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Continuous low dose antibiotic prophylaxis versus no antibiotics with respect to urinary tract infection and biofilm formation in the patients with double-j stents: A prospective randomized study

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Abstract

Objective: To evaluate effects of Continuous low dose antibiotic prophylaxis versus no antibiotics in the patients with DJ stents with respect to urinary tract infection (UTI and biofilm formation).

Material and Methods: A prospective randomized study in 36 patients being stented for stone disease, pelvi-ureteric junction obstruction (PUJO), were divided into 2 groups. Group 1 containing 18 patients received T. Nitrofurantoin 100mg once a day after stenting and Group 2 containing 18 patients received no antibiotic after stenting. Both the groups received pre-op single dose intravenous (IV) Levoflox and Amikacin according to their body weight. After stent removal, stents were sent in normal saline for evaluation of Culture and Biofilm formation. Positive stent cultures were processed for the formation of biofilm using Christensen's Tube method.

Results: 2 out of 18 pre-stent removal cultures in group 1, 7 out of 18 pre-stent removal cultures in group 2 were positive. Biofilm was not detected in any of the groups. Febrile urinary tract infection was not seen in any of the groups. Dysuria and pain abdomen were most common presenting symptoms in stented patients.

Conclusion: The incidence of infection in both the groups is same. There was no added advantage of prophylactic antibiotics for patients on DJ-stent. Unnecessary and irrational use of antibiotics should be avoided to prevent bacterial resistance in future. Studies on antibiotic prophylaxis in patients on DJ-stents are sparse. Larger studies are required to confirm the findings.

Keywords: Stent, biofilm, urine culture, stent culture, Christenson's tube method

Introduction

Double-J (DJ) stenting is the commonest procedure performed in urology. Patients with stent, develop stent infections and stent-related symptoms. Use of antibiotics in patients with DJ stent is rampant. No uniform data is there to prove advantage of antibiotic prophylaxis. Colonial way of life of microorganisms, complex microbial assemblages are responsible for formation of biofilm. Both gram positive and gram negative bacteria produces biofilm. Biofilm is an important virulence factor and is main cause of many chronic infections and multi-drug resistant strains resulting in treatment failure.

Microbially derived sessile communities containing cells that are attached to a substratum or to each other are called biofilms. They are embedded in a matrix which they have produced containing extracellular polymeric substances (EPS) and exhibit an altered phenotype with respect to growth rate and gene transcription ^[1].

"Quorum sensing" is a phenomenon where-in bacteria communicate with each other within a biofilm, by producing chemotactic particles or pheromones ^[2]. Some factors which influence biofilm formation are availability of key nutrients, Chemotaxis towards surface, motility of bacteria, surface Adhesins and presence of surfactants ^[2].

Microbes growing in a biofilm are more resistant to antimicrobial agents. High antimicrobial concentrations are required to kill these organisms. There can be a 1000 fold increase in antibiotic resistance with biofilm formation ^[3]. This study is done to evaluate effects of Continuous low dose antibiotic prophylaxis versus no antibiotics in the patients with DJ stents with respect to urinary tract infection (UTI) and biofilm formation at our institute.

Material and Methods

This is a prospective randomized study conducted in our institute from January 2017 to December 2017 in 36 patients being stented for stone disease, pelvi-ureteric junction obstruction (PUJO) (Figure 1). Informed consent is taken from all the patients enrolled in the study. Ethical committee approval is also taken from the Institute. These patients are divided into two groups. Group 1 has 18 patients who are given Tab. Nitrofurantoin 100mg once a day after stenting and Group 2 has 18 patients who are not given any antibiotics after stenting. Pre-operative positive urine cultures are excluded from the study. Both the groups received pre-op single dose intravenous (IV) Levofloxacin and Amikacin according to their body weight. Pre-stent-removal urine cultures are done in all patients. After stent removal, stents are sent in normal saline for Culture

and evaluation of Biofilm formation. Positive stent cultures are processed for Biofilm formation using Christensen's Tube method.

Analysis done by using SPSS software.

Results

Table 1 shows Demographic data of both study groups. 2 out of 18 stent removal cultures in group 1, 7 out of 18 stent cultures in group 2 are positive (figure 2). Biofilm is not detected in any of the groups. Culture and sensitivity pattern after stent culture in both the groups are shown in table 2. Febrile urinary tract infection is not seen in any of the groups (Table 3). Dysuria and pain abdomen are the most common presenting symptoms in stented patients (figure 3).

Table 1: Demographic data in two different groups

Variables	Group1	Group2
No. of patients	18	18
Age range (years)	6-60	8-63
Male/ Female	11/7	9/9
Stent indwelling time (days)	15-75	12-60

Table 2: Culture and sensitivity pattern of the removed stents in both the groups.

S. No	Stent culture	Group	Sensitivity	Biofilm
1	<i>Pseudomonas aeruginosa</i>	2	Gentamicin, Amikacin, Piperacillin + Tazobactam, Netilmicin, Imipenem	-
2	<i>Pseudomonas aeruginosa</i>	2	Ciprofloxacin, Norfloxacin, Ofloxacin, Amoxicillin, Piperacillin + Tazobactam, Imipenem, Ceftazidime + Clavulonic acid	-
3	<i>Citrobacter</i> sp	2	Amikacin, Imipenem	-
4	<i>Staphylococcus aureus</i>	2	Tetracyclin, Piperacillin + Tazobactam, Cefoperazone + Sulbactam, Amikacin, Ceftriaxone, Azithromycin, Linezolid	-
5	<i>Citrobacter freundii</i>	2	Ampicillin, Amoxicillin, Gentamicin, Amikacin, Imipenem	-
6	<i>Staphylococcus aureus</i>	1	Tetracyclin, Piperacillin + Tazobactam, Cefoperazone + Sulbactam, Amikacin, Linezolid	-
7	<i>Candida</i> sp.	2		-
8	<i>Candida</i> sp.	1		-
9	<i>Klebsiella pneumonia</i>	2	Piperacillin + Tazobactam, Imipenem	-

Table 3: Febrile urinary tract infections in both the groups

Studies	Group 1	Group 2
Felix Moltzahn <i>et al.</i> (126 pts.)	1%	9.5 %
Krishna Ramaswamy <i>et al.</i> (48 pts.)	2%	2%
Our study (36 pts.)	0	0

Table 4: various studies showing sensitivity and specificity of Christensen's tube method.

Studies	Sensitivity	Specificity
Mathur T <i>et al.</i> [13]	73.6%	92.6%
Hassan A <i>et al.</i> [14]	73%	92.5%
Oliveira A <i>et al.</i> [15]	100%	100%
Afreenish <i>et al.</i> [16]	73%	92.5%
Our study	71.88%	88.89%

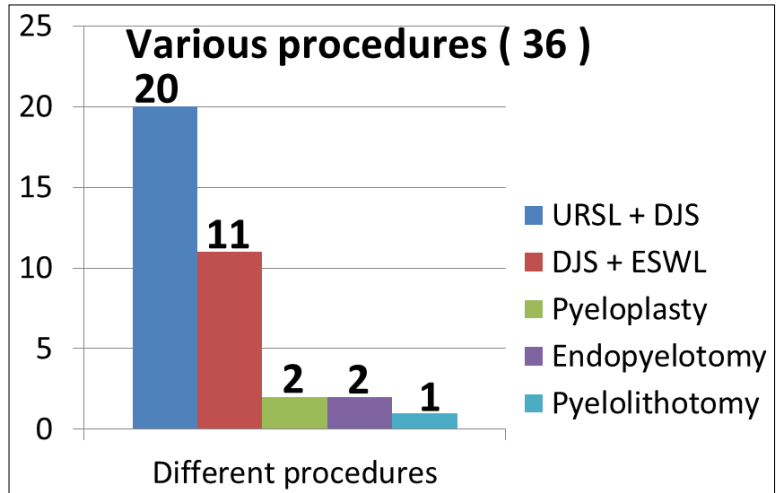


Fig 1: Various procedures performed prior to double-J stenting.

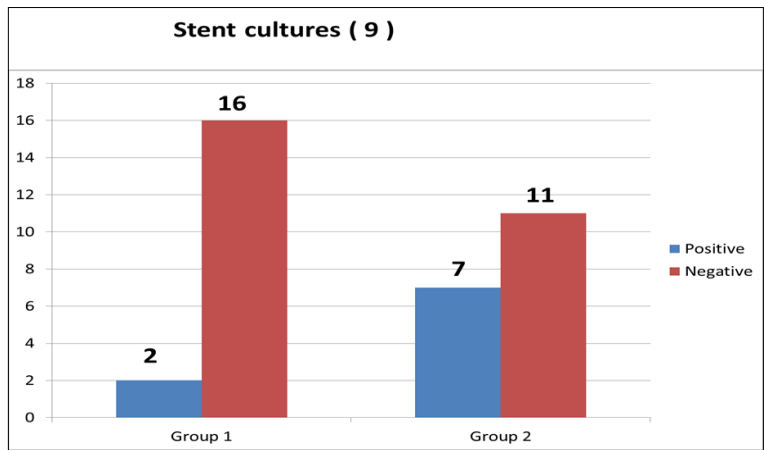


Fig 2: Stent cultures after double-J stent removal

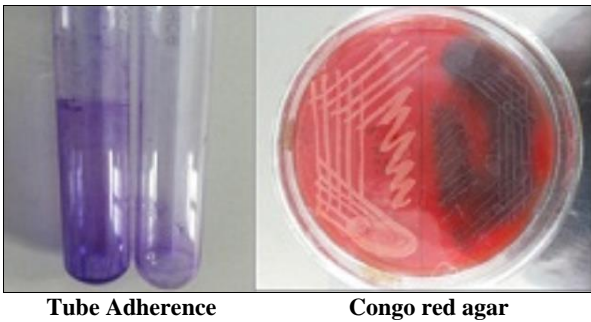


Fig 3: Tube adherence method showing biofilm as bluish tinge on Glas and Congo red agar plate showing biofilm as black colonies

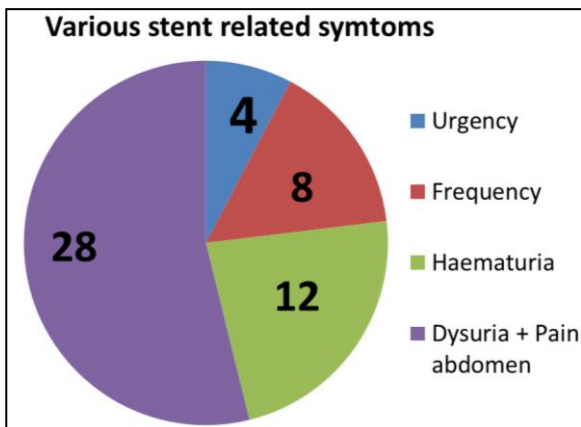


Fig 4: Stent related symtoms in all the patients.

Discussion

More than 80% of all infections involve biofilms as per the publication by the National Institutes of Health [4]. Biofilms are seen in upper respiratory tract infections, peritonitis, and urinary tract infections. They are also seen on implanted devices and dental plaque [5]. Not much data is available regarding association of biofilms and Stents. Bacteria's like *Enterococcus faecalis*, *Staphylococcus aureus*, *Staphylococcus epidermoid*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis* and *Pseudomonas aeruginosa* produce biofilms [6].

Various methods to detect biofilm production include the Tissue Culture Plate method (TCP) [7], Tube method (TM) [8], Congo Red Agar method (CRA) [9], Bio-luminescent Assay [10], Piezoelectric sensors [11], And Fluorescent microscopic examination [12].

Tissue culture plate method

Christensen *et al.* described this test [7]. This is a quantitative test and is considered to be the gold-standard method for biofilm detection [13]. Organisms isolated from fresh agar plates are inoculated in 10 mL of trypticase soy broth with 1% glucose. Broths are incubated at 37 °C for 24 hours. The cultures were then diluted 1:100 with fresh medium. Individual wells of sterile 96 well-flat bottom polystyrene tissue culture treated plates (Sigma-Aldrich, Costar, USA) are filled with 200 µL of the diluted cultures. The control organisms are also incubated, diluted and added to tissue culture plate. Negative control wells contained inoculated sterile broth. The plates are incubated at 37 °C for 24 hours. After incubation, gentle tapping of the

wells is done to remove excess contents. The wells are washed four times with 0.2 mL of phosphate buffer saline (pH 7.2) to remove free-floating bacteria. 2% sodium acetate is used for fixing the biofilm which is formed by bacteria adherent to the wells and is stained by crystal violet (0.1%). Excess stain is removed by using deionized water and plates are kept for drying.

Tube method

This is described by Christensen *et al.* [8]. This is a qualitative method for detection of biofilm. A loopful of test organisms is inoculated in 10 mL of trypticase soy broth with 1% glucose in test tubes. The tubes are incubated at 37 °C for 24 hours. Tubes are decanted and washed with phosphate buffer saline (pH 7.3) and incubated. Tubes are dried. Tubes are then stained with crystal violet (0.1%). Excess stain is washed with deionized water. Tubes are dried in inverted position. When a visible film lined the wall and the bottom of the tube, biofilm formation was considered positive (figure 4). Ring formation at the liquid interface is not indicative of biofilm formation. In our study, we used Christensen's Tube method.

Congo Red Agar (CRA) method

Freeman *et al.* have described this method [9]. This is a qualitative method. CRA medium is prepared with brain heart infusion broth (Oxoid, UK) 37 g/L, sucrose 50 g/L, agar No. 1 (Oxoid, UK) 10 g/L and Congo Red indicator (Oxoid, UK) 8 g/L. Congo Red stain is prepared as an aqueous solution and autoclaved at 121 °C for 15 minutes separately, from the other medium constituents. This stain is added to the autoclaved brain heart infusion agar with sucrose at 55 °C [5]. CRA plates are inoculated with test organisms and incubated at 37 °C for 24 hr aerobically. Black colonies indicated biofilm production [5].

Antibiotic susceptibility test of biofilm producing bacteria is done on Mueller Hinton agar (Oxoid, UK) using the following antibiotic discs: ampicillin, cotrimoxazole, ciprofloxacin, aztreonam, meropenem, Cefoperazone-Sulbactam, chloramphenicol, vancomycin, erythromycin, amoxicillin-clavulanic acid, oxacillin, linezolid, penicillin.

The sensitivity and specificity of Tube Method followed in our study is comparable with other studies by Mathur T *et al.* [13], Hassan *et al.* [14], Oliveira *et al.* [15], Afreenish *et al.* [16].

The limitation of this study is that this is a single institutional study and there is a need to enroll more number of cases to further validate the results.

Conclusion

There is no added advantage of prophylactic antibiotics for patients on DJ-stent. Unnecessary and irrational use of antibiotics should be avoided to prevent bacterial resistance in future. Biofilm is not detected in any of the study groups.

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