

Efficacy of 1 Versus 3 Days of Intravenous Amikacin as a Prophylaxis for Patients Undergoing Transurethral Resect Prostate: A Prospective Randomized Trail

ABDUL BASIT NIAZI¹, RASHID ALI², HIRA ANIS BUMBIA³, MUHAMMAD ASIF⁴, MUHAMMAD AMMAR⁵, HALEEMULLAH⁶

¹Assistant Professor Urology, Niazi Medical & Dental College Sargodha

²MBBS, FCPS, Consultant Urologist, Balochistan Institution of Nephrology and Urology, Quetta

³Consultant urologist, Dr Ziauddin Hospital, Karachi

⁴Associate Professor of Urology, Azra Naheed Medical College, Lahore

⁵Senior Registrar Urology, Chaudhary Muhammad Akram Teaching and Research Hospital/ Azra Naheed medical college Lahore

⁶Senior Resident Medical Officer, Institute: Sindh Institute of Urology and Transplant, Karachi

Corresponding author: Hira Anis Bumbia, Email: Hirabumbia@gmail.com

ABSTRACT

Background: The goal of the current study was to investigate the safety of a single dose of IV Amikacin given a period of three days as compared to a single dose of one and two days, when used as a surgical prophylactic antibiotic prior to transurethral prostate resection.

Study Design: This was a randomized and prospective study conducted at Urology Department of Niazi Medical & Dental College Sargodha for the duration of six-months from May 2022 to October 2022.

Methods: There were 300 men who participated in total and had their prostates transurethral resected (TURP). Three groups, A, B, and C, each with 100 participants, were created randomly from among the participants. The participants will either be assigned at random to receive a single dose of Amikacin that complies with recommendations for groups A, B, and C on days 1, 2, and 3. Follow Up until day 30 following surgery, routinely gathered data from TURP will be the end of the study. Within 60 minutes of the incision, all patients received a single dose of prophylactic antibiotics.

Results: The Groups A and B had higher rates of significant bacteriuria than Group C, the intention-to-treat analysis determined that this difference was not statistically significant. The results of a per-protocol analysis were similar. ($p=0.88$; 0.13). This suggests that postoperative bacteriuria poses a significant risk for the emergence of UTI symptoms ($p=0.002^{**}$). Antibacterial drug resistance has a significant relationship with the progression of infectious complications and was associated with a history of diabetes (95% [CI]: $0.08-3.11$, $OR=0.33$; $p=0.01^{*}$) and surgical history and ESBL positivity were indicate infection-related issues (95% [CI]: $1.51-1.86$, $OR=5.1$; $p=0.023$ and 95% [CI]: $2.55-13.1$, $OR=4.90$; $p<0.0001^{***}$).

Conclusions

The Amikacin was safe for surgical prophylaxis in single dose until 3 days as compared to 1 and 2 days because of the incidence of postoperative complication such as UTI reduced. It was greater role to decrease antibiotic resistance.

Keyword: Bacterial infection, Urinary tract, Antibiotics.

INTRODUCTION

The surgical treatment of lower urinary tract symptoms brought by benign prostatic obstruction (BPO), transurethral resection of the prostate (TURP), also known as monopolar transurethral resection of the prostate, is both clinically and financially advantageous. Urethral strictures after TURP, regardless of the energy source, are one of the most frequent late complications and have been identified as the main cause of iatrogenic urethral strictures in patients over the age of 45 who underwent urethroplasty. An overview of the epidemiology, aetiology, and management of TURP stricture. The rate of intraoperative and postoperative complications following TURP is still quite high.¹ Internalized gonococci with phagocytic vacuoles cause the majority of anterior urethral strictures and also cause inflammatory infiltrates in the submucosa, which leads to fibrosis and stricture the relationship between the rate of reoperation after TURP due to urethral stricture or bladder neck contracture and pathologically confirmed prostatic inflammation.²

It may not be possible to avoid the bacterial role in the pathophysiology of prostate hyperplasia, particularly in the development of an inflammatory response. The microbial makeup of tissues, its relationship to inflammation, and the impact of clinically isolated bacteria on prostate epithelial cells are all examined.³ Depending on the population under consideration and the type of UTI, behavioural, anatomical, or genetic risk factors for urinary tract infections (UTIs) may exist.^{4, 5} Lower urinary tract symptoms (LUTS) have a significant negative impact on men's quality of life and were a common issue. Historically, prostatic enlargement—which frequently results in bladder outlet obstruction—has been linked to LUTS. Transurethral resection of the prostate was the mainstay of operative procedure for LUTS induced by prostatic obstruction. These patients are at a significant risk for urethritis (UTIs). Many of these patients depend on a brief

or prolonged catheterization before receiving further treatment, despite the potential for the development of residual urine, which serves as a growth medium for bacteria.^{6, 7} Antibiotic use as a preventative measure is intended to stop local or systemic postoperative infection. Infections of four different types are frequently linked to urologic surgery. In the first, an endoscopic or endoluminal procedure that results in an infection of the urinary tract (UTI) may be used. Both open and laparoscopic surgeries can result in it, and it typically happens when catheters and stents are placed or when a hidden bacterial load is detected. After open and laparoscopic surgeries, the second type is an infection of the surgical wound. The male genital system is affected by the third type of infection (prostatitis, epididymitis, and orchitis). In the fourth form, bloodstream-borne sepsis secondary to urologic instrumentation which associate with infections. The most effective procedure for benign prostate surgery is thought to be transurethral removal of the prostate. Despite advancements in prostate surgery, postoperative infectious complications, particularly UTIs, are still common and frequently lead to bacteremia and potentially fatal sepsis. Additionally, there is still debate regarding antibiotic prophylaxis for prostatic surgery, as there is for other urologic surgeries, despite the fact that it helps reduce postoperative infectious complications.⁸ The goal of the current study was to investigate the safety of a single dose of IV Amikacin given over a period of three days as compared to a single dose of one and two days, when used as a surgical prophylactic antibiotic prior to transurethral prostate resection.

METHODS

This was a randomized and prospective study conducted at Urology Department of Niazi Medical & Dental College Sargodha for the duration of six-months from May 2022 to October 2022. There were 300 men who participated in total and had their

prostates transurethral resected (TURP). Three groups, A, B, and C, each with 100 participants, were created randomly from among the participants. Participants will either be assigned at random to receive a single dose of Amikacin that complies with recommendations for groups A, B, and C on days 1, 2, and 3. Up until day 30 following surgery, routinely gathered data from TURP will be the foundation of the trial. Within 60 minutes of the incision, all patients received a single dose of prophylactic antibiotics. When the surgery is scheduled, informed consent will take place at the outpatient clinic. According to inclusion criteria: The age >20 years, normal kidney condition, and hyperplasia and obstructive prostrate. Exclusion criteria: Nephrotoxic, immune compromised, over weight and pediatric participants. At one month, follow-up was conducted. Experienced surgeons performed every procedure. The data was analyzed with SPSS 21. The categorical data will be displayed as frequency, percentage, mean, and standard deviation (SD). The

variables had changed significantly, as evidenced by the p=0.05 value.

RESULTS

Amikacin (15 mg/kg) was administered intravenously to each patient prior to the induction. Participants in groups A, B and C were received injections of Amikacin on days 1, 2, and 3. As per the established protocol, TURP was performed on the participants. On day 3, the urinary catheter was taken out, and on day 4, the postoperative urine culture was transmitted. On day 7, every patient was available for the follow-up, but after a month, some participants were no longer available. The analyses used were per-protocol and intention-to-treat. Adverse events linked to Amikacin were nonexistent.

Table 1: Demographic characteristics of the participants

| Variables | Total No. of Participants, N=300(%) | | | P=value |
|--|-------------------------------------|-----------------|-----------------|-----------|
| | Group A (100) | Group B (n=100) | Group C (n=100) | |
| | Day 1 Amikacin | Day 2 Amikacin | Day 3 Amikacin | |
| Age | 66.9±7.6 | 67.5±7.5 | 67.9±7.9 | 0.116 |
| PSA ^a | 0.85±0.4 | 0.89±1.0 | 0.88±0.6 | 0.333 |
| Prostate volume, cc | 35.1±23.2 | 36.1±22.4 | 35.8±20.1 | 0.561 |
| ESBL positivity | 10(10%) | 20(20%) | 80(80%) | 0.0001*** |
| Diabetes mellitus | 65(65%) | 60(60%) | 20(20%) | 0.01* |
| IPSS | | | | 0.082 |
| Mild(≤7) | 0 | 0 | 0 | |
| Moderate(8-19) | 15(15%) | 16(16%) | 11(11%) | |
| Severe(20-35) | 35(35%) | 34(34%) | 49(49%) | |
| Post void residue (PVR)ml before surgery | 82(16-250) | 82(10-255) | 81(15-260) | 0.627 |
| Prostate grade | | | | |
| 1 | 25(25%) | 15(15%) | 15(15%) | |
| 2 | 70(70%) | 75(75%) | 77(77%) | 0.221 |
| 3 | 5(5%) | 10(10%) | 8(8%) | |
| Surgery time (min) | 42 | 42 | 42 | ----- |
| Operative history | 40(40%) | 45(45%) | 35(35%) | 0.023 |
| Prostatitis history | 6(6%) | 8(8%) | 7(7%) | 0.002** |
| UTI history | 8(8%) | 6(6%) | 3(3%) | 0.651 |
| Surgeon experience | | | | |
| > 5 year | 60(60%) | 65(65%) | 70(70%) | 0.66 |
| < 5 year | 40(40%) | 35(35%) | 30(30%) | 0.63 |

Mean ± SEM: ANOVA SPS Test* p< 0.0; **p<0.0; ***p<0.00:

Table 2: To evaluate the bacterial infection in Urinary tract after 4th day of operation

| Infection | G-A(PP) | G-B(PP) | G-C(PP) | G-A(ITT) | G-B(ITT) | G-C(ITT) | P=value |
|-----------|----------|-----------|----------|----------|-----------|----------|---------|
| | N=33 | N=34 | N=33 | N=33 | N=34 | N=33 | |
| Yes | 25(76%) | 27(79.4%) | 5(15.1%) | 26(79%) | 27(79.4%) | 8(24.2%) | 0.88 |
| No | 8(24.2%) | 6(18%) | 28(85%) | 7(21.2%) | 6(18%) | 25(76%) | 0.13 |

Mean ± SEM: ANOVA SPS Test* p< 0.0; **p<0.0; ***p<0.00:

Table 3: Infective complications after operation in three groups related to PP and ITT

| Parameters | G-A(PP) | G-B(PP) | G-C(PP) | G-A(ITT) | G-B(ITT) | G-C(ITT) | P=value |
|---------------------------|-----------|-----------|---------|----------|-----------|----------|---------|
| | N=33 | N=34 | N=33 | N=33 | N=34 | N=33 | |
| Sepsis after operation | 11(33.3%) | 10(29.4%) | 1(3%) | 9(27.2%) | 11(32.3%) | 1(3%) | 0.075 |
| Readmit after 1 month UTI | 3(9%) | 5(15%) | 0(0%) | 5(15.1%) | 3(9%) | 0(0%) | 0.113 |
| Symptoms of UTI | 7(21.2%) | 6(18%) | 1(3%) | 9(27.2%) | 8(24%) | 2(6%) | 0.002** |

Mean ± SEM: ANOVA SPS Test* p< 0.0; **p<0.0; ***p<0.00:

Abbreviation: IPSS international prostate symptom score; PVR post void residue.

The participants were divided into three Day 1, 2 and 3 of Amikacin single dose by intravenous. The demographic characteristics of participants were similar in thrice group A, B and C related to age, IPSS, PVR and prostrate grade and there was no significant changes. But the diabetes and history of prostatitis were significantly change (p=0.01*; p=0.002**). The ESBL positivity was show significant result (p=0.0001***) from the culture reports before surgery of TRUP.

Abbreviation: PP per protocol; ITT intention to treat analysis.

Finding the prevalence of bacterial infection four days after surgery was the main result. Diabetes, surgeon experience, resection time, or the amount of prostatic tissue removed—all risk factors

examined in this trial—did not have any impact on patients' development of significant bacteriuria or UTI at day 4 or 1 month, respectively. Although the rate of significant bacteriuria in Group A and B was greater than Group C, this was not statistically significant as per the intention-to-treat analysis. Per-protocol analysis also showed similar results (p=0.88; 0.13) were seen Table 2.

These groups had comparable rates of postoperative sepsis, antibiotic use, and readmissions. Even though Groups A and B had more UTIs at one month, this difference was not statistically significant. Significant bacteriuria was present in the patients in Groups A and B who had UTI at one month, compared to Group C. This suggests that postoperative bacteriuria poses a significant risk for the emergence of UTI symptoms (p=0.002**). When compared

to a single dose, the (NNT) number needed to prevent bacteriuria and urinary tract infection when giving 1, 2, and 3-day course of injection Amikacin, the NNT to give 3 days of Amikacin to prevent one episode of bacteriuria and a UTI.

Table 4: To evaluate the clinical variables with infectious complications by using Multivariate regression analysis.

| Clinical variables | Multivariate | | | P=value |
|-----------------------|--------------|--------|-------|------------|
| | OR | 95% CI | | |
| | | lower | Upper | |
| Amikacian Group | | | | |
| A-----DAY-1 | 3.69 | 0.78 | 10.2 | 0.19 |
| B-----DAY-2 | 3.66 | 0.75 | 9.9 | 1.34 |
| C-----DAT-3 | 2.99 | 0.65 | 7.5 | 0.066 |
| Age | 0.81 | 0.85 | 1.5 | 0.342 |
| D.M | 0.33 | 0.08 | 3.11 | 0.01* |
| Operative history | 5.1 | 1.51 | 1.86 | 0.023* |
| Prostatitis history | 0.0 | NA | NA | |
| ESBL positive | 4.90 | 2.55 | 13.1 | <0.0001*** |
| Bacteriuria infection | 4.48 | 2.79 | 13.98 | <0.001** |

Mean \pm SEM: ANOVA SPS Test* p<0.0; **p<0.0; ***p<0.00:

By using multivariate analysis, Amikacin, it was show that a prior surgical history within the previous five months and ESBL positivity were indicate infection-related issues (95% [CI]: 1.51-1.86, OR=5.1; p=0.023 and 95% [CI]: 2.55-13.1,OR=4.90; p<0.0001***) strongly linked to complications. Antibacterial drug resistance has a significant relationship with the progression of infectious complications and was associated with a history of diabetes (95% [CI]: 0.08-3.11, OR=0.33; p=0.01*). The other parameters, had no significant impact seen in Table 4.

Table 5: Urine culture after postoperative cases

| Participants | Group | Infections | Urine culture | Blood culture | ESBL positivity |
|--------------|---------|---------------------------|------------------|---------------|-----------------|
| 1 | Group A | Antibacterial prophylaxis | Enterococcus spp | No growth | Yes |
| 2 | Group A | UTI, bacteriemia | E.coli | E.coli | Yes |
| 3 | Group B | sepsis | No growth | E.coli | No |
| 4 | Group B | Antibiotic prophylaxis | E.coli | No growth | Yes |
| 5 | Group C | sepsis | E.coli | E.coli | Yes |

The details of the pathogens cultured from infected patients shown in Table 5.

DISCUSSION

The main urogenital tract pathogens are particularly prone to antimicrobial resistance. High levels of antimicrobial resistance are found in isolates from urological patients. The frequent and extensive use of antimicrobial agents, including for AP in typical urological procedures, has been used and to accompanied by rising levels of resistance.^{9, 10} In single-dose antibiotics have been demonstrated to be comparable to a short course of antibiotics in previous studies of patients with sterile urine in terms of lowering the incidence of postoperative bacteriuria and complications. However, some studies have found that short-course antibiotic protocols (based on cephalosporin's) are more effective than single-dose regimens.^{11, 12} In our study to found that Amikacin was frequently suggested as the first choice of antibiotic for TURP prophylaxis due to its simplicity of administration, greater systemic absorption and a safe low toxicity in urinary tract tissues and helped to lower the rate of infectious complications following surgery. However, the steadily rising antibacterial resistance prevalence and the associated infectious complications are worrisome in most nations and could have economically greater impact. Amikacin was selected because of the prostatic tissue's high concentration of the drug with a single dose administered at 3 days and the low rate of Amikacin resistance of isolated pathogens from prostate specimens. The pathogens that were isolated from the participants were all Amikacin-susceptible isolates of *E. coli*,

with the patient who had ESBL-positive *E. coli*. Appropriate antimicrobial prophylaxis, such as Amikacin prophylaxis, cannot completely eradicate the infectious complications following TURP. In our earlier research, we looked into whether using Amikacin after TRUP would lower the incidence of infectious complications.^{13, 14} In our finding to found that Amikacin did reach significant concentrations in the prostate tissue after a single dose at 3 days as opposed to 1 and 2 days and that *E. coli* are extremely vulnerable to it, and decreased incidence of infections following TURP when using Amikacin prophylaxis. Gentamicin, an additional aminoglycoside, decreased postoperative infectious complications. We are agree with the previous study.^{15, 16} In our study, the total participants n=300, who had after TURP, participants in Groups A and B who received Amikacin on Days 1 and 2 experienced infectious complications. TURP compared ESBL producing and non-producing *E. coli* isolated from these participants. Amikacin activity, for example, was significantly decreased in ESBL-positive *E. coli* (95% [CI]:2.55-13.1, OR=4.90; p=0.0001***). If antibiotic resistance is low, extended antibiotic prophylaxis may be beneficial. However, our findings show that when participants have antibiotic-resistant bacteria, especially ESBL-positive bacteria, antibiotic prophylaxis has constraints. While in Group C, which was treated with Amikacin for three days, there was a reduction in ESBL production in the *E.coli*. Urinary tract infections (UTI) caused by Enterobacteriaceae producing extended-spectrum beta-lactamase (ESBL) are becoming more common worldwide. More importantly, it has been reported that two-thirds of UTIs caused by ESBL-producing Enterobacteriaceae recur with ESBL-producing Enterobacteriaceae.¹⁷ Diabetes and earlier surgery were revealed to be possible causes for antimicrobial resistance (95% [CI]: 0.08-3.11, OR=0.33;p=0.01*) and (95% [CI]: 1.51-1.86, OR=5.1;p=0.02*). These outcomes corresponded with a previous study's having found that diabetes was dramatically associated with an elevated risk of post-prostate infectious diseases.^{18, 19} The beneficial effect of 3 days of Amikacin IV therapy was explained by the fact that the delivery of therapy was adequate recovery or postoperative complications and early systemic treatment, thereby improving pathologic outcomes after resection. In the PP and ITT analyses, subsequent analysis revealed that Amikacin had a beneficial effect after 3 days when compared to a single dose. The subgroup with PP analysis demonstrated a decrease in infectious complications following surgery in 3 days after receiving an Amikacin dose. Furthermore, no statistically significant variations between the studies were discovered.^{20, 21}

CONCLUSIONS

The Amikacin was safe for surgical prophylaxis in a single dose at 3 days as compared to 1 and 2 days, s because of the incidence of postoperative complication such as UTI reduced. It was greater role to decrease antibiotic resistance.

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