	99	124	76	92	16	1	3		78	99	124	76	92	16	1	3		N		N		N	N	N	N	N	N	5
82	99	122	78	92.6667	13	1	3		80	99	120	80	93.3333	13	1	3		80	99	120	80	93.3333	13	1	2		80	99	120	80	93.3333	13	1	2		Y	60 MIN	N		N	N	N	N	N	N	4
75	99	112	72	85.3333	13	1	1		75	99	115	74	87.6667	12	1	1		75	99	115	74	87.6667	12	1	1		75	99	115	74	87.6667	12	1	1		Y	30 MIN	N		N	N	N	N	N	N	5
78	99	112	74	86.6667	12	1	2		76	99	122	75	90.6667	13	1	3		76	99	122	75	90.6667	13	1	3		76	99	122	75	90.6667	13	1	3		N		N		N	N	N	N	N	N	4
72	99	118	72	87.3333	14	2	2		78	99	116	80	92	16	2	2		78	99	116	80	92	16	2	4	Inj. Diclofenac	78	99	116	80	92	16	2	2		N	Postoperative at 105 MINS	N		N	N	N	N	N	N	3
72	99	118	72	87.3333	14	2	2		78	99	116	80	92	16	2	2		78	99	116	80	92	16	2	4	Inj. Diclofenac	78	99	116	80	92	16	2	2		N	Postoperative at 105 MINS	N		N	N	N	N	N	N	3
84	98	128	80	96	14	1	1		81	99	124	82	96	11	1	1		81	99	124	82	96	11	1	2		81	99	124	82	96	11	1	2		N		Y	10 MINS	N	N	N	N	N	N	5
80	99	120	74	89.3333	12	1	2		78	99	118	74	88.6667	13	1	2		78	99	118	74	88.6667	13	1	1		78	99	118	74	88.6667	13	2	2		N		N		N	N	N	N	N	N	5
76	99	122	70	87.3333	13	2	3		79	99	126	71	89.3333	15	2	3		79	99	126	71	89.3333	15	2	2		79	99	126	71	89.3333	15	1	2		N		N		N	N	N	N	N	N	5
74	99	126	72	90	13	1	2		76	99	128	72	90.6667	15	1	2		76	99	128	72	90.6667	15	1	2		76	99	128	72	90.6667	15	1	2		N		N		N	N	N	N	N	N	4
69	99	120	80	93.3333	13	2	3		70	99	121	82	95	13	1	3		70	99	121	82	95	13	1	1		70	99	121	82	95	13	1	1		N		N		N	N	N	N	N	N	5
86	99	124	80	94.6667	14	1	2		80	99	122	80	94	14	1	3		84	99	124	80	94.6667	14	1	3		84	99	122	80	94	14	1	3		N		N		N	N	N	N	N	N	5
66	100	106	72	83.3333	14	1	1		70	99	134	85	101.333	14	1	3		70	99	134	85	101.333	14	1	3		61	99	134	85	101.333	14	2	3		Y	Postoperative at 30 MIN	N		N	N	N	N	N	N	4