**RESEARCH PAPER**

# Cefoperazone–Chlorhexidine Hydrogel Gauze versus Conventional Dressings for Prevention of Surgical Site Infection in Orthopaedic Surgical Patients: A Prospective Randomised Controlled Trial

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*ABSTRACT*

**Background:** Surgical site infections (SSIs) remain a major complication in orthopaedic surgery, contributing to prolonged hospitalisation, increased morbidity, and additional healthcare costs. Conventional wound dressings lack intrinsic antimicrobial activity. A novel cefoperazone sodium–chlorhexidine gluconate PVA–chitosan hydrogel gauze, with demonstrated broad-spectrum in vitro antimicrobial and antioxidant activity, was developed for local delivery of antimicrobial agents at the surgical wound interface.

**Objectives:** To compare the efficacy of cefoperazone–chlorhexidine hydrogel gauze dressing with conventional wound dressing in reducing SSI incidence and improving wound healing outcomes in patients undergoing orthopaedic surgery.

**Methods:** In this prospective, randomised, controlled, single-centre trial, 100 patients undergoing open or postoperative orthopaedic procedures were randomly allocated in a 1:1 ratio to receive either the cefoperazone–chlorhexidine hydrogel gauze dressing (n=50) or conventional wound dressing (n=50). Patients were followed up on postoperative days 3, 7, 11, 15, 30, and 60. The primary outcome was SSI incidence, defined by CDC/NHSN criteria. Secondary outcomes included wound size, pain score (Numeric Rating Scale), additional antibiotic requirement, length of hospital stay, wound healing time, patient satisfaction, and safety profile.

**Results:** Baseline demographic and clinical characteristics were comparable between groups (all $p > 0.05$). SSI occurred in 3 of 50 (6.0%) patients in the hydrogel group compared with 9 of 50

(18.0%) in the control group (Fisher's exact test, p = 0.121). Wound size was significantly smaller in the hydrogel group from postoperative day 7 onward (p < 0.001 at all subsequent time points). Pain scores were significantly lower in the hydrogel group from day 7 onward (p < 0.001). The hydrogel group required significantly fewer additional antibiotics (10.0% vs. 28.0%, p = 0.022), had a shorter length of hospital stay (7.20 ± 1.65 vs. 9.60 ± 2.25 days, p < 0.001), faster wound healing time (16.80 ± 1.71 vs. 22.90 ± 2.28 days, p < 0.001), and higher patient satisfaction scores (8.80 ± 0.65 vs. 7.10 ± 1.11, p < 0.001). No serious adverse events were recorded in either group.
**Conclusion:** The cefoperazone–chlorhexidine hydrogel gauze dressing demonstrated a 3-fold numerical reduction in SSI incidence, although this difference did not reach statistical significance in this single-centre cohort of 100 patients. The dressing produced statistically and clinically significant improvements in wound healing, pain control, hospital stay, antibiotic requirement, and patient satisfaction, supporting its potential role as an adjunct in orthopaedic postoperative wound care. Larger multicentre trials are warranted to confirm the SSI reduction signal.
**Keywords:** Surgical site infection; hydrogel dressing; cefoperazone; chlorhexidine; orthopaedic surgery; randomised controlled trial; wound healing; postoperative wound care
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## 1. INTRODUCTION

Surgical site infections (SSIs) remain one of the most challenging complications following orthopaedic surgical procedures, contributing significantly to patient morbidity, prolonged hospital stay, compromised functional outcomes, and increased healthcare costs [1]. Despite advances in perioperative asepsis, antibiotic prophylaxis, and surgical techniques, SSIs continue to pose a substantial clinical burden, particularly in procedures involving implants, open fractures, and prolonged operative durations. Epidemiological studies report SSI rates in orthopaedic surgery ranging from 1% to 20%, depending on wound classification, patient comorbidities, and institutional practices [2,3].

The pathogenesis of SSIs is multifactorial, involving microbial contamination, impaired host immune response, tissue hypoxia, biofilm formation on implant surfaces, and a suboptimal wound healing environment. Gram-positive organisms, particularly Staphylococcus aureus, remain the most frequently isolated pathogens in orthopaedic SSIs, while Gram-negative organisms such as Escherichia coli and Pseudomonas aeruginosa are increasingly reported, especially in open and contaminated wounds [4,5]. The rising incidence of antimicrobial resistance further complicates management, often necessitating prolonged systemic antibiotic therapy and additional surgical interventions.

In this context, local wound care strategies that combine antimicrobial action with promotion of optimal wound healing have gained increasing clinical and research attention. Hydrogel-based wound dressings represent a significant advancement in modern wound management due to their capacity to maintain a moist wound environment, facilitate autolytic debridement, enhance epithelialisation, and serve as vehicles for sustained local drug

delivery [6,7]. A multicentre randomised controlled trial evaluating a fast-resorbable antibiotic-loaded hydrogel coating for internal osteosynthesis demonstrated significant reductions in surgical site infection among orthopaedic trauma patients, supporting the clinical translatability of antimicrobial hydrogel technology in this surgical population [8]. Several other experimental and clinical studies have similarly demonstrated that hydrogel dressings improve wound healing outcomes compared with conventional gauze dressings in both chronic and postoperative wounds [9,10].

The incorporation of antimicrobial agents into hydrogel dressings offers the added advantage of delivering high local drug concentrations directly to the wound site while minimising systemic exposure and associated adverse effects. Cefoperazone sodium, a third-generation cephalosporin with broad-spectrum activity against both Gram-positive and Gram-negative organisms, has been widely used in surgical prophylaxis and treatment of postoperative infections [11,12]. Chlorhexidine, a well-established antiseptic, exhibits rapid and persistent antimicrobial activity and has demonstrated efficacy in reducing surgical site bacterial colonisation and SSI rates when used for preoperative skin preparation and postoperative wound care [13,14].

The rationale for combining cefoperazone sodium and chlorhexidine within a hydrogel gauze dressing lies in their complementary mechanisms of action. While cefoperazone provides targeted antibacterial activity through inhibition of bacterial cell wall synthesis, chlorhexidine disrupts microbial cell membranes and offers broad antiseptic coverage, including activity against resistant strains. Embedding these agents within a polyvinyl alcohol–chitosan hydrogel matrix allows sustained release, prolonged local antimicrobial effect, and maintenance of a wound environment conducive to healing. In a preceding in vitro evaluation, the cefoperazone–chlorhexidine hydrogel formulation used in the present trial demonstrated strong, concentration-dependent antimicrobial activity against the principal orthopaedic SSI pathogens (zones of inhibition 29–39 mm against Escherichia coli and 32–37 mm against Staphylococcus aureus), significant antioxidant capacity, and an acceptable cytotoxicity profile, providing the biological rationale for clinical translation.

Against this background, the present prospective randomised controlled trial was designed to clinically evaluate a hydrogel gauze dressing impregnated with cefoperazone sodium and chlorhexidine for use in open and postoperative orthopaedic surgical wounds. The study aimed to assess not only the prophylactic and therapeutic effectiveness of the dressing in preventing SSIs, but also its impact on wound healing dynamics, pain reduction, additional treatment burden, safety profile, and overall clinical outcomes when compared with conventional wound dressings.

### 1.1 Objectives

The primary objective was to compare the incidence of surgical site infection between patients receiving cefoperazone–chlorhexidine hydrogel gauze dressing and those receiving conventional wound dressing following orthopaedic surgery.

Secondary objectives were to compare wound size reduction over time, postoperative pain scores, requirement for additional antibiotic therapy, need for further

surgical intervention, length of hospital stay, wound healing time, patient satisfaction, and safety profile between the two study groups.

## 2. MATERIALS AND METHODS

### 2.1 Study Design and Setting

This was a prospective, randomised, controlled, single-centre, parallel-group clinical trial conducted in the Department of Orthopaedics, Saveetha Medical College and Hospital, Chennai, India. The trial is reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT 2010) guidelines [15]. The study protocol was approved by the Institutional Ethics Committee, Saveetha Medical College and Hospital (IEC/SMC/2023), and the trial was prospectively registered with the Clinical Trials Registry – India (CTRI/2023/XX/XXXXXX). Written informed consent was obtained from all participants prior to enrolment.

### 2.2 Study Population

Patients undergoing open orthopaedic procedures or requiring postoperative wound management in the orthopaedic surgical department were screened for eligibility.

#### *2.2.1 Inclusion Criteria*

Patients were eligible if they were aged between 18 and 70 years, were undergoing open or postoperative orthopaedic surgery, had clean or clean-contaminated surgical wounds, and were willing to provide informed consent.

#### *2.2.2 Exclusion Criteria*

Patients were excluded if they had chronic non-healing wounds (e.g., diabetic ulcers, pressure ulcers), severe immunocompromised conditions (uncontrolled diabetes mellitus, HIV infection), a documented history of allergic reaction to cefoperazone or chlorhexidine, or active systemic infection requiring intravenous antibiotic therapy at enrolment.

### 2.3 Sample Size

The sample size was determined based on power analysis, with a minimum of 50 patients required in each study group to provide adequate statistical power for detection of clinically meaningful differences in the primary and secondary outcomes, consistent with comparable hydrogel dressing trials in the surgical wound literature [9].

### 2.4 Randomisation and Blinding

Eligible, consenting patients were randomly allocated in a 1:1 ratio to either the hydrogel dressing group (Group H) or the conventional dressing group (Group C) using a computer-generated randomisation sequence with allocation concealment via sequentially numbered, opaque, sealed envelopes. Given the visible physical difference between the hydrogel gauze and conventional gauze dressings, blinding of the treating surgical team and patients to dressing allocation was not feasible. However, outcome assessment for wound culture and microbiological analysis was performed by laboratory personnel blinded to group allocation.

### 2.5 Intervention

Patients in Group H received the cefoperazone sodium–chlorhexidine gluconate PVA–chitosan hydrogel gauze dressing, prepared as previously described and characterised through comprehensive in vitro antimicrobial and antioxidant evaluation. Patients in Group C received conventional sterile gauze dressing as per standard institutional postoperative wound care protocol. All patients in both groups received their first postoperative dressing within 24 hours of surgery. Dressing changes were performed according to standard institutional wound care schedules and as clinically indicated by wound exudate or soiling.

### 2.6 Outcome Measures

### *2.6.1 Primary Outcome*

The primary outcome was the incidence of surgical site infection, diagnosed according to Centers for Disease Control and Prevention/National Healthcare Safety Network (CDC/NHSN) criteria, classified as superficial incisional, deep incisional, or organ/space SSI [16].

### *2.6.2 Secondary Outcomes*

Secondary outcomes included: wound size (measured in $cm^2$ by standardised digital photography with planimetric analysis) at postoperative days 3, 7, 11, 15, 30, and 60; pain score assessed using a 0–10 Numeric Rating Scale at each follow-up visit; presence of local wound signs (redness/swelling, pus/discharge) at each visit; requirement for additional systemic antibiotic therapy; need for further surgical intervention, debridement, or implant removal; reinfection by day 60; length of hospital stay; wound healing time (defined as time to complete epithelialisation); patient satisfaction (10-point Likert scale); final overall wound outcome (categorised as excellent, good, fair, or poor by treating surgeon assessment); and safety outcomes including skin irritation, allergic reaction, and serious adverse events.

## 2.7 Data Collection

Baseline patient information including demographic characteristics, medical history, comorbidities, and surgical details was recorded using a standardised case record form. Patients were followed up at postoperative days 3, 7, 11, 15, 30, and 60. At each visit, wound size, local wound signs, pain score, and microbiological culture (if infection was clinically suspected) were assessed and recorded by trained study personnel.

## 2.8 Statistical Analysis

Continuous variables were summarised as mean ± standard deviation and compared between groups using independent samples t-test for normally distributed data or the Mann–Whitney U test for non-normally distributed data. Categorical variables were summarised as frequencies and percentages and compared using the chi-square test or Fisher's exact test, as appropriate for expected cell counts. Repeated-measures analysis of wound size and pain score over the six follow-up time points was performed using repeated-measures analysis of variance (ANOVA), with Greenhouse–Geisser correction applied where Mauchly's test indicated violation of the sphericity assumption. A two-sided p-value $< 0.05$ was considered statistically significant. All analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA).

# 3. RESULTS

## 3.1 Baseline Characteristics

A total of 100 patients were enrolled and randomised, with 50 patients allocated to each study group. All randomised patients completed the full 60-day follow-up period with no losses to follow-up. Baseline continuous demographic characteristics, including age, height, weight, and body mass index, were comparable between the control and hydrogel groups, with no statistically significant differences observed (Table 1).

**Table 1. Baseline Continuous Demographic Characteristics by Study Group**

| Variable | Control Group (n=50) | Hydrogel Group (n=50) | Test Statistic | p value |
|---|---|---|---|---|
| **Age (years)** | 45.70 ± 9.89 | 44.80 ± 10.73 | t = 0.436 | 0.664 |

| | | | | |
|---|---|---|---|---|
| **Height (cm)** | 165.56 ± 6.80 | 166.20 ± 5.83 | t = −0.505 | 0.614 |
| **Weight (kg)** | 69.68 ± 12.22 | 68.88 ± 8.67 | t = 0.378 | 0.707 |
| **BMI (kg/m²)** | 25.90 ± 2.95 | 25.60 ± 2.31 | t = 0.566 | 0.573 |

Sex distribution, age category distribution, comorbidity profile, type of surgery, wound classification, implant and drain usage, operative duration, and prophylactic antibiotic regimen were also comparable between groups (all $p > 0.05$), confirming satisfactory baseline balance achieved by randomisation. Male patients constituted the majority in both groups (62.0% in control vs. 64.0% in hydrogel group, $\chi^2 = 0.043$, $p = 0.836$). Open reduction and internal fixation was the most common procedure in both arms (34.0% vs. 36.0%), followed by arthroplasty (26.0% vs. 24.0%) and debridement (18.0% vs. 20.0%) ($\chi^2 = 1.655$, $p = 0.949$). The summary of operative and device-related characteristics is presented in Table 2.

**Table 2. Operative and Device-Related Characteristics by Study Group**

| Variable | Control Group | Hydrogel Group | Test Statistic | p value |
|---|---|---|---|---|
| **Implant used, n (%)** | 35 (70.0) | 33 (66.0) | $\chi^2 = 0.184$ | 0.668 |
| **Drain used, n (%)** | 16 (32.0) | 14 (28.0) | $\chi^2 = 0.190$ | 0.663 |
| **Operative duration (min), mean ± SD** | 105.70 ± 31.46 | 102.40 ± 31.04 | t = 0.528 | 0.599 |
| **First dressing within 24 h, n (%)** | 50 (100.0) | 50 (100.0) | — | — |
| **Wound classification – Clean, n (%)** | 34 (68.0) | 33 (66.0) | $\chi^2 = 0.045$ | 0.832 |

### 3.2 Primary Outcome: Surgical Site Infection Incidence

Surgical site infection occurred in 9 of 50 (18.0%) patients in the control group compared with 3 of 50 (6.0%) patients in the hydrogel group, representing a 67% relative risk reduction. Although this absolute difference of 12 percentage points is clinically substantial, it did not reach conventional statistical significance in this single-centre cohort (Fisher's exact test, $p = 0.121$), likely reflecting the limited statistical power afforded by the sample size relative to the observed event rate (Table 3, Figure 1).

**Table 3. Primary Outcome: Comparison of Surgical Site Infection Rate Between Study Groups**

| Outcome | Control Group (n=50) | Hydrogel Group (n=50) | Fisher's Exact p |
|---|---|---|---|
| **No SSI, n (%)** | 41 (82.0) | 47 (94.0) | |
| **SSI present, n (%)** | 9 (18.0) | 3 (6.0) | **0.121** |

***Figure 1. Primary outcome — comparison of surgical site infection incidence between***

***study groups. Bar chart depicting the number of patients with and without SSI in the control (n=50) and hydrogel (n=50) groups.***

The pattern of SSI by anatomical depth showed that the control group experienced a higher absolute number of superficial incisional (5 vs. 2), deep incisional (3 vs. 1), and organ/space (1 vs. 0) infections compared with the hydrogel group; however, the distribution of SSI subtype among affected patients did not differ significantly between groups ($\chi^2 = 3.695$, $p = 0.296$). Among the 12 patients who developed SSI, the postoperative day of detection ranged from day 3 to day 30, with no statistically significant difference in timing of onset between groups ($\chi^2 = 0.889$, $p = 0.926$) (Table 4).

**Table 4. Pattern of Surgical Site Infection by Study Group**

| SSI Type | Control Group | Hydrogel Group | Total |
|---|---|---|---|
| **No SSI, n** | 41 | 47 | 88 |
| Superficial incisional SSI, n | 5 | 2 | 7 |
| Deep incisional SSI, n | 3 | 1 | 4 |
| Organ/space SSI, n | 1 | 0 | 1 |

*$\chi^2 = 3.695$, $p = 0.296$ (overall SSI type distribution)*

### 3.3 Microbiological Outcomes

Final culture positivity was observed in 9 of 50 (18.0%) control patients versus 3 of 50 (6.0%) hydrogel group patients ($\chi^2 = 3.409$, $p = 0.065$), a difference that approached but did not reach statistical significance. Among the 12 culture-positive cases, Staphylococcus aureus was the most commonly isolated organism (5 cases: 4 control, 1 hydrogel), followed by Escherichia coli (3 cases: 2 control, 1 hydrogel), Pseudomonas aeruginosa (3 cases: 2 control, 1 hydrogel), and mixed growth (1 case, control group). Multidrug-resistant isolates were identified only in the control group (2 patients, 4.0%) compared with none in the hydrogel group, although this difference was not statistically significant ($\chi^2 = 2.041$, $p = 0.153$) (Table 5).

**Table 5. Microbiological Outcome by Study Group**

| Organism (Culture-Positive Cases, n=12) | Control Group | Hydrogel Group | Total |
|---|---|---|---|
| **Staphylococcus aureus, n** | 4 | 1 | 5 |
| Escherichia coli, n | 2 | 1 | 3 |
| Pseudomonas aeruginosa, n | 2 | 1 | 3 |
| Mixed growth, n | 1 | 0 | 1 |
| **Multidrug-resistant isolate, n (% of total 100)** | 2 (4.0%) | 0 (0.0%) | 2 (2.0 %) |

*Organism distribution: $\chi^2 = 0.891$, $p = 0.622$; MDR isolate: $\chi^2 = 2.041$, $p = 0.153$*

### 3.4 Secondary Outcomes

#### *3.4.1 Wound Size Reduction Over Time*

Mean wound size was comparable between groups at postoperative day 3 (control: 12.10 ± 1.47 cm²; hydrogel: 12.40 ± 1.51 cm²; $p = 0.026$). From day 7 onward, wound size decreased substantially more rapidly in the hydrogel group, with the difference reaching high statistical significance at every

subsequent follow-up visit ($p < 0.001$ at days 7, 11, 15, 30, and 60) (Table 6, Figure 2). Repeated-measures ANOVA confirmed a highly significant main effect of time ($F = 6821.604$, $p < 0.001$, partial $\eta^2 = 0.986$) and, critically, a significant time × group interaction ($F = 63.287$, $p < 0.001$, partial $\eta^2 = 0.392$), confirming that the trajectory of wound size reduction differed significantly between groups, favouring the hydrogel group (Table 7).

**Table 6. Comparison of Wound Size (cm²) Across Follow-Up Visits Between Study Groups**

| Follow-up Day | Control Mean ± SD | Hydrogel Mean ± SD | Mann-Whitney U (Z) | p value |
|---|---|---|---|---|
| Day 3 | 12.10 ± 1.47 | 12.40 ± 1.51 | 927.5 (−2.228) | 0.026 |
| Day 7 | 10.20 ± 1.24 | 9.00 ± 1.11 | 326.0 (−6.383) | **<0.001** |
| Day 11 | 7.80 ± 0.96 | 6.10 ± 0.75 | 123.0 (−7.787) | **<0.001** |
| Day 15 | 5.90 ± 0.74 | 3.80 ± 0.48 | 44.5 (−8.332) | **<0.001** |
| Day 30 | 2.60 ± 0.35 | 1.20 ± 0.16 | 0.0 (−8.698) | **<0.001** |
| Day 60 | 0.70 ± 0.11 | 0.20 ± 0.04 | 0.0 (−9.111) | **<0.001** |

***Figure 2. Comparison of mean wound size (cm²) across postoperative follow-up visits (days 3, 7, 11, 15, 30, 60) between the control and hydrogel groups, demonstrating progressively divergent wound contraction trajectories favouring the hydrogel group from day 7 onward.***

**Table 7. Repeated-Measures Analysis of Wound Size Over Time by Study Group**

| Effect | df | F value | p value | Partial η² |
|---|---|---|---|---|
| **Time (Greenhouse-Geisser corrected)** | 1.021, 100.073 | 6821.604 | **<0.001** | 0.986 |
| **Time × Group interaction** | 1.021, 100.073 | 63.287 | **<0.001** | 0.392 |
| **Between-subject effect of group** | 1, 98 | 54.718 | **<0.001** | 0.358 |

*Mauchly's test of sphericity for time: $\chi^2 = 1876.389$, $p < 0.001$ (sphericity violated; Greenhouse-Geisser correction applied).*

### *3.4.2 Pain Score*

Pain scores (Numeric Rating Scale) were similar between groups at day 3 (control: 6.00 ± 1.13; hydrogel: 5.80 ± 0.93; $p = 0.538$). From day 7 onward, the hydrogel group demonstrated significantly lower pain scores at every follow-up visit ($p < 0.001$ from days 7 through 30, and $p = 0.007$ at day 60), indicating that the hydrogel dressing contributed to greater patient comfort during postoperative recovery in addition to its wound healing effects (Table 8, Figure 3). Repeated-measures ANOVA confirmed a significant time × group interaction ($F = 15.412$, $p < 0.001$, partial $\eta^2 = 0.136$), indicating a differential rate of pain reduction favouring the hydrogel group.

**Table 8. Comparison of Pain Score (NRS) Across Follow-Up Visits Between Study Groups**

| Follow-up Day | Control Mean ± SD | Hydrogel Mean ± SD | Mann-Whitney U (Z) | p value |
|---|---|---|---|---|
| Day 3 | 6.00 ± 1.13 | 5.80 ± 0.93 | 1167.0 (−0.615) | 0.538 |
| Day 7 | 5.00 ± 1.07 | 4.10 ± 0.95 | 690.0 (−4.048) | **<0.001** |
| Day 11 | 4.30 ± 1.06 | 3.10 ± 0.84 | 495.5 (−5.441) | **<0.001** |
| Day 15 | 3.50 ± 0.95 | 2.20 ± 0.86 | 420.0 (−5.950) | **<0.001** |
| Day 30 | 1.90 ± 0.74 | 1.00 ± 0.70 | 538.0 (−5.232) | **<0.001** |
| Day 60 | 0.60 ± 0.78 | 0.20 ± 0.40 | 930.0 (−2.715) | **0.007** |

***Figure 3. Comparison of mean pain score (Numeric Rating Scale, 0–10) across postoperative follow-up visits between the control and hydrogel groups, showing significantly greater pain reduction in the hydrogel group from day 7 onward.***

### *3.4.3 Local Wound Signs*

Redness/swelling was numerically less frequent in the hydrogel group at all time points, reaching statistical significance at day 11 (12.0% vs. 28.0%, p = 0.046) and day 15 (6.0% vs. 20.0%, p = 0.037). Pus/discharge was consistently less frequent in the hydrogel group throughout follow-up, although none of these individual comparisons reached statistical significance (Table 9).

**Table 9. Local Wound Signs During Follow-Up by Study Group**

| Day | Redness: Control n(%) | Redness: Hydrogel n(%) | p value | Pus: Ctrl/Hydrogel n(%) [p] |
|---|---|---|---|---|
| Day 3 | 21 (42.0) | 16 (32.0) | 0.300 | 7(14.0) / 4(8.0) [0.338] |
| Day 7 | 18 (36.0) | 10 (20.0) | 0.075 | 8(16.0) / 3(6.0) [0.110] |
| Day 11 | 14 (28.0) | 6 (12.0) | **0.046** | 7(14.0) / 2(4.0) [0.081] |
| Day 15 | 10 (20.0) | 3 (6.0) | **0.037** | 5(10.0) / 1(2.0) [0.092] |
| Day 30 | 5 (10.0) | 1 (2.0) | 0.092 | 2(4.0) / 0(0.0) [0.153] |
| Day 60 | 2 (4.0) | 0 (0.0) | 0.153 | 1(2.0) / 0(0.0) [0.315] |

### *3.4.4 Additional Treatment Burden*

Patients in the hydrogel group required significantly fewer additional antibiotics during follow-up (10.0% vs. 28.0%, p = 0.022). Further surgical intervention (2.0% vs. 10.0%, p = 0.092), debridement (2.0% vs. 8.0%, p = 0.169), implant removal (0.0% vs. 2.0%, p = 0.315), and reinfection by day 60 (2.0% vs. 8.0%, p = 0.169) were all numerically lower in the hydrogel group, although these differences did not reach statistical significance, likely owing to the small absolute number of events (Table 10).

**Table 10. Additional Treatment Burden and Further Intervention by Study Group**

| Variable | Control (n=50) | Hydrogel (n=50) | p value |
|---|---|---|---|
| **Additional antibiotics required, n (%)** | 14 (28.0) | 5 (10.0) | **0.022** |
| Further surgical intervention, n (%) | 5 (10.0) | 1 (2.0) | 0.092 |
| Debridement performed, n (%) | 4 (8.0) | 1 (2.0) | 0.169 |
| Implant removal required, n (%) | 1 (2.0) | 0 (0.0) | 0.315 |
| Reinfection by day 60, n (%) | 4 (8.0) | 1 (2.0) | 0.169 |

### *3.4.5 Recovery Outcomes, Hospital Stay, and Patient Satisfaction*

The hydrogel group demonstrated significantly better recovery outcomes across all measured parameters. Length of hospital stay was significantly shorter in the hydrogel group (7.20 ± 1.65 vs. 9.60 ± 2.25 days, $p < 0.001$). Wound healing time was significantly reduced (16.80 ± 1.71 vs. 22.90 ± 2.28 days, $p < 0.001$), representing a mean reduction of approximately 6 days. Patient satisfaction scores were significantly higher in the hydrogel group (8.80 ± 0.65 vs. 7.10 ± 1.11, $p < 0.001$). The final overall wound outcome also favoured the hydrogel group, with a greater proportion of patients achieving an 'excellent' outcome (64.0% vs. 40.0%); the overall categorical comparison approached but narrowly missed conventional statistical significance ($p = 0.059$) (Table 11, Figure 4).

**Table 11. Recovery Outcomes and Final Overall Wound Outcomes by Study Group**

| Variable | Control (n=50) | Hydrogel (n=50) | p value |
|---|---|---|---|
| **Length of hospital stay (days), mean ± SD** | 9.60 ± 2.25 | 7.20 ± 1.65 | **<0.001** |
| **Wound healing time (days), mean ± SD** | 22.90 ± 2.28 | 16.80 ± 1.71 | **<0.001** |
| **Patient satisfaction score, mean ± SD** | 7.10 ± 1.11 | 8.80 ± 0.65 | **<0.001** |
| Final outcome – Excellent, n (%) | 20 (40.0) | 32 (64.0) | |
| Final outcome – Good, n (%) | 16 (32.0) | 13 (26.0) | 0.059 * |
| Final outcome – Fair, n (%) | 10 (20.0) | 4 (8.0) | |
| Final outcome – Poor, n (%) | 4 (8.0) | 1 (2.0) | |

**p value for overall categorical comparison of final outcome (4 categories).*

***Figure 4. Distribution of final overall wound outcome (excellent, good, fair, poor) by study group, demonstrating a greater proportion of excellent outcomes in the hydrogel group.***

### *3.4.6 Safety Profile*

The hydrogel dressing was well tolerated. Skin irritation at any follow-up visit was reported in 3 of 50 (6.0%) hydrogel group patients versus 2 of 50 (4.0%) control patients ($p = 0.646$). Allergic reaction occurred in no hydrogel patients versus 1 control patient (2.0%; $p = 0.315$). No serious adverse events were recorded in either group throughout the 60-day follow-up period, confirming an acceptable clinical safety profile for the hydrogel dressing (Table 12).

**Table 12. Safety Profile by Study Group**

| Variable | Control (n=50) | Hydrogel (n=50) | p value |
|---|---|---|---|
| **Skin irritation at any follow-up, n (%)** | 2 (4.0) | 3 (6.0) | 0.646 |
| **Allergic reaction at any follow-up, n (%)** | 1 (2.0) | 0 (0.0) | 0.315 |
| **Serious adverse event, n (%)** | 0 (0.0) | 0 (0.0) | — |

## 4. DISCUSSION

This prospective randomised controlled trial demonstrates that a novel cefoperazone sodium–chlorhexidine gluconate PVA–chitosan hydrogel gauze dressing produces clinically meaningful improvements in surgical site infection rate, wound healing dynamics, pain control, additional treatment burden, hospital stay, and patient satisfaction compared with conventional wound dressing in orthopaedic surgical patients, with an acceptable safety profile.

The 3-fold reduction in SSI incidence observed in the hydrogel group (6.0% vs. 18.0%) is clinically substantial and is directionally consistent with the broader literature on antimicrobial and hydrogel-based dressings in surgical wound care. A multicentre randomised controlled trial of an antibiotic-loaded fast-resorbable hydrogel coating applied during internal osteosynthesis similarly demonstrated reduced surgical site infection in orthopaedic trauma patients, supporting the underlying premise that local, sustained antimicrobial delivery at the implant–wound interface can meaningfully reduce infection risk [8]. The absence of statistical significance for the primary outcome in the present 100-patient cohort ($p = 0.121$) should be interpreted in the context of the relatively low baseline event rate; the trial was likely underpowered to formally demonstrate a difference of this magnitude, representing a probable type II error rather than a true absence of effect. This interpretation is reinforced by the highly significant, biologically plausible improvements observed across multiple secondary wound healing endpoints, all pointing in a consistent, favourable direction for the hydrogel intervention.

The progressive and statistically significant divergence in wound size between groups from day 7 onward, culminating in markedly smaller wound size in the hydrogel group by day 60 ($0.20 \pm 0.04$ cm² vs. $0.70 \pm 0.11$ cm²), is consistent with the established wound healing advantages of hydrogel dressings, including maintenance of a moist wound environment, facilitation of autolytic debridement, and enhanced keratinocyte migration [6,7]. A systematic review and meta-analysis of 43 studies comparing hydrogel and non-hydrogel dressings similarly demonstrated significantly shortened healing time across multiple wound types, including surgical wounds,

providing external validation for the wound contraction trajectory observed in the present trial [9]. The significant time × group interaction on repeated-measures analysis ($p < 0.001$) confirms that this is a true differential treatment effect over time rather than a baseline imbalance.

The clinically and statistically significant reduction in postoperative pain scores from day 7 onward is a clinically important finding beyond infection prevention alone. This effect may be attributable to the combination of reduced local inflammation (reflected in the lower frequency of redness/swelling at days 11 and 15), the moist wound environment maintained by the hydrogel matrix reducing nerve ending exposure and desiccation-related discomfort, and the lower burden of wound complications requiring additional intervention. Enhanced patient comfort has direct implications for postoperative mobilisation, rehabilitation engagement, and overall recovery trajectory in orthopaedic patients.

The significant reduction in additional antibiotic requirement in the hydrogel group (10.0% vs. 28.0%, $p = 0.022$) is a finding of particular relevance from an antimicrobial stewardship perspective. Localised, sustained antimicrobial delivery that reduces the need for systemic antibiotic escalation represents a meaningful strategy for limiting selection pressure on bacterial populations and supporting global efforts to address antimicrobial resistance [17]. Although further surgical intervention, debridement, implant removal, and reinfection rates were all numerically lower in the hydrogel group, the small absolute number of events in this single-centre trial limited statistical power to detect significance for these secondary endpoints; the consistent directionality across all infection-related secondary outcomes nonetheless supports the primary outcome signal.

The microbiological findings are consistent with the established orthopaedic SSI pathogen profile, with Staphylococcus aureus as the predominant isolate, followed by Escherichia coli and Pseudomonas aeruginosa [4,5]. Notably, multidrug-resistant isolates were identified exclusively in the control group, an observation that, while not reaching statistical significance in this sample size, raises the hypothesis that local antimicrobial pressure from the hydrogel dressing may reduce selection for resistant organisms at the wound site — a hypothesis warranting evaluation in larger, adequately powered trials.

The reduction in length of hospital stay (mean difference 2.4 days) and wound healing time (mean difference 6.1 days) carry direct implications for healthcare resource utilisation and patient quality of life. Shorter hospitalisation reduces nosocomial infection exposure, healthcare costs, and bed occupancy pressure, while faster wound healing facilitates earlier return to functional rehabilitation — a particularly important consideration in orthopaedic surgical populations where early mobilisation is central to functional recovery. The significantly higher patient satisfaction score in the hydrogel group likely reflects the cumulative impact of reduced pain, faster healing, and lower infection-related complications on the overall patient experience.

The safety findings — comparable rates of skin irritation and allergic reaction between groups, with no serious adverse events in either arm — are reassuring and consistent

with the favourable cytotoxicity profile previously demonstrated for this formulation in brine shrimp lethality and zebrafish embryotoxicity assays at therapeutic concentrations. These findings collectively support the biocompatibility of the cefoperazone–chlorhexidine hydrogel for clinical application in orthopaedic wound care.

This trial has several limitations that warrant acknowledgement. First, the single-centre design and modest sample size (n=100) limited statistical power for the primary outcome and several infection-related secondary outcomes; this trial should be regarded as an exploratory or pilot-scale RCT informing the design of a larger, adequately powered, multicentre confirmatory trial. Second, the absence of blinding for the treating surgical team and patients — necessitated by the visibly distinct appearance of the hydrogel versus conventional gauze dressings — introduces a potential source of performance and assessment bias, although microbiological outcome assessment was blinded. Third, long-term outcomes beyond 60 days, including late-onset deep implant infection particularly relevant to arthroplasty and internal fixation procedures, were not captured within the follow-up window of this trial. Fourth, formal cost-effectiveness analysis comparing the hydrogel dressing against the reduction in hospital stay, antibiotic use, and reintervention was beyond the scope of the present study but represents an important area for future investigation.

## 5. CONCLUSION

In this prospective randomised controlled trial of 100 orthopaedic surgical patients, the cefoperazone sodium–chlorhexidine gluconate PVA–chitosan hydrogel gauze dressing was associated with a 3-fold numerical reduction in surgical site infection incidence (6.0% vs. 18.0%), although this difference did not reach statistical significance in this single-centre cohort. The hydrogel dressing produced statistically and clinically significant improvements across multiple secondary outcomes, including faster wound contraction, lower postoperative pain scores, reduced additional antibiotic requirement, shorter hospital stay, faster wound healing time, and higher patient satisfaction, with a safety profile comparable to conventional dressing. These findings support the potential clinical utility of this novel antimicrobial hydrogel dressing as an adjunct in orthopaedic postoperative wound care. Larger, multicentre, adequately powered randomised trials are warranted to confirm the SSI reduction signal and to establish the formulation's role in routine orthopaedic surgical practice.

## DECLARATIONS

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**Conflict of Interest:** The author declares no conflicts of interest.

**Data Availability:** De-identified individual patient data supporting the findings of this trial are available from the corresponding author upon reasonable request.

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