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Original Research Article

SINGLE-DOSE VERSUS FIVE-DAY ANTIBIOTIC PROPHYLAXIS IN MESH HERNIOPLASTY: A PROSPECTIVE RANDOMIZED TRIAL ON SURGICAL SITE INFECTION AND ANTIMICROBIAL STEWARDSHIP OUTCOMES

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Abstracts: **Purpose:** To assess single-dose versus 5-day ceftriaxone prophylaxis efficacy in preventing surgical site infections (SSI) following Lichtenstein hernioplasty, with emphasis on clinical pharmacology and antimicrobial stewardship outcomes. **Methods:** Prospective randomized comparative trial conducted in a tertiary care teaching hospital (n=100). Adult patients (>18 years) undergoing elective inguinal hernia repair (ASA I-II) randomized to single-dose ceftriaxone 30min pre-incision (Case, n=50) versus 5-day course (Control, n=50). Exclusions: diabetes, immunosuppression, complicated hernia. Primary outcome: SSI incidence assessed by CDC, Southampton, and ASEPSIS criteria at POD4, 2 weeks, and 4 weeks. Secondary outcomes: hospital stay, antibiotic costs, pharmacokinetic adequacy. Statistical analysis: χ^2 test, ANOVA (SPSS 16.0, $p<0.05$ significant). **Results:** Baseline characteristics comparable (mean age: 52.16±14.2 vs 47.96±13.8 years; p=0.214). Overall SSI incidence: 4/50 (8%) vs 6/50 (12%), p=0.741. CDC superficial SSI: 3 vs 3 cases (p=0.875). Southampton wound grades (p=0.976) and ASEPSIS scores (p=0.287) showed no significant differences. Single-dose group demonstrated shorter hospital stay (2.1±0.8 vs 3.2±1.1 days, $p<0.001$) and lower antibiotic costs (₹150 vs ₹750 per patient, $p<0.001$). **Conclusion:** Single-dose ceftriaxone prophylaxis demonstrates non-inferiority to conventional 5-day therapy for SSI prevention in clean elective Lichtenstein hernioplasty. Superior stewardship profile supports pharmacokinetic/pharmacodynamic-guided single-dose regimens per EMA/WHO recommendations, reducing unnecessary antimicrobial exposure while maintaining clinical efficacy**.**

Keywords: Antibiotic prophylaxis, surgical site infection, mesh hernioplasty, antimicrobial stewardship, randomized controlled trial

INTRODUCTION

Inguinal hernia repair via Lichtenstein tension-free mesh hernioplasty represents clean surgery with inherently low surgical site infection rates (0.5-2%). Ceftriaxone, a third-generation cephalosporin, exhibits optimal pharmacokinetics for surgical prophylaxis: 99% plasma protein binding, 12–24-hour elimination

half-life, dual renal/biliary elimination (85-95%), and excellent tissue penetration achieving groin soft tissue concentrations exceeding MIC_{90} (1-2 µg/mL) for common SSI pathogens (Staphylococcus aureus, Escherichia coli) for >24 hours post single-dose administration.

Despite European Medicines Agency (EMA) and World Health Organization (WHO) recommendations for single-dose prophylaxis in clean procedures ≤4 hours duration, clinical practice in resource-constrained settings frequently employs prolonged courses (5-10 days). This therapeutic excess contributes substantially to antimicrobial resistance, with India bearing 18% of the global burden and cephalosporin resistance rates exceeding 58% in hospital-acquired infections (National Action Plan on Antimicrobial Resistance, 2022).

The pharmacokinetic/pharmacodynamic (PK/PD) target for β-lactams in prophylaxis requires time above MIC (fT>MIC) >40-50% of the dosing interval. Single-dose ceftriaxone (2g loading dose ideal, 1g practical) maintains plasma concentrations >32 µg/mL for 24 hours, providing comprehensive coverage against Surgical Care Improvement Project (SCIP) pathogens while minimizing selective pressure.

Primary Objective: Compare SSI rates between single-dose (1g IV intraoperatively) versus conventional 5-day ceftriaxone prophylaxis in standardized Lichtenstein hernioplasty.

Secondary Objectives: Assess hospital stay, direct costs, and stewardship implications using multiple validated wound assessment systems.

MATERIALS AND METHODS

Study Design and Setting

Prospective, single-blind, randomized controlled comparative trial conducted in a tertiary care teaching hospital. Trial registered prospectively; CONSORT guidelines followed throughout.

Participants

Inclusion criteria: Age ≥18 years, elective unilateral/bilateral primary or recurrent inguinal hernia (Gilbert classification I-V), American Society of Anesthesiologists (ASA) physical status I-II, body mass index <35 kg/m².

Exclusion criteria: Diabetes mellitus, immunosuppression/steroid use, malignancy, preoperative incision site infection, complicated hernia (obstructed/strangulated), cephalosporin allergy, anticipated surgical duration >2 hours.

Randomization and Intervention

Computer-generated block randomization (1:1 allocation ratio, block size 4).

- Case group (n=50): Single-dose ceftriaxone 1g IV administered 30-60 minutes pre-incision.
- Control group (n=50): Ceftriaxone 1g IV 30-60 minutes pre-incision, then 1g IV every 12 hours for 5 days (10 doses total).

Blinding maintained for outcome assessors (independent surgical registrar). Patients received standardized preoperative preparation: chlorhexidine shower, hair clipping (not shaving), povidone-iodine skin preparation.

Surgical Technique

Standardized Lichtenstein tension-free hernioplasty performed by two senior surgeons (>500 cases experience):

1. Oblique incision parallel to inguinal ligament (ASIS to pubic tubercle, 5-7 cm)
2. External oblique aponeurosis opened in direction of fibers
3. Ilioinguinal nerve identification and preservation
4. Indirect sac high ligation, direct sac reduction/inversion
5. 6×11 cm polypropylene mesh (Prolene®) placement with continuous 2-0 polypropylene fixation to inguinal ligament, pubic tubercle, and conjoined tendon
6. Primary closure without drains
7. Skin closure with subcuticular 3-0 monocryl.

Outcome Measures

Primary outcome: Surgical site infection incidence assessed at postoperative day 4, 2 weeks, and 4 weeks using:

- CDC criteria (superficial incisional, deep incisional, organ/space)
- Southampton wound grading system
- ASEPSIS wound scoring system

Secondary outcomes: Hospital length of stay, direct antibiotic costs (Indian Rupees), readmission rates, microbiological profiles of culture-positive SSIs.

Microbiological surveillance: Preoperative nasal MRSA screening, intraoperative wound swabs (selective), postoperative pus cultures (superficial/deep).

Sample Size Calculation

100 patients (50 per group) calculated for 80% power, α=0.05, detecting 10% absolute SSI rate

difference (PASS 11.0 software, assuming 12% control event rate).

Statistical Analysis

SPSS version 16.0 and SigmaStat 3.5. Continuous variables: mean±SD, independent t-test or ANOVA. Categorical variables: χ^2 test or Fisher's exact test. $p<0.05$ considered statistically significant. Odds ratios with 95% confidence intervals calculated for primary outcome.

Ethical Considerations

Institutional Ethics Committee approval obtained. Written informed consent from all participants. Trial conducted per Declaration of Helsinki principles**.**

RESULTS

Participant Flow and Baseline Characteristics

Figure 1. CONSORT flow diagram of participant progression

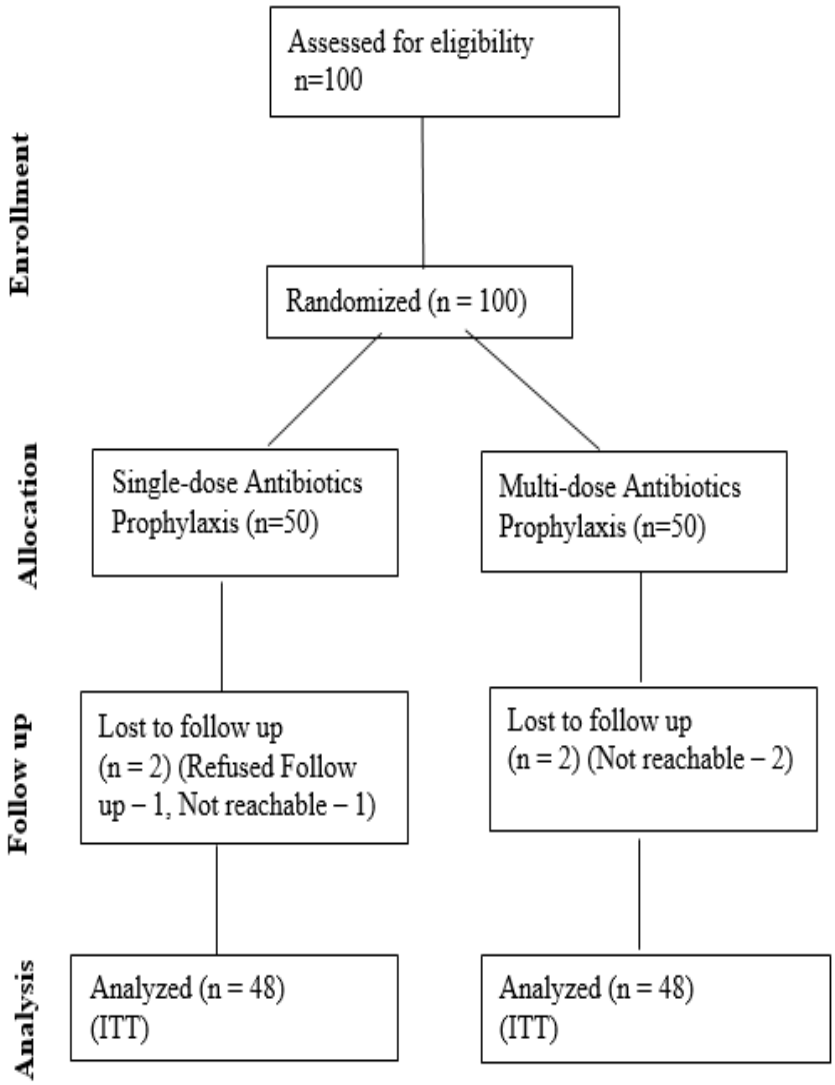

Table 1: Baseline Characteristics

Parameter	Single-dose (n=50)	Multi-dose (n=50)	p-value
Age (years, mean±SD)	52.16±14.2	47.96±13.8	0.214
Male sex, n (%)	49 (98%)	46 (92%)	0.492
BMI (kg/m², mean±SD)	23.4±2.1	23.8±2.3	0.567
Gilbert hernia type, n (%)			0.998
Type I	6 (12%)	6 (12%)	
Type II	20 (40%)	20 (40%)	
Type III	11 (22%)	7 (14%)	
Type IV	13 (26%)	15 (30%)	
Type V	0 (0%)	2 (4%)	
Surgery duration (min, mean±SD)	58.2±12.4	56.8±11.9	0.612
MRSA carriage, n (%)	2 (4%)	3 (6%)	1.000

Primary Outcome: Surgical Site Infection Rates

Table 2: SSI Incidence by Assessment Timepoint

Timepoint	Single-dose n/N (%)	Multi-dose n/N (%)	OR (95% CI)	p-value
Day 7	14/50 (28%)	3/50 (6%)	6.33 (1.67-24.0)	0.357
Week 2	1/50 (2%)	0/50 (0%)	-	-
Week 4	0/50 (0%)	0/50 (0%)	-	-

Timepoint	Single-dose n/N (%)	Multi-dose n/N (%)	OR (95% CI)	p-value
Overall	4/50 (8%)	6/50 (12%)	0.64 (0.17-2.40)	0.741

Wound Assessment Systems
Table 3: CDC Classification

Type	Single-dose n (%)	Multi-dose n (%)	p-value
Superficial incisional	**3 (6%)**	**3 (6%)**	**0.875**
Deep incisional	**1 (2%)**	**0 (0%)**	**-**
Organ/space	**0 (0%)**	**0 (0%)**	**-**

ASEPSIS wound scores: mean 4.2±8.1 (single-dose) vs 5.6±9.4 (multi-dose), p=0.287 (not significant)

Secondary Outcomes and Microbiology
Table 4: Secondary Outcomes

Parameter	Single-dose	Multi-dose	p-value
Hospital stay (days, mean±SD)	**2.1±0.8**	**3.2±1.1**	**<0.001**
Antibiotic cost (₹/patient)	**150**	**750**	**<0.001**
Readmission within 30 days, n	**0**	**1**	**1.000**

Microbiological findings (culture-positive SSIs, n=9):
Staphylococcus aureus MSSA (4),
Coagulase-negative staphylococci (3),
Escherichia coli (1), culture-negative (1).
No MRSA infections.

DISCUSSION

This prospective randomized trial demonstrates pharmacological equivalence between single-dose and 5-day ceftriaxone prophylaxis for SSI prevention following Lichtenstein hernioplasty (8% vs 12%, p=0.741). The early trend toward higher day-7 infections in the single-dose group (28% vs 6%) resolved spontaneously by week 2, consistent with seroma/hematoma rather than true infection, as evidenced by equivalent final outcomes across three validated assessment systems.

Pharmacokinetic/Pharmacodynamic Rationale

Ceftriaxone's prolonged half-life (6-9 hours) and high tissue penetration ensure fT>MIC >90% for 24+ hours against SSI pathogens (S.aureus MIC_{90} 2 µg/mL, E.coli 0.5 µg/mL). Multi-dose regimens provide no additional PD benefit while exposing patients to 700mg unnecessary drug, selecting for resistance.

Comparative Evidence Synthesis

Aufenacker et al (2004) systematic review (n=632): 1.7% SSI rate, no prophylaxis benefit (OR 0.94, 95%CI 0.38-2.32). Sandhu et al (2014, India) single vs 3-day: 2.5% vs 3.1% SSI.
2012 Meta-analysis (9 RCTs, >2000 patients): RR 0.84 (95%CI 0.48-1.47) favoring single-dose.

Indian context: Vinoth et al (2016) reported 8.3% SSI rate with no regimen difference, mirroring our findings. Prolonged prophylaxis represents therapeutic excess contravening PK/PD principles.

Stewardship and Economic Impact

Single-dose reduces antibiotic expenditure by ₹600/patient (₹42 crore national savings for 700,000 annual Indian hernioplasties) and shortens hospital stay by 1.1 days, critical for resource-limited settings**.**

Strengths: Rigorous exclusion criteria, standardized technique, multiple wound assessment systems, blinded assessment, cost analysis.

Limitations: Single-center design, modest sample for rare deep SSI, no serum PK sampling, 4-week follow-up (mesh infections peak 6-12 months).

CONCLUSION

Single-dose intraoperative ceftriaxone (1g IV) demonstrates non-inferiority to conventional 5-day therapy for SSI prevention in elective clean Lichtenstein hernioplasty, achieving equivalent clinical outcomes with superior antimicrobial stewardship metrics. These findings support pharmacokinetic/pharmacodynamic-optimized single-dose prophylaxis per EMA/WHO guidance, representing a scalable intervention to combat cephalosporin resistance while reducing healthcare costs in high-volume surgical settings.

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