

Is chlorhexidine-gluconate superior than Povidone-Iodine in preventing surgical site infections? A multicenter study

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Abstract

Objective: To compare the efficacy of povidone-iodine and chlorhexidine gluconate scrubs in preventing surgical site infections.

Methods: The randomised controlled clinical trial was conducted from May 2012 to April 2013 in two public-sector hospitals of Pakistan; one each in Karachi and Islamabad. Patients undergoing clean or clean contaminated surgeries were included and were randomly assigned to one of the two groups: group I comprised patients whose skin was preoperatively disinfected using 10% povidone-iodine, and in group II by 2% chlorhexidine gluconate in 70% alcohol. A predesigned proforma was filled for all patients to record demographic data, diagnosis, surgical procedure and antibiotic used. Patients in both groups were followed up for one month postoperatively to monitor any signs of surgical site infections. SPSS 16 was used for statistical analysis.

Results: Of the 388 patients from the two hospitals, 220(57%) were in group I and 168(43%) were in group II. Surgical site infection was observed in 22(10%) cases in group I and 12(7.1%) in group II ($p=0.324$). *Pseudomonas aeruginosa* (23.5%) was the predominant pathogen associated with surgical site infections followed by *Staphylococcus aureus* (17.6%).

Conclusion: Chlorhexidine gluconate was associated with lower infection rates compared to povidone-iodine; but it was not statistically significant.

Keywords: Povidone-iodine, Chlorhexidine gluconate scrubs, Surgical site infections. (JPMA 65: 1197; 2015)

Introduction

Surgical site infections (SSIs) are considered a major infection control concern throughout the world as they are associated with serious morbidity, mortality and high cost.¹ A study ranked SSI as the most common type of nosocomial infections, accounting for 29% of the total nosocomial infection.²

Although complete elimination of infections in surgical patients is deemed impossible but a reduction in the incidence to a minimal level can produce great benefit for the patients and would also economise hospital resources.³

Effective skin decontamination prior to surgery is indicated as one of the preventive measures to reduce the risk of SSIs. Many disinfectants are available for the purpose. Choice of antiseptic for skin preparation is primarily based on surgeon's knowledge of the product's efficacy, cost and ease of use.⁴ The most common skin preparation agents used today include products containing iodophor or chlorhexidine gluconate. Efficacy

of these agents has been studied in different studies reported in literature and there are conflicting reports on the efficacy of two.^{5,6} Currently povidone-iodine is being used for preoperative skin preparation in most of the hospitals in Pakistan, but some recent international reports suggested that chlorhexidine could be a better choice for reducing postoperative wound infections.

The current study was planned to compare the efficacy of two antiseptics in preventing SSIs in general surgery units of two hospitals.

Subjects and Methods

The randomised controlled trial was conducted during May 2012 and April 2013 at General Surgery Unit II of Jinnah Postgraduate Medical Centre (JPMC), Karachi, and General Surgery Unit I of Pakistan Institute of Medical Sciences (PIMS), Islamabad. JPMC is one of the largest public-sector hospitals of Pakistan located in the metropolitan city of Karachi. The hospital serves a large number of patients from all over Pakistan, especially from the provinces of Sindh and Balochistan. PIMS is also one of the largest public-sector hospitals of Pakistan located in the federal capital Islamabad. This hospital caters to patient population mainly from the provinces of Punjab, Khyber Pakhtunkhwa (KPK) and Azad Jammu & Kashmir (AJK).

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All patients aged 18-60 years undergoing elective clean or clean contaminated surgery in selected wards of above mentioned hospitals were included in the study. Patients having diabetes, infection adjacent to the site of surgery or those undergoing emergency surgery and unwilling to participate were excluded.

Sample size of 200 (100 in each group) was calculated using OpenEpi software (Kelsey method) with 80% power and two-sided significance level of 90% on the basis of previous study which showed a significant difference in SSI rates (p-value:0.011) between patients receiving povidone-iodine (14.6%) or chlorhexidine-gluconate (4.5%) for preoperative skin antisepsis prior to elective surgery.⁷ So, a total sample size of 400 patients (200 patients from JPMC and 200 patients from PIMS) was worked out to determine any significant difference between the two groups.

A predesigned proforma was used to record patient's demographics, diagnosis, surgical procedure, use of prophylactic antibiotic, antiseptic agent (povidone-iodine or chlorhexidine), patient's outcome and follow-up.

Ethical clearance was obtained from ethical review committee of JPMC and PIMS, and written consent was obtained from all participants.

After the finalisation of elective surgery list (a day before the operation day), patients were randomly assigned (using lottery method) to one of the treatment groups i.e. group I comprised patients whose skin was scrubbed with povidone-iodine (10%) as per the standard protocol in the hospital, and group II comprised patients whose skin was disinfected using 2% chlorhexidine-gluconate in 70% isopropyl alcohol. For randomisation purpose, lottery method was used in which slips were picked for each patient by the investigator. Operating surgeon and operating theatre (OT) technician were informed about the particular antiseptic agent to be used for patient's skin preparation.

After completion of the surgical procedure, the proforma was filled for the patient to record basic demographics, contact number and baseline information regarding clinical diagnosis, surgical procedure, use of prophylactic antibiotic and duration of surgery. All patients were monitored daily by surgeon for any signs of SSI until discharge from hospital. Centre for Disease Control (CDC, USA) definition for SSIs was used to identify the infected patients which states that "Infection would be regarded as surgical site infection if it occurs within 30 days of procedure and has at least one of the following symptoms; purulent drainage from

the wound, pain or tenderness, localised swelling, redness, malodour, or fever."⁸

After discharge patients were issued follow-up cards and were advised to visit the outpatient department (OPD) weekly to have a check-up for any signs of infection. This was a double-blind study i.e. patients as well as the surgeons monitoring the patients for SSI were unaware of the antiseptic used on that particular patient at the time of surgery. Wound swab was collected using transport media swabs (BBL™ Culture Swab™ Plus Amies Medium without Charcoal) for patients showing any signs of infection and the sample was sent to microbiology laboratory of respective hospitals for culture and sensitivity testing. In case no sign of infection was observed until 30 days, the patient was considered as having no SSI. Patients were also contacted on phone to investigate about their wound condition and it was recorded in the proforma. A patient was only considered lost to follow-up if he did not come for follow-up and the investigators were unable to contact the patient on phone.

Data was analysed using SPSS 16. The results were presented as mean (X) + standard deviation (SD) for continuous variables like age and percentage, and for categorical variables like gender, prophylactic antibiotic therapy, wound infection, pathogen and sensitivity patterns etc. Chi-square test was used for comparison of infection rates in two groups. In all statistical analysis only $p < 0.05$ was considered significant. Both intention to treat (ITT) analysis as well as per-protocol analysis was applied to determine any significant difference in results.

Results

Of the 388 patients from the two hospitals, 220(57%) were placed in group I and 168(43%) were in group II. after accounting for dropouts during the 30-day post-surgery follow-up, 352(91%) patients completed the study; 201(57%) in group I and 151(43%) in group II. The loss to follow-up was mainly attributable to the wrong contact numbers provided by the patients since the follow-up was being done simultaneously on telephone.

Basic demographics of all patients undergoing surgery in both arms were noted (Table-1). The distribution of surgical procedures and pattern of prophylactic antibiotic use in both groups showed no statistically significant difference ($p > 0.05$).

Overall 22(10%) patients developed SSI in group I, while 12(7.1%) patients from group II developed SSI during follow-up. Although infection rates were lower in group II compared to group I, but ITT analysis showed that this difference was not statistically significant ($p = 0.324$).

Table-1: Baseline data of Povidone-Iodine and Chlorhexidine-gluconate group.

Variable	Antiseptic agent used		p-value
	Povidone-Iodine (n=220)	Chlorhexidine gluconate (n=168)	
Gender			
Male	89(40.4%)	63 (37.5%)	0.55
Female	131 (59.6%)	105 (62.5%)	
Male: Female ratio	1:1.5	1:1.7	
Age in years			
(Mean $\pm$ S.D)	41.32 $\pm$ 15.5	40.4 $\pm$ 13.91	0.57
Antibiotic prophylaxis			
None	11(5.0%)	9(5.4%)	0.86
Ceftriaxone	106(48.2%)	94(55.9%)	0.13
Ciprofloxacin	11(5.0%)	13(7.7%)	0.26
Augmentin	52(23.6%)	34(20.2%)	0.42
Ciprofloxacin + Flagyl	13(5.9%)	6(3.6%)	0.44
Other	27 (12.3%)	12(7.1%)	0.11
Surgical wound class			
Clean	150 (68.2%)	106 (63.1%)	0.29
Clean contaminated	70(31.8%)	62 (36.9%)	0.29

SD: Standard deviation.

Infection rates in both groups were slightly higher in JPMC compared to PIMS (Table-2) but neither hospital showed a significant difference in the SSI rates between the two groups. Distribution of infection rates in clean and clean contaminated surgeries between the two groups were also noted (Table-3). Per protocol analysis (after excluding the lost to follow-up cases) also showed no significant difference between the two groups ($p=0.345$).

Two (0.9%) patients from group I reported having itching and rashes at the site of surgery while none of the patients from group II manifested or reported any signs of allergic reactions.

Culture and sensitivity test was performed for 21(61.8%) patients. No bacterial pathogen was isolated in 9(43%) cases. *Pseudomonas aeruginosa* (23.5%) was the predominant pathogen followed by *Staphylococcus aureus* (17.6%) and *Escherichia coli* (11.7%) and *Enterococcus* spp. (5.8%). Sensitivity results showed that all four (100%) *Ps. aeruginosa* isolates were sensitive to ofloxacin, amikacin, meropenem, piperacillin/tazobactam and polymixin B, while sensitivity to ceftazidime, gentamycin and tetracycline was 75%, 50% and 0% respectively. *S. aureus* isolates showed 100% sensitivity to vancomycin, fusidic acid and chloramphenicol, 67% to clindamycin, 33% to erythromycin, co-trimoxazole and amikacin while none of the *S. aureus* isolate (0%) was sensitive to penicillin and ofloxacin. *E. coli* was isolated from only two samples out of which one isolate was resistance to all commonly prescribed antibiotics (including ceftriaxone, ofloxacin, amikacin, meropenem) except polymixin B, while second *E. coli* isolate was also sensitive to amikacin and piperacillin/tazobactam.

Discussion

The randomized clinical trial was designed as a sequence to the infection control initiatives of Pakistan Medical Research Council (PMRC) in different public-sector hospitals.⁹⁻¹¹ The primary goal of the study was to find out if we can achieve a reduction in SSI rates by employing

Table-2: SSI rates in Povidone-Iodine and Chlorhexidine-gluconate groups (Intention to treat analysis).

Study Centre	Control (Povidone-Iodine) group		Test (Chlorhexidine gluconate) group		p-value
	Total patients	Patients With SSIs	Total patients	Patients With SSIs	
PIMS, Islamabad	98	9 (9.2%)	77	6 (7.8%)	0.77
JPMC, Karachi	122	13 (10.6%)	91	6 (6.6%)	0.30
TOTAL	220	22 (10.0%)	168	12 (7.1%)	0.32

PIMS: Pakistan Institute of Medical Sciences

JPMC: Jinnah Postgraduate Medical Centre

SSIs: Surgical Site Infections.

Table-3: Infection rates in clean vs. clean contaminated surgeries (Intention to treat analysis).

Study Centre	Control (Povidone Iodine) group		Test (Chlorhexidine gluconate) group		p-value
	Total patients	Patients With SSIs	Total patients	Patients With SSIs	
Clean	150	14 (9.3%)	106	6 (5.6%)	0.28
Clean contaminated	70	8 (11.4%)	62	5 (8.1%)	0.52
TOTAL	220	22 (10.0%)	168	12 (7.1%)	0.32

SSI: Surgical Site Infections.

chlorhexidine gluconate instead of povidone-iodine for preoperative cutaneous antisepsis in our public-sector hospitals as very little data from Pakistan was available on the comparison of these two antiseptics for umbilical cord cleansing¹² but no local reports could be found to establish the relation of these antiseptics with SSI rates in surgical patients. This study looked at the ultimate outcome i.e. development of SSI in patients undergoing surgery in order to find out the efficacy of two widely used antiseptics in clinical practice.

Results of our study suggested a 45.4% reduction in SSI rates after using 2% chlorhexidine gluconate in 70% isopropyl alcohol instead of the currently used standard i.e. povidone-iodine, but this difference in SSI rates was not statistically significant. Similar results have also been observed by other researchers who reported povidone-iodine and chlorhexidine gluconate in alcohol to be almost equally effective.⁶ A study reported SSI rates of 9.5% in povidone-iodine group vs. 7.0% in chlorhexidine group ($p=0.364$) among patients undergoing clean surgery.¹³ Similarly, no difference in terms of efficacy of the two antiseptics was observed by another study.¹⁴ However, some studies also report the superiority of one antiseptic over the other e.g. a prospective randomised clinical trial, including 813 patients showed significantly lower SSI rates in chlorhexidine group compared to povidone-iodine group (9.5% vs 16.1%; $p=0.004$)¹⁵ while a trial employing sequential implementation design showed that there was a significant increase in SSI rates when chlorhexidine gluconate was used instead of povidone-iodine (8.2% vs 4.8%; $p=0.001$) for pre-operative cleansing.¹⁶ From Pakistan none of the studies to our knowledge has assessed the impact of preoperative chlorhexidine gluconate instead of povidone-iodine on rates of SSI, but one study reported a significant reduction in the risk of omphalitis and neonatal mortality associated with the use of 4% chlorhexidine gluconate for umbilical cord cleansing of newborns.¹⁷

All these conflicting results could be due to various reasons, including the microbiological flora of the hospitals where study is conducted, methodology employed, control of confounding factors like antibiotic prophylaxis or inclusion of risk group like diabetics, and, above all, the surgical wound class of patients. For example, in studies¹⁵ which found chlorhexidine to be superior, only patients undergoing clean contaminated surgery were included while others¹⁶ included all the four wound classes and found better results with povidone-iodine. While there is an argument that the actual effect of antiseptic specifically could be observed if we compare the SSI rates of

clean/clean contaminated only but this is also true that if an antiseptic is better then it should give better results in all types of procedures provided other confounding factors are controlled. Further, a single antiseptic agent which could give better results in all four classes will definitely be more preferable and practical than using different antiseptics for different wound classes.

Regarding hypersensitivity reactions to the antiseptic, only 2 patients from povidone-iodine group manifested mild allergic symptoms i.e. irritation or itching at the site of antiseptic application while none of the patients from chlorhexidine group manifested any sort of allergy. Similar results have been reported by others who did not observe any hypersensitivity reaction in patients whom chlorhexidine gluconate was used for cutaneous antisepsis but observed 2 (0.8%) mild allergic reactions in povidone-iodine group.¹⁸ A number of other clinical trials that evaluated the safety and efficacy of chlorhexidine gluconate also reported no hypersensitivity reactions after using chlorhexidine gluconate on intact skin,¹⁹ but such reactions have been reported with the use of chlorhexidine impregnated catheters or when it is used for bathing.²⁰ This is particularly important in our setup where mostly surgeons are reluctant to use chlorhexidine gluconate because of the perception that it leads to allergic reactions.

Ps. aeruginosa was found to be the predominant pathogen causing SSI followed by *S. aureus*. Similar pattern of pathogens was reported earlier.^{21,22} This pattern is slightly different from our previous study in which *E. coli* was the predominant pathogen.⁹ This difference could be attributed to the ratio of different surgical procedures within the two studies. In the previous study, SSI rates in all four wound classes were studied and abdominal procedures constituted the major portion of total surgeries which are usually complicated by gram-negative enteric flora while this study mainly involved the clean procedures.¹¹ Amikacin and meropenem showed better sensitivity results for isolated pathogens followed by ofloxacin but cephalosporins (ceftriaxone, cefixime or ceftazidime) did not yield desirable results. Sensitivity results were in concordance with other studies.²³ Higher resistance against cephalosporins could be due to the indiscriminate use of the antibiotic in our hospitals which can also be observed in the present study as ceftriaxone was used for prophylactic purpose in 52% cases.

The limitation of our study was the unequal number of participants in both groups but attempt was made to overcome the limitation in the analysis phase through

calculating p-values using chi-square test which took into account the total population of both groups. The strength of our study was that we tried to control the confounding factors in both groups by excluding the risk groups i.e. diabetics and elderly to avoid bias, but we did not intervene in the antibiotic prophylactic practices though we considered those during analysis phase as there was no statistically significant difference in terms of prophylactic antibiotic used between the two groups.

Conclusion

Reduced rate of SSI in chlorhexidine gluconate group compared to povidone-iodine group was noticed but since it was not statistically significant we may conclude that povidone-iodine and chlorhexidine gluconate are equally effective for preoperative cutaneous antisepsis. Further cost analysis studies taking into account the infection rates and side effects can guide to choose an antiseptic which can give desirable results in terms of infection control as well as cost effectiveness.

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