SINGLE DOSE OF PRE-OPERATIVE INTRAVENOUS ANTIBIOTIC IS SUFFICIENT FOR UPPER TRACT UROLITHIASIS PROCEDURES

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Abstract

Background: Infection is one of the major complications in endourological procedures, and may range in severity from mild fever to septic shock. A survey on postoperative antibiotic usage showed varied usage. No clear guidelines exist for the same. The objective of this study is to rationalise the usage of post-operative antibiotics in urine culture negative patients with symptomatic upper urinary tract calculi.

Materials and Methods: A prospective randomised controlled study done from March 2021 to February 2022. A total of 250 cases operated for upper urinary tract calculi at our institution with sterile urine culture are considered. All the patients received only single dose of prophylactic antibiotic before surgery and no postoperative antibiotics were given. They were divided into 2 groups to assess the local antibiotic (gentamycin) implications in reducing the usage of post-operative antibiotics. Postoperatively fever was assessed along with other signs of infection like pyelonephritis, symptomatic urinary tract infection (UTI) and sepsis. Statistical analysis is done and p value <0.05 is considered significant.

Results: A total of 19 patients (8%) developed fever among 250 patients. Among the 124 Percutaneous Nephrolithotomy (PCNL) patients, 11 developed fever and among 126 Ureterorenoscopic lithotripsy (URSL) patients, 8 developed fever. Overall fever incidence is similar with gentamycin (7.5%) or standard normal saline (NS) irrigation (7.7%). None of the patients developed pyelonephritis, UTI or sepsis.

Conclusion: Single dose of pre-operative intravenous (IV) antibiotic is sufficient for upper tract urolithiasis procedures. There is no significant role of local antibiotic instillation in irrigation fluid, on the post-operative infections.

Keywords: Antibiotic usage; PCNL; URSL; Upper tract Urolithiasis.
Introduction

Infection is one of the major complications in Ureterorenoscopic Lithotripsy (URSL) and Percutaneous Nephrolithotomy (PCNL) surgeries. It may range in severity from mild fever to septic shock. Bacteria and endotoxins from stones are released during the stone fragmentation step of PCNL/URSL and may result in post-operative fever or sepsis. We have conducted a survey which showed varied practice of postoperative antibiotics for 3 to 5 days in patients undergoing PCNL and URSL. There are numerous studies with varied antibiotic protocols. Some have suggested postoperative antibiotics for 3-5 days and some guidelines published there is no need for any postoperative antibiotics.

Aims and objectives:
Our primary objective was to rationalise the post-operative antibiotic practice in upper tract urolithiasis procedures and the secondary objective was to analyse whether there is any role of local antibiotic instillation (in irrigation fluid during the procedure) in reducing the symptomatic postoperative infections.

Materials and Methods
This is a prospective randomised controlled study done from March 2021 to February 2022. A total of 250 patients undergoing PCNL or URSL surgeries at our institution are considered for the study. Institutional Ethical Committee approval obtained and an informed written consent was obtained from every patient. Inclusion criteria were all renal and ureteric calculi patients with sterile urine culture who underwent PCNL and URSL. Exclusion criteria were all the patients with positive urine culture, indwelling catheter, previous antibiotic usage within 2 weeks of the admissions, allergy to antibiotics, refusal to enroll in the study and paediatric patients.

All the 250 renal and ureteric calculi cases are divided into 2 groups by double blinded randomization.

Randomization technique: Randomization was done by asking each patient to pick up a paper slip from a box containing a bunch of slips with either group written on it. The ward nurse will take the box containing slips to the patient and the patient will pick up one slip. Based on that slip, patient is included in the respective group. This technique is adopted to eliminate the selection bias. Group 1 patients will undergo PCNL or URSL with Normal saline (NS) irrigation fluid. Group 2 patients will undergo PCNL or URSL with Gentamycin instillation into the normal saline irrigation.

120mg/3ml of gentamycin was instilled into each litre NS irrigation fluid. This amount of dilution was decided based on the minimal inhibitory concentration (MIC)
of gentamycin (0.94 ug/ml). Both the groups have received only one dose of preoperative intravenous (IV) antibiotic (cefaperazone + sulbactum 1.5 gm), given 1 hour before surgery and no post-operative antibiotics are given. Height of the irrigation bottle is 60 cm above the pelvis and only 3 litres irrigation bottle is used for all the cases. Post-operative fever > 100 °F is considered standard and marked in both groups. Post operatively ultrasound abdomen, total counts, complete urine examination and Serum Creatinine are done in both the groups. Any signs and symptoms of pyelonephritis, urinary tract infection (UTI) and sepsis are marked in both the groups. All patients had a Double J (DJ) stent placed post operatively. All stents were removed 15 days after surgery. Stent related infective complications were noted postoperatively. All the patients who develop fever received further antibiotic treatment.

**Statistical analysis:**
Statistical significance was analysed using Chi square test. Statistical analysis was done by using IBM SPSS version 24.0 software. P value < 0.05 is considered as statistically significant.

**Results**

Out of the total 250 patients who underwent PCNL and URSL, only 8% of them developed fever. Among the patients who underwent PCNL and URSL, 8.8% and 6.3% developed fever respectively Table I.

<table>
<thead>
<tr>
<th></th>
<th>Fever present</th>
<th>%</th>
<th>Fever absent</th>
<th>%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCNL</td>
<td>11</td>
<td>8.8</td>
<td>113</td>
<td>91.2</td>
<td>124</td>
</tr>
<tr>
<td>URSL</td>
<td>8</td>
<td>6.3</td>
<td>118</td>
<td>93.7</td>
<td>126</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>8</td>
<td>231</td>
<td>92</td>
<td>250</td>
</tr>
</tbody>
</table>
A total of 250 patients were randomised into 2 groups. Gentamycin irrigation group consisted of 120 patients and Normal saline irrigation group consisted of 130 patients. Among 120 patients, only 9 developed fever post-operatively in gentamycin group. Among 130 patients, 10 developed fever post-operatively in NS irrigation group Table II. The p value is 0.954, which is not significant.

Table II: Incidence of fever in both the groups.

<table>
<thead>
<tr>
<th></th>
<th>Fever present</th>
<th>%</th>
<th>Fever absent</th>
<th>%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamycin group</td>
<td>9</td>
<td>7.5</td>
<td>111</td>
<td>92.5</td>
<td>120</td>
</tr>
<tr>
<td>NS group</td>
<td>10</td>
<td>7.7</td>
<td>120</td>
<td>92.3</td>
<td>130</td>
</tr>
</tbody>
</table>

Chi-square value = 0.003, P Value = 0.954 (Not Sig.)

In patients who underwent PCNL, total 11 patients developed fever out of 124 patients among which 7 were in gentamycin irrigation group and 4 in NS irrigation group (Table III).

Table III: Incidence of fever in patients who underwent PCNL

<table>
<thead>
<tr>
<th></th>
<th>Fever present</th>
<th>%</th>
<th>Fever absent</th>
<th>%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamycin group</td>
<td>7</td>
<td>12.3</td>
<td>50</td>
<td>87.7</td>
<td>57</td>
</tr>
<tr>
<td>NS group</td>
<td>4</td>
<td>6</td>
<td>63</td>
<td>94</td>
<td>67</td>
</tr>
</tbody>
</table>

Chi-square value = 1.517, P Value = 0.218 (Not Sig.)
In patients who underwent URSL, total 8 patients developed fever out of 126 patients among which 2 were in gentamycin irrigation group and 6 in NS irrigation group Table 4. No patients developed postoperative pyelonephritis, UTI or sepsis.

**Table IV: Incidence of fever in patients who underwent URSL**

<table>
<thead>
<tr>
<th></th>
<th>Fever present</th>
<th>%</th>
<th>Fever absent</th>
<th>%</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamycin group</td>
<td>2</td>
<td>3.2</td>
<td>61</td>
<td>96.8</td>
<td>63</td>
</tr>
<tr>
<td>NS group</td>
<td>6</td>
<td>9.5</td>
<td>57</td>
<td>90.5</td>
<td>63</td>
</tr>
</tbody>
</table>

Chi-square value = 2.136, P Value = 0.144 (Not Sig.)

**Discussion**

Gentamycin is a type of aminoglycoside with bactericidal action. It can be given intravenously, intramuscularly or topically. It is active against a wide range of bacterial infections, mostly Gram-negative bacteria including Pseudomonas, proteus, E.coli, klebsiella pneumoniae, Enterobacter aerogenes, Serratia, and the Gram-positive Staphylococcus. Gentamycin has been known in urology for bladder irrigation in cases of recurrent UTI. It has shown decrease in symptomatic UTI episodes because of its direct action. Locally intravesical gentamycin precludes systemic toxicity and development of antimicrobial resistance is unlikely because of high urinary concentration and lack of selective pressure on commensal gut flora.

There are many studies on usage of prophylactic or preoperative antibiotics but there are no studies in recent times about the usage of postoperative antibiotics in endourology\(^1\text{-}^4\) (Table 5). Our idea was to see whether Gentamycin irrigation decreases the post-operative infections in upper tract endoscopy. We have conducted
a survey among urologists from various parts of our country practicing in different types of hospital setups, which showed 80% of them used postoperative antibiotics for 3 to 5 days in patients undergoing PCNL and URSL. This practice needs to be rationalized and a proper protocol developed regarding antibiotic usage as irrational use has lead to evolution of multi drug resistant organisms. For prevention, various antibiotics have been considered. The American Urological Association (AUA) recommended practice statement suggests combining metronidazole or clindamycin with a first and second-generation cephalosporin or an aminoglycoside. Ampicillin/sulbactam or even a fluoroquinolone are two alternatives. Antibiotic recommendations from the European Association of Urology (EAU 2020) recommend using a second or third or third-generation cephalosporin, trimethoprim-sulfamethoxazole, or aminopenicillin with a β-lactamase inhibitor. In this study, we have used cefaperazone (third generation cephalosporin) with sulbactum(β-lactamase inhibitor) similar to EAU guidelines. The AUA recommended practice policy statement now suggests a single dosage on the day of the procedure. To lower the risk of clinical urine infection after percutaneous nephrolithotomy, the EAU guidelines 2020 advocate using single dose antibiotic prophylaxis.

Dogan and colleagues conducted the first prospective research to assess the duration of treatment in 2002. In this study, PCNL patients in one group received a single 200 mg dosage of ofloxacin during anaesthesia induction, while those in the control group received 400 mg of ofloxacin daily from the day of the surgery until the nephrostomy tube was removed. There were no differences in postoperative fever, bacteremia, or bacteriuria between the two groups. Further investigations in 2012 and 2013 verified the single-dose antibiotic regimen's efficacy. In addition, with a single pre-operative antibiotic treatment,
we saw a much lower percentage of patients (8%) with post-operative fever.

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Tuzel and colleagues then conducted a prospective research in which they analyzed the use of a single dosage of ceftriaxone at the time of operation to a regime of a pre-procedural dose with continuing antibiotic treatment till the period of nephrostomy tube removal². There were no differences in the incidence of postoperative fever or bacteriuria between the groups. Therefore, it appears that a single dosage of a broad-spectrum antibiotic shortly prior to PCNL provides good infection prevention. Similar results are seen in this study also where single preoperative antibiotic dose is effective against infectious complications.

Though gentamycin has been known for its use in bladder irrigation for recurrent UTI, there is no data of its usage in upper tract endoscopic procedures. We are trying to find out its local antibiotic implications in endourology procedures by this study. Our study was not statistically significant (p value=0.954) in this aspect, clearly indicating that there is no role for gentamycin instillation into irrigation fluid in reducing postoperative infections. The main limitation of this study was that it was conducted at a single institution with a small number of patients. Further studies with more patients will be needed.
**Conclusion**

Single dose of pre-operative IV antibiotic is sufficient for upper tract urolithiasis procedures. There is no significant role of local antibiotic instillation in irrigation fluid, on the post-operative infections.

**References**


5. G. Bonkat, R. Bartoletti, F. Bruyère, et al., editors. EAU guidelines on urological infections 2020..


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Ethical Approval: Approved by the institutional review board committee

Authors contribution:

Concept and design: 1
Data collection and analysis: 1
Responsibility for statistical analysis: 1,2
Writing the article: 3
Critical review: 1,2,3,4
Final approval of the article: 1,2,3,4

Each author believes that the manuscript represents honest work and certifies that the article is original, is not under consideration by any other journal, and has not been previously published.

Availability of Data and Material:
The corresponding author is prompt to supply datasets generated during and/or analyzed during the current study on wise request.

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