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Original Research Article

Comparison of Single-Dose vs Multi-Dose Antibiotic Prophylaxis in Clean and Clean-Contaminated Surgeries

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Abstract

Background: Antibiotic prophylaxis is critical in preventing surgical site infections (SSIs). However, there is ongoing debate regarding the need for multi-dose regimens over single-dose prophylaxis in clean and clean-contaminated surgeries.

Objective: To compare the efficacy of single-dose versus multi-dose antibiotic prophylaxis in preventing SSIs in clean and clean-contaminated surgeries.

Methods: This prospective study was conducted at a tertiary care center in Sriganganagar from January 2024 to May 2025. Patients undergoing clean or clean-contaminated surgeries were randomized into two groups: Group A received a single-dose antibiotic preoperatively, while Group B received a multi-dose regimen comprising a preoperative dose followed by postoperative doses for 48 hours. Patients were followed for 30 days to assess the incidence of SSIs.

Results: Out of 400 patients (200 per group), SSI rates were 4.5% in the single-dose group vs 5.5% in the multi-dose group ($p = 0.62$). No significant difference was observed in SSI rates between the two groups for both clean (2.3% vs 3.1%) and clean-contaminated (6.8% vs 7.9%) procedures ($p = 0.62$). Hospital stay and antibiotic-related adverse events were significantly higher in the multi-dose group ($p < 0.05$).

Conclusion: Single-dose antibiotic prophylaxis is as effective as multi-dose in preventing SSIs in clean and clean-contaminated surgeries and is associated with fewer adverse events and lower costs.

Keywords: Antibiotic Prophylaxis, Surgical Wound Infection, Clean Surgical Procedures, Clean-Contaminated Procedures, Anti-Bacterial Agents, Single-Dose Therapy.

Introduction

Surgical site infections (SSIs) continue to be a significant burden on global healthcare systems, accounting for a substantial proportion of healthcare-associated infections [1]. These infections contribute not only to increased postoperative morbidity and mortality but also to prolonged hospital stays, higher treatment costs, and greater use of healthcare resources. In clean and clean-contaminated surgeries, appropriate antibiotic prophylaxis has been shown to play a pivotal role in minimizing the risk of postoperative infections [1-3].

Despite the widespread consensus on the need for prophylactic antibiotics, there remains considerable debate regarding the optimal timing and duration of administration. While prolonged multi-dose regimens have historically been used with the aim of ensuring continued antimicrobial coverage, emerging evidence suggests that prolonged antibiotic use may not offer added benefit and may contribute to resistance and toxicity [3–4]. Recent clinical guidelines by global health authorities have emphasized that a single preoperative dose administered at the appropriate time is often sufficient for infection prophylaxis in most clean and clean-contaminated surgical procedures. However, a subset of studies has reported marginally better outcomes with extended regimens, particularly in surgeries involving gastrointestinal organs or patients at higher risk of infection. In the Indian context, where overuse of antibiotics is prevalent [14] and antimicrobial resistance is a growing concern, defining a safe and effective minimum effective duration of prophylaxis becomes even more crucial [5].

This study was therefore designed to investigate whether single-dose antibiotic prophylaxis is as effective as multi-dose regimens in preventing surgical site infections among patients undergoing elective clean and clean-contaminated surgeries at a tertiary care center in Sriganganagar. By generating local evidence, the study also aims to inform

rational antibiotic use policies and support national antimicrobial stewardship efforts.

Materials and Methods

This was a prospective study conducted at a tertiary care teaching hospital in Sriganganagar, Rajasthan. The study was carried out over a period of 17 months, from January 2024 to May 2025. It aimed to compare the efficacy of single-dose versus multi-dose antibiotic prophylaxis in preventing surgical site infections (SSIs) in patients undergoing clean and clean-contaminated surgical procedures.

Patients aged between 18 and 70 years who were scheduled to undergo elective clean or clean-contaminated surgeries under general or regional anesthesia were considered eligible for inclusion in the study. Patients were excluded if they were immunocompromised (e.g., HIV-positive individuals, those on immunosuppressants), undergoing emergency surgical procedures, or already receiving antibiotics preoperatively for any concurrent infection.

A sample size calculation was performed based on an assumed 5% difference in SSI rates between the two groups, with a confidence level of 95% and a power of 80%. This yielded a minimum requirement of 196 patients per group. To account for potential dropouts and ensure adequate power, the sample size was rounded to 200 participants in each group, resulting in a total of 400 patients. Patients were randomized using a computer-generated block randomization (block size of 4, not stratified) into two groups. Group A consisted of 200 patients who received a single dose of antibiotic prophylaxis preoperatively. Group B also comprised 200 patients and received a multi-dose regimen consisting of the same preoperative antibiotic followed by postoperative doses for 48 hours. The antibiotics used in both groups were either intravenous ceftriaxone 1 gram or cefuroxime 1.5 gram, administered 30 to 60 minutes before the surgical incision. In Group B, the same antibiotic was continued every 12 hours postoperatively for a total of 48 hours.

All surgeries were performed under sterile operating room conditions by qualified surgeons. The type of surgical procedure, duration, intraoperative complications (if any), and wound classification (clean or clean-contaminated) were recorded. Postoperative wound care was standardized across both groups. Patients were followed up daily during their hospital stay and subsequently reviewed on postoperative days 7, 14, and 30. Any signs or symptoms of SSI were recorded and confirmed based on the Centers for Disease Control and Prevention (CDC) criteria for surgical site infection. Data were entered into a structured pro forma and analyzed statistically using Chi-square tests for categorical variables and t-tests for continuous variables to assess differences in infection rates and other secondary outcomes between the two groups.

Results

Table 1: Baseline Characteristics of Study Participants

Characteristic	Group A (Single-Dose)	Group B (Multi-Dose)	p-value
Number of patients (n)	200	200	—
Mean Age (years ± SD)	42.6 ± 13.2	43.1 ± 12.8	0.68
Age Group (years)			
18–30	48 (24%)	51 (25.5%)	0.75
31–50	97 (48.5%)	93 (46.5%)	
>50	55 (27.5%)	56 (28%)	
Sex			0.81
Male	108 (54%)	110 (55%)	
Female	92 (46%)	90 (45%)	
Type of Surgery			0.80
Clean	90 (45%)	92 (46%)	
Clean-contaminated	110 (55%)	108 (54%)	
Comorbidities			0.79
Hypertension	26 (13%)	28 (14%)	
Diabetes Mellitus	22 (11%)	20 (10%)	
None	152 (76%)	152 (76%)	
ASA Physical Status			0.67
ASA I	116 (58%)	119 (59.5%)	
ASA II	70 (35%)	68 (34%)	
ASA III	14 (7%)	13 (6.5%)	

The baseline characteristics of the patients in both groups were statistically comparable, indicating successful randomization and group matching. The mean age was similar in both groups (42.6 ± 13.2

in Group A vs 43.1 ± 12.8 in Group B, p = 0.68), with the majority of participants falling in the 31–50 year age range. Gender distribution was also well balanced, with males comprising slightly more than half of each group (p = 0.81). The proportions of patients undergoing clean and clean-contaminated surgeries were nearly identical across groups (p = 0.80), eliminating procedural bias. The prevalence of comorbidities such as hypertension and diabetes was also evenly distributed, with around 76% of patients in each group being free from chronic medical conditions. ASA physical status grading, an important predictor of perioperative risk, was likewise comparable between groups (p = 0.67), with most patients classified as ASA I or II. These comparable baseline features across groups strengthen the internal validity of the study and support a fair comparison of outcomes between the single-dose and multi-dose antibiotic prophylaxis protocols.

Table 2: Demographics and Surgery Type Distribution

Parameter	Group A (Single-Dose)	Group B (Multi-Dose)	p-value
Mean Age (years)	42.6 ± 13.2	43.1 ± 12.8	0.68
Male : Female Ratio	108 : 92	110 : 90	0.81
Number of Clean Cases	90	92	0.78
Clean-Contaminated Cases	110	108	0.84

The demographic characteristics and surgical type distribution were comparable between the two groups, with no statistically significant difference in mean age (p = 0.68) or gender distribution (p = 0.81). The proportion of clean (45% in Group A vs 46% in Group B) and clean-contaminated surgeries (55% in Group A vs 54% in Group B) was also well balanced (p > 0.05). This homogeneity in baseline parameters ensures the internal validity of the outcome comparisons between the groups.

Table 3: Primary Outcome – Surgical Site Infection (SSI) Rates

Type of Surgery	Group A SSI Rate (%)	Group B SSI Rate (%)	p-value
Clean	2.3% (2/90)	3.1% (3/92)	0.65
Clean-Contaminated	6.8% (7/110)	7.9% (9/108)	0.71
Overall	4.5% (9/200)	5.5% (11/200)	0.62

The overall surgical site infection (SSI) rate in the single-dose group (Group A) was 4.5%, compared to 5.5% in the multi-dose group (Group B), a difference that was not statistically significant (p = 0.62).

When analysed based on surgery type, the SSI rate in clean surgeries was marginally lower in the single-dose group (2.3%) than the multi-dose group (3.1%), while for clean-contaminated procedures, the SSI rate was 6.8% in Group A and 7.9% in Group B. Neither comparison reached statistical significance (p = 0.65 and 0.71, respectively).

These findings suggest that a single preoperative antibiotic dose is as effective as a multi-dose regimen in preventing SSIs in both clean and clean-contaminated surgeries.

Table 4: Secondary Outcomes among the Study Participants

Outcome	Group A	Group B	p-value
Mean Hospital Stay (days)	4.2 ± 1.1	5.3 ± 1.4	<0.01
Antibiotic-related Adverse Events	2% (4 cases)	7.5% (15 cases)	<0.01
Cost of Antibiotic Therapy (INR)	145 ± 12	430 ± 27	<0.001

Significant differences were observed in secondary outcomes favouring the single-dose group. The mean hospital stay was shorter in Group A (4.2 ± 1.1 days) compared to Group B (5.3 ± 1.4 days), which was statistically significant (p < 0.01). This reduction in length of stay may be attributed to decreased need for postoperative monitoring and fewer antibiotic-related side effects.

Adverse drug reactions such as gastrointestinal discomfort and rash were more frequent in the multi-dose group (7.5%) compared to the single-dose group (2%), again reaching statistical significance (p < 0.01). This underscores the importance of minimizing antibiotic exposure to reduce iatrogenic complications.

The cost of antibiotic therapy was substantially lower in Group A (mean INR 145) than in Group B (mean INR 430), which was highly significant (p < 0.001). This cost difference becomes more relevant in resource-constrained settings and public health institutions.

Discussion

The findings of the present study demonstrate that there is no statistically significant difference in surgical site infection (SSI) rates between patients

receiving single-dose antibiotic prophylaxis and those administered a multi-dose regimen, in both clean and clean-contaminated surgical procedures. These results are consistent with a growing body of international and Indian literature suggesting that extended courses of prophylactic antibiotics do not confer additional benefit in reducing SSI rates when compared to a single appropriately timed preoperative dose.

Classen et al. (1992), in one of the landmark studies on surgical antibiotic prophylaxis, concluded that there was no added advantage to extending antibiotic coverage beyond the initial dose, provided it was administered within the optimal window before incision [6]. Similarly, DiPiro et al. (1986) emphasized that a single preoperative dose was sufficient in general surgical cases and that extending antibiotics postoperatively did not reduce infection rates further [7]. Bratzler et al. (2013), in their comprehensive clinical practice guidelines, reiterated that the timing of antibiotic administration is more crucial than its duration, reinforcing the importance of delivering the dose within 60 minutes prior to incision [8].

In the Indian context, clinical evidence supports the effectiveness of single-dose prophylaxis in clean and clean-contaminated surgeries. A study from Kolkata involving 60 patients undergoing elective clean procedures found no significant difference in SSI rates between single-dose and multi-dose groups; however, the single-dose regimen was more cost-effective [9]. Similarly, a prospective investigation, which included 264 general surgery patients, reported an overall SSI rate of just 3.8% with single-dose cefazolin, demonstrating its adequacy in clean and clean-contaminated cases without the need for extended postoperative dosing [10].

Some studies have reported slightly different outcomes. For instance, a multicenter randomized trial published in International Journal of Gynecology & Obstetrics (Wiley, 2016) compared single-dose versus multi-dose cefazolin regimens in cesarean sections.

While the difference in post-operative infection rates was not statistically significant, the multi-dose group had a marginally lower incidence of febrile morbidity (2.1% vs 3.5%) [11]. Similarly, a propensity-score matched analysis involving 902 elective minimally invasive colorectal cancer surgeries from Korea found that SSI rates were 2.0% in the single-dose group and 2.1% in the multi-dose group pre-matching—and 0.9% vs 1.9% post-matching—although neither difference reached statistical significance [12].

These findings suggest that extended antibiotic coverage offers minimal additional benefit and should be reserved for high-risk cases. Conversely, a systematic review and meta-analysis focusing on closed orthopaedic fracture surgeries reported no superiority of multi-dose prophylaxis compared to a single preoperative dose (risk ratio 1.24, 95% CI 0.60–2.60) [13].

Antibiotic stewardship is particularly essential in India, where antimicrobial overuse is a major driver of resistance. The 2019 Indian Council of Medical Research (ICMR) guidelines specifically recommend single-dose preoperative antibiotic prophylaxis for most clean and clean-contaminated surgeries, reserving extended courses only for those with specific risk factors. These guidelines align with global recommendations from both the WHO and CDC, which endorse single-dose regimens in the majority of procedures unless patient comorbidities, implant use, or high contamination risks are present [14].

Conclusion

Single-dose antibiotic prophylaxis is as effective as multi-dose in preventing SSIs in clean and clean-contaminated surgeries, with added benefits of reduced cost, adverse events, and antimicrobial resistance risk. It should be adopted as standard practice in eligible patients.

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