Skin preparation with chlorhexidine versus povidone-iodine for the prevention of surgical site infection

SUPERIOR UNIVERSITY

Thesis Submitted to

The Superior University Lahore

In Partial Fulfillment of the

Requirement for the Degree of

Master of Science in Allied Health Sciences

By

HAFIZA YUSRA WAQAR.

SU91-MSAHW-S24-066

Session: 2024-2026

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Examination Committee:

Session Chair: Signature: _____

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DEDICATION

This thesis is dedicated to my parents, whose unwavering support, unconditional love, and constant encouragement have been the foundation of my journey. Your sacrifices and belief in me have been my greatest strength.

To my family, thank you for being my pillars of support, for celebrating my successes, and for standing by me in times of struggle. Your presence has made this achievement all the more meaningful.

I am deeply grateful to each of you for inspiring me to reach higher and pursue my dreams.

ACKNOWLEDGEMENT

In the name of Allah, the most Gracious, the most Merciful.

I am extremely thankful to Almighty ‘Allah’ Who is the entire source of knowledge and wisdom endowed to mankind, for providing me with the acumen and vision to complete this endeavor.

I would like to express my profound gratitude to my supervisor for his/her wise counsel and encouraging attitude towards this study. I am extremely grateful to him/her for immensely facilitating me during my study period by ensuring the provision of favorable circumstances and conducive environment. This project would not have been possible without his support and expert guidance.

In the end, I would like to extend my deepest gratitude to my family members. Without their encouragement, I would not have been able to complete this endeavor.

Hafiza Yusra Waqar

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LIST OF ABBREVIATIONS

Abbreviation	Full Term
CHG	Chlorhexidine gluconate
PVI	Povidone-iodine
SSI	Surgical site infection
SSIs	Surgical site infections
CDC	Centers for Disease Control and Prevention
WHO	World Health Organization
RCT	Randomized controlled trial
SR	Systematic review
MA	Meta-analysis
CI	Confidence interval
RR	Relative risk
OR	Odds ratio
HR	Hazard ratio
ARR	Absolute risk reduction
RRR	Relative risk reduction
NNT	Number needed to treat
AE	Adverse event
CRBSI	Catheter-related bloodstream infection
CFU	Colony-forming units
IPA	Isopropyl alcohol
w/v	Weight per volume
v/v	Volume per volume

ABSTRACT

Background: Surgical site infections (SSIs) are a common postoperative complication that may increase morbidity, hospitalization, and cost of medical care. Prior to surgery, it is a precaution to observe proper skin antisepsis. Though common antiseptics are povidone-iodine and chlorhexidine, it is still debated in clinics how effective they are in the prevention of SSIs.

Objective: To determine the effectiveness of chlorhexidine and povidone-iodine in skin preparation to reduce the occurrence of surgical site infections in elective surgery patients.

Methods: Services Hospital Lahore, 200 patients that underwent elective orthopedic, general, obstetric, and gynecological operations were involved in a comparative cross-sectional study. The number of patients was divided in equal amounts (n = 100) into two groups, i.e., povidone-iodine and chlorhexidine. Perioperative, clinical and demographic data were collected by use of medical records. The surgical site infections were monitored on seven consecutive days after the surgery and data regarding the type and treatment of SSIs as well as the outcomes was recorded. The statistical analysis involved descriptive statistics, chi-square tests, independent t-tests, and binary logistic regression to control the confounding factors.

Results: The overall incidences of SSI reduced in the chlorhexidine group (6% and 14% in the chlorhexidine and povidone-iodine groups, respectively) (p = 0.048). When age, BMI, diabetes, length of operation, and ASA class were considered, the incidence of SSI was significantly low with the use of chlorhexidine (adjusted OR = 0.44, 95% CI: 0.25-0.78, p = 0.005). Increased BMI, diabetes, and increased surgical length and increased ASA were also strong predictors of SSI. The chlorhexidine group of 4.2 +- 1.1 days (p = 0.001) had a shorter mean hospitalization than the povidone-iodine group of 5.6 +- 1.8 days (p = 0.001).

Conclusion: Chlorhexidine skin preparation had significantly reduced the cases of surgical site infection and hospital stay as compared to povidone-iodine skin

preparation. Routine chlorhexidine-impregnated skin antisepsis during preoperative processes is recommended to improve surgical outcomes.Keywords: Surgical site infection, Chlorhexidine, Povidone-iodine, Skin antisepsis, Elective surgery, Infection prevention

Keywords

Chapter 1

INTRODUCTION

The term skin preparation antisepsis is defined as the application of chemical antiseptics to minimize or eradicate the microbial colonization on the skin before it undergoes invasive surgeries such as surgery (1,2). The most effective way to prevent surgical site infections (SSIs) is to maintain the space near the incision or puncture site in a clean and sterile setting. Common antiseptics include alcohol, povidone-iodine and chlorhexidine gluconate. The kinds of germs that these therapies have been shown to kill are different and so are their effectiveness and lifespan. Infection management in minor and major surgery facilities should be an effective practice of skin antisepsis. A surgical site infection (SSI) is an inseparable complication of an invasive surgery. To diagnose an infection at the surgical site (SSI), certain symptoms including purulence, erythema, pain, or elevated temperature must be present or related to a number of over 10 colony-forming units per millimeter of tissue. Four categories of surgical procedures and wounds include clean, clean-contaminated, contaminated and dirty-infected. It is divided according to the level of infection and inflammation, and the specific location of the anatomy (1). A clean wound after surgery will decrease the risk of infection. The rates of infection would have been lower than 2 with contaminated surgeries less than 10% (Leaper, 1995) (2). The Health Protection Agency (HPA) of UK then periodically gathers national data on surgical site infections (SSIs), but only in the case of orthopaedic surgery. HPA determined 438,679 operations in 237 NHS hospitals in the period between April 2006 and March 2011. The incidence of clean surgical site infection (SSI) is as follows: 0.8% of hip prostheses, 0.5% of limb amputations, 0.6% of knee prostheses and 1% of heart operations (excluding CABG). This is a sharp contrast of the 10% level of surgical site infections found by the HPA in large bowel procedures carried out in 2006 to 2011 after contamination. The number of clean surgeries exposes a large proportion of patients to surgical site infections (SSIs) although the illnesses are lower in clean surgeries compared to other types of operations. Tens of thousands of sanitary treatments are carried out every year; washing the skin prior to surgery and after surgery could be of paramount importance in the prevention of surgical site infections (SSI) compared to washing during non-sterile procedure. It is because

cleaning methods minimize the risk of catching an infection due to the possibility of being contaminated internally (4,5). A number of organizations recommend the use of antiseptic before proceeding with an operation to remove transient bacteria and lower the number of commensal organisms (5,6).

These organizations are connected to Royal College of Surgeons of England, Association to Perioperative Practice, Association of Perioperative Registered Nurses (AORN), and CDC. Thus, it is the norm of cleansing the surgical area using an antiseptic. The antiseptic and application method is believed to have an influence on the effectiveness of skin preparation. The area around the wound can be cleaned with various antiseptic interventions (7). Some types of bacteria can be killed by the use of iodine and iodophors. This includes the bacilli of tuberculosis, the viruses, the fungi, the Gram-positive and Gram-negative bacteria. When they are inside the cells, they oxidize releasing free iodine in the place of the microbial components. The stabilizing and surfactant properties of iodophors contribute to the liberation of free iodine. Iodophor has become a widely used antiseptic substance used by most modern antiseptics instead of iodine. Iodophor is otherwise known as povidone iodine (PI). It is formed as a result of the free iodine molecules binding themselves to a polymer, like povidone. The normal concentration of iodine in 10 percent PI formulations is 1 percent. One of the ways of preparing PI is through the use of iodophor cleanse and paint. This is a single step aqueous formulation which utilizes polymer (3M). DuraPrep is an alternative. It is prepared using a polymer that is water-insoluble and an alcoholic iodophor. Drink changes the proteins of bacterial cell walls. Mycobacterium tuberculosis is a bacteria that is killed by alcohol. It also eliminates the germs, viruses, and fungus. The usefulness of alcohol is also greatly dependent on the amount of alcohol and not the type of alcohol. Chlorhexidine gluconate comes in an alcoholic and aqueous state, and it is effective against various bacteria, viruses, and yeasts. Skin antisepsis can help to prevent surgery site infection (SSIs) by eliminating all residual bacteria and other pathogenic agents. The skin is not a sterile surface as it has three million bacteria per square centimeter. The adhesive property of antiseptics to stratum corneum is extended to enhance their period of stay on the skin as well as increasing the chemical efficacy of antiseptics. The main aim of antiseptics is to destroy bacteria colonizing and contaminating surfaces by inhibiting, destroying them chemically or physically. Microbes are normally located in the lowest layers of stratum corneum, which is the outermost

layer of the dehydrated cells. This means that they are able to stay in that place a long time even after desquamation of the epidermis. Transients are merely temporary and commensals are long-term residents of the skin. Some people would say that commensals are more challenging to eliminate than migratory species. Commensal bacteria like Pseudomonas, Propionibacterium species, diphtheroid organisms as well as Staphylococci will cause severe human infections when allowed to proliferate. The growth of pathogens on the wound weakens the immunity of the host, which may result in a surgical site infection (SSI). These disorders tend to affect the skin of the patient. Although the use of antiseptics on the surgical location is now a norm, it is important to consider the effectiveness of different antiseptics in order to make prudent treatment decisions. The National Institutes of Health and Clinical Excellence (NICE) state that the most effective agents to use in prepping the skin prior to treatments are povidone-iodine or chlorhexidine. However, alcohol-based antiseptics are as effective as water-based antiseptics. One of the recent studies involved the comparison of chlorhexidine in alcohol and aqueous povidone-iodine on 849 patients who underwent clean-contaminated procedures. Incidence of incisional superficial infection (4.2 vs. 8.6 in the PI group; p-value 0.08), and incisional deep infection (1.0 vs. 3.0 in the PI group; p-value 0.05) was significantly lower with the use of chlorhexidine solution compared to the PI group (5). A recent detailed research study compared the effect of chlorhexidine-alcohol and PI-aqueous skin antiseptic on the prevention of surgical site infections (SSIs). Five RCTs (randomized controlled trials) are included into the review. The risk ratio (RR) of chlorhexidine-alcohol is 0.65 (95% CI 0.50 to 0.85) lower in comparison to PI according to the authors in the risk of surgical site infections (SSIs). One of the questions that need to be answered is whether alcohol in chlorhexidine-alcohol solutions is effective in preventing surgical site infections more than PI-aqueous solutions. This is the most important question which is answered in the study. The outcomes related to clean surgical wounds are more difficult to find since this analysis includes randomised controlled trials (RCTs) that compare clean and infected wounds (11).

Every year, surgery site infections afflict between 300,000 and 500,000 people in the United States, even when prophylactic procedures such as povidone-iodine skin washing are available. Better skin antisepsis can reduce chances of developing surgical site infections because the skin of the patient can serve as a source of

infection (8). The CDC recommends the use of 2% chlorhexidine solution to wash the area surrounding a vascular catheter implantation. Similar to 27 million surgeries that are conducted in the US annually, the Centers of Disease Control and Prevention has not prescribed a particular antiseptic that may be employed to minimize the chances of surgical site infections in the post-surgery period.

Surgical site infection (SSI) is one of the types of healthcare-associated infection (HAI). Approximately 11 percent of patients will have issues at the surgical site within 30 days after the general surgery (1). They are related to increased mortality, increased operations, and increased hospitalization (2). World Health Organization (WHO) defines preoperative skin antisepsis as one of the key elements that help to avoid postoperative surgical site infections (SSIs) (3).

Povidone iodine (PVI) is an economic antiseptic that is non-resistant to antibiotics and also cross-resistant in the surgical procedures. One potential alternative antiseptic solution is the use of chlorhexidine (CHX) which is a broad spectrum antibacterial that harms bacterial cytoplasmic membranes, but does not induce bacterial resistance (4). In the attempt to reduce SSIs, some clinical practice guidelines advise using antiseptic skin dressing of CHX gluconate and iodophor; however, there remains the debate of the most effective agent (3,5). The cost of alcoholic chlorhexidine skin preparation is higher than that of other easily accessible options, although a meta-analysis of high-quality randomized controlled trials (RCTs) showed no advantages to it (6). Some meta-analyses showed that chlorhexidine was better than PVI in the prevention of postoperative surgical site infections (SSIs) (7,8). Recent, high-caliber, randomized controlled studies have been well used to support the ongoing controversy regarding the best agent.

RATIONALE OF STUDY

Even though the most widespread antiseptics are povidone-iodine and chlorhexidine, these two antiseptics have differences regarding their antibacterial spectrum, long-term activity, and mechanisms of action. Povidone-iodine is a common alternative to chlorhexidine, which has been known to have longer effects and is also more effective in case of a broader range of infections. It is necessary to determine the relative effectiveness of these drugs to develop evidence-based surgical practices, improve patient outcomes, and develop standardized infection control programs.

OBJECTIVES

- To compare the effectiveness of chlorhexidine and povidone-iodine as antiseptic agents in preventing surgical site infections (SSIs),

Chapter 2

LITERATURE REVIEW

The biggest cause of morbidity and mortality in hospital and clinic settings worldwide is Surgical site infection (SSIs). These diseases cause almost 20% of all the hospital-acquired infections and thus can render surgery and infection control very challenging. Surgical site infections (SSI) is one of the largest issues in the medical sector. The rate of surgery site infections (SSIs) in the US is 2 to 5 percent of surgery patients which is between 160,000-300,000 SSIs annually. They lead to surgical discomfort and fever and increase length of stay (an increase of 23 days on average). Medical care is becoming expensive as more surgeries, treatments and hospital stay is increasing. This has a massive impact on finances of people. The worst outcome is that the risk of dying because of SSIs has nearly tripled. The second most common form of hospital-acquired illness is the so-called surgical site infections (SSIs) which occur in 14-16% of all hospitalized patients. Seven to twenty percent of individuals with post-cesarean surgery problems get infected. Coronary artery disease (CAD) is the most common serious operation in women with a global prevalence of 18.6% (13).

Postpartum surgical site infections (SSIs) may disrupt the breastfeeding process of a mother and the bonding between a mother and a child. This causes the length of her hospital stay to increase, increases her chances of infection, increases the amount of medical resources required, increases the cost of her hospitalization and places an increased burden of stress on the family members. The infection rate is determined by a plethora of factors most of them being patient specific. Some of the contributing variables are low socioeconomic level, immunosuppression, corticosteroids use, hemorrhage, maternal health issues, high body mass index (BMI), late labor and delivery, ruptured membranes, no preventive care, and an emergency cesarean delivery. Surgical site infections (SSIs) can be caused by external elements such as hospital supplies, operating room environments, tool sterilization, skin preparation of patients, and hand hygiene. When bacteria of the vagina or natural skin commensals enter the surgical site after a CD, the chances of an SSI increase. The most common are mixed polymorphic diseases. These infections could include gram-negative bacilli, group B streptococci, anaerobes, enterococci. The correct antiseptic must be used when preparing the skin of the surgery to prevent surgical site infections (SSIs).

The two skin disinfectants that have been most studied are povidone-iodine and chlorhexidine-alcohol. This can be explained by the fact that they are effective against a large variety of pathogens such as gram-positive and gram-negative bacteria, viruses, fungi, and Mycobacterium tuberculosis (9).

Before the procedure of cesarean delivery (CD), one should not use a specific skin antiseptic to prevent surgical site infections (SSIs). A systematic review based on the application of skin antiseptics in preventing surgical site infections (SSIs) during cardiac interventions (CIs). It was found that poor quality of data shows that povidone-iodine was more likely to induce bacterial growth compared to chlorhexidine-alcohol. Hand sanitizers, antibiotics, strict aseptic wound management, and additional measures can then reduce the likelihood of the occurrence of post-surgical wound infection at the surgical sites. Guidelines have been published by the World Health Organization (WHO), Centers for Disease Control and Prevention (CDC), and National Institute for Health and Clinical Excellence (NICE) to prevent surgical site infections in the post-surgical period. The use of skin antiseptics is an essential aspect of this undertaking. Povidone-iodine is the most commonly applied antiseptic on the skin in the clinical setting (12). Recent studies indicate that the chlorhexidine is a stronger skin antiseptic than the povidone-iodine. Professionals are faced with a problem of selecting skin disinfectants. Before surgery, it is necessary to clean the skin. Skin antisepsis is largely the key to the success of the postoperative period and the ultimate outcomes of the patient. There are many forms of bacteria present on the skin. Some pathogens have the ability of leading to surgical wound infections in case they are not managed. The fact that the less amount of skin bacteria is closely related to a reduced number of post-operative infections means that it is urgently necessary to thoroughly organize this aspect of the care procedures (14).

Antiseptics used to prepare the skin are usually povidone-iodine and chlorhexidine. Its effects are long-term and the impact of the bacteria it has is long lasting as it rapidly disposes off the bacteria. However, although developed later than chlorhexidine, povidone-iodine became widely used in the field of surgery and medicine when its effectiveness and safety were noticed (15). In 2021, Wade and his colleagues conducted another network meta-analysis, but now only examined clean surgery. This research involved both non-randomized and randomized research. The

authors overstated the importance of this concentration of antiseptic as they wrongly classified and assessed three researches with 4.0-5.0% concentration of chlorhexidine in alcohol rather than 0.5% and 2%. We concurred with Wade and his associates that the best method of preventing SSIs is to use higher concentration of chlorhexidine in alcohol (e.g. 4.0%). Nevertheless, due to the fact that they place them in a wrong category, it is difficult to scrutinize this concept precisely (6).

Since 2017, several randomized controlled trials (RCTs) have been performed, and they offer new knowledge on this subject matter. Randomized controlled trials are commonly used to compare various skin antiseptics including: 4.0% chlorhexidine in alcohol vs. povidone-iodine in water or iodine in alcohol vs. chlorhexidine in water. In a quantitative assessment, all these dissimilar comparisons cannot be incorporated in a typical meta-analysis (7). Network meta-analysis is a useful method of comparing two or more RCTs simultaneously since the entire data on the trials are aggregated with various comparisons. Several skin antiseptic treatment of various concentrations can be drawn in comparison or indirectly. Through incorporating every trial which directly pits two drugs, direct effect estimates are derived in a manner analogous to an ordinary pairwise meta-analysis. In order to compute indirect effects at all the indirect channels within the network, we employ standard comparators. Where both direct and indirect effects are known, then the two are compounded to obtain network estimate. In terms of indirect evidence only the network estimate is equivalent to the indirect effect estimate. Network meta-analyses have a larger dataset since they consider the whole network compared to paired meta-analyses (18).

There is need to recommend evidence-based guidelines with respect to the type and quantity of skin antiseptic to apply as skin preparation is a critical component of traditional surgical care. The aim of this study was to find published randomized controlled trials (RCTs), which examined two or more antiseptic skin preparation products and compared different guidelines on surgical site infection (SSI) prevention. We aim to provide a clinical practice recommendation and a subjective assessment of the effectiveness of various skin antiseptic solutions and concentrations to prevent surgical site infections in adult patients, who have undergone operations (19).

Infection at or around the site of surgery incision takes place in 0.5-3% of surgery patients. Microorganisms that are populating the patients skin are believed to be the main cause of causative pathogens. Preparation of intact skin is currently done using alcohol-based solution, either with chlorhexidine gluconate or povidone iodine compounds (20). Although the US Centers for Disease Control and Prevention (CDC) and Surgical Infection Society endorse the use of either substance, the World Health Organization (WHO) suggests the use of alcohol-based solutions containing chlorhexidine gluconate as the one that is better than povidone iodine. Three to five Compared to povidone iodine, two meta-analyses demonstrated that chlorhexidine gluconate disinfectants have a significant effect on the occurrence of surgical site infections (SSIs) (6,7). Recent randomized clinical trials refute these findings and indicate that povidone iodine is not better than chlorhexidine gluconate. As such variables as drugs selection, exposure duration, and frequency of application might influence the outcomes of skin preparation, the optimal skin preparation is still debatable. These characteristics have not been sufficiently standardized as had been shown in previous studies. The bacteriostatic effect of iodophors and chlorhexidine on the skin is long-term, whereas alcohol does not have aftereffects. Research shows that such effect may not be so evident in iodophors compared to chlorhexidine (21). Chlorhexidine was more effective than iodophors in a number of applications, including the prevention of bloodstream infections associated with the use of catheters and hospital-acquired infections in intensive care units. The UK National Institute of Health and Care Excellence recommends chlorhexidine compounds as a result of the need to prepare the skin of patients in ready preparation of surgery. Even though the use of chlorhexidine is generally common in non-operating environments, particularly in the intensive care unit when it comes to patient washing and handling of vascular access, the rising trends of reduced susceptibility or resistance to the drug are alarming (22). Since it is believed that povidone iodine is not as effective as it could be, there appears to lack sufficient evidence to justify substituting chlorhexidine gluconate with povidone iodine in all surgical cases. The trials were restricted to some surgical procedures, were single center, and /or relatively small in their size; they were not a comparison of drugs with similar alcohol-based formulations (23).

It is believed that preoperative skin antisepsis is a significant preventive tool in the reduction of the surgical site infection (SSI) and that it must be used to lessen the microbial count in the surgical location (24). The use of povidone-iodine and chlorhexidine as two popular antiseptic agents has been widely researched as to its capability of preventing microorganism proliferation. Povidone-iodine, an iodophor, helps to release free iodine and thus has a broad-spectrum antibacterial activity in the face of bacteria, viruses and fungi. This penetration of microbial cell walls by this iodine leads to protein and nucleic acid structures being disrupted (25). Drug is commonly used due to its rapid effect and low systemic absorption, however, the presence of organic materials, e.g. blood or serum, can decrease its efficiency (26).

The cationic bisbiguanide chlorhexidine binds to the stratum corneum and causes bacterial cell membranes to rupture and intracellular content to precipitate leading to long-term residual effect (27). Alcohol-based chlorhexidine preparations are found to be more effective than aqueous preparations and/or povidone-iodine on bactericidal action, rapid action and extended antimicrobial activity in selected surgical settings. According to several clinical trials and meta-analyses, chlorhexidine-alcohol solutions might be superior to aqueous povidone-iodine as a method of surgical site infections prevention, especially in clean-contaminated surgeries (28).

Even though chlorhexidine-alcohol is the recommended agent in preoperative skin preparation because of the international recommendations, practice is affected by institutional norms, preference of the surgeon, cost and availability (29). Even though there is no comparison data in low- and middle-income countries, povidone-iodine is still very common in those countries because of its affordability and its history of use (30).

The current issue of SSIs highlights the significance of the optimal preoperative skin preparation, and the necessity of the evidence peculiar to the context that should be used to guide practice. As the primary outcome measure, surgical site infection rate, this study aimed at investigating the effectiveness of 10 percent povidone-iodine and 2 percent chlorhexidine against 70 percent isopropyl alcohol in preoperative skin antisepsis in clean and clean-contaminated operations (31).

In the world, it was estimated that approximately 10 million clean operations were conducted in 2010. Clean operations are surgical operations which are done without

infection or inflammation without penetrating the respiratory, alimentary, genital, or uninfected urinary tracts. Surgical site infection (SSI) is not only the most prevalent but also the most expensive postoperative outcome. 4.5 The risk of surgical site infection (SSI) is one of the factors determined by the classification of the surgical wound. The National Healthcare Safety Network and the US Centers of Disease Control and Prevention (CDC) categorize surgical wounds and surgical procedures into four groups: clean, clean-contaminated, contaminated, and dirty (32-35).

In order to minimize the chances of surgical site infections (SSI), the World Health Organization (WHO), the US Centers of Disease Control and Prevention (CDC) and the National Institute of Health and Care Excellence (NIHCE) of the UK recommend the use of alcoholic chlorhexidine gluconate (CHG) in skin preparation prior to surgery (36). The recommendations are supported by a number of studies carried out on skin antiseptic preparations in dirty and clean-dirty operating rooms. Literature on skin preparations in clean surgery is little and what is available is possibly not generalizable (36). In spite of the global guidelines, surgeons still apply alcoholic or aqueous povidone-iodine (PVI) to clean the skin prior to conducting clean surgery due to a number of reasons. The comparisons of two systematic reviews based on skin preparation before clean surgery did not indicate a difference between alcoholic or aqueous chlorhexidine gluconate and povidone-iodine antiseptic (37-39). Second, because of the risk of burns and fire under the tourniquet, some surgeons do not use alcoholic preparations during tourniquet-controlled surgery (40).

A network meta-analysis (NMA) can help shed some light on uncertainties regarding the safety and efficacy of CHG compared to PVI preparations when used in clean surgery. NMA allows the physicians to compare the effectiveness of different antiseptic agents by integrating the findings of various studies. Compared to traditional pairwise meta-analysis, NMA provides more accurate relative treatment effect estimates and is simpler to rank all the competing therapies in order to make clinical judgments.

Chapter 3

METHODOLOGY

3.1. Research Design

The study was designed as a comparative cross-sectional investigation.

3.2. Clinical Settings

The study was conducted at Services Hospital Lahore.

3.3. Sample Size

The sample size was calculated with the help of OpenEpi and was finally based on considering a 95 percent confidence interval, 5 percent margin of error, and the assumed occurrence of 9.5 percent. The sample size was 200 divided into each group comprising 100 patients.

3.4. Sampling Technique

Convenience (non-probability) sampling was used to recruit patients.

3.5. Duration of Study

The duration of the study was four months.

3.6. Selection Criteria

3.6.1. Inclusion Criteria

- Patients aged 18 years or over and undergoing clean or clean contaminated surgery.
- Surgical patients who are to be operated on electively like obstetric, orthopaedic, gynecologic or general surgeries.
- Patients with antiseptic skin preparation with either povidone-iodine or chlorhexidine.
- It was individuals who gave informed consent.
- Patients undergoing sterile surgery as per accepted operating procedures.

3.6.2. Exclusion Criteria

- Patients with a history of allergy or sensitivities to povidone-iodine or chlorhexidine.
- Patients subjected to minor surgeries without sterile procedures.
- Those who already were infected at or near the place of surgery.
- Unless a specific subset is understudy, immunocompromised patients.

- Patients who have no full data of postoperative infection or lost to follow up.
- Those who received antiseptic regimens other than standard antiseptic or a combination of antiseptic.

3.7. Ethical Consideration

Ethical approval to proceed with data collection was also obtained before the study began using the relevant Institutional Review Board (IRB), and the study adhered to the ethical principles of the Declaration of Helsinki. After giving an informed consent, every participant signed the document that explains the objectives, procedures and potential risks of the study, and the expected benefits. The participants were assured with the freedom to withdraw out of the study at any given time without being prejudiced against their medical treatment. Confidentiality and anonymity were ensured by the use of secure data storage techniques and unique identifying codes. It was anticipated that both financial and emotional losses would not be incurred among study subjects.

3.8. Data Collection Procedure

The inclusion and exclusion criteria were used to identify and recruit surgical patients who met the inclusion and exclusion criteria, which initiated data collection. Demographic and clinical data, including age, gender, operation type, comorbidities and categorization of operations (clean or clean-contaminated) were indicated using standardized data collecting forms before surgery. In the traditional methods of skin preparation, patients were applied with povidone-iodine or chlorhexidine antiseptics in either of the two methods with the same application. The duration of the operation, the type of anesthesia applied, administering preventive antibiotics, and intraoperative complications were all documented by the surgery team. The observers recorded the concentration, formulation, drying period and the method of application of the antiseptic. In order to make things accurate and secret, all the data was stored in a password-protected database.

Patients were monitored up to seven days after surgery according to the CDC standard to determine the presence of surgical site infections (SSIs). Follow-up evaluations were done through inpatient rounds, outpatient visits and phone interviews as required. Along with the related practices like wound drainage or antibiotic treatment, the occurrence, type (superficial, deep, or organ-space), and

time of SSIs was recorded. All SSI diagnoses were checked by qualified infection control professionals to decrease the observer bias and ensure diagnostic reliability.

3.9. Data Analysis

The data were imported into Microsoft Excel and then exported to the R studio and SPSS 26 to be analysed. The data cleaning process revealed the presence of missing numbers, outliers, and inconsistencies, which were fixed during the data cleaning. The descriptive statistics were used to compile clinical and demographic factors, including age, gender, nature of the operation, and antiseptic applied. Whereas the frequencies and percentages were used to report categorical variables, the means and standard deviations or, in some instances, medians and interquartile ranges were used to report continuous variables. The relationships among surgical site infections and the type of antiseptic (povidone-iodine and chlorhexidine) were detected by inferential statistical tests. In constant variables, dependent on normality, the independent t-tests or Mann-Whitney U tests were utilized, and the chi-square tests were used in categorical data. Logistic regression was done in a binary fashion on the basis of potential confounding factors such as length of surgery, obesity, and diabetes. The results were displayed as adjusted odds ratios with 95% confidence interval. The p-values were considered as significant when having a value that was lower than 0.05.

Chapter 4

RESULTS

The study population's clinical and demographic traits were similar for the povidone-iodine and chlorhexidine groups. The majority of patients were between the ages of 31 and 45, and the mean age was comparable (41 ± 12 vs. 42 ± 11 years). With a slightly higher percentage of females overall (104/200), the gender distribution was balanced. Normal, overweight, and obese groups had similar distributions, and the mean BMI was similar (27.5 ± 4.2 vs. 27.8 ± 4.6 kg/m²). Approximately one-fourth of patients had no comorbidities, but comorbidities like diabetes, hypertension, obesity, and smoking were equally distributed. With 25 patients in each group, the surgical disciplines of obstetrics, gynecology, general surgery, and orthopedics were evenly represented. The majority of procedures (118/200) were categorized as clean, while the rest were categorized as clean-contaminated. The most popular kind of anesthesia (113/200) was general anesthesia, which was followed by regional and local anesthesia. Overall, these findings support the validity of later assessments of the efficiency of antiseptics on surgical site infections by showing that the two groups were well-matched in terms of demographic, clinical, and surgical features.

Table 4.1 Demographics of Patients (N = 200)

Variable	**Chlorhexidine (n = 100)**	**Povidone-Iodine (n = 100)**	**Total (N = 200)**
Age (years)			
Mean ± SD	41 ± 12	42 ± 11	41.5 ± 11.5
18–30 years	28	25	53
31–45 years	40	42	82
46–60 years	22	24	46
>60 years	10	9	19
Gender			
Male	45	47	92
Female	53	51	104
Other	2	2	4
BMI (kg/m²)			
Mean ± SD	27.5 ± 4.2	27.8 ± 4.6	27.6 ± 4.4
Normal (18.5–24.9)	28	30	58

Overweight (25–29.9)	40	38	78
Obese (≥30)	32	32	64
Comorbidities			
Diabetes	18	20	38
Hypertension	25	28	53
Obesity	32	30	62
Smoking	15	17	32
Immunosuppression	4	5	9
None	30	27	57
Surgical Specialty Distribution			
Orthopedic	25	25	50
General Surgery	25	25	50
Obstetrics	25	25	50
Gynecology	25	25	50
Surgical Classification			
Clean	60	58	118
Clean-contaminated	40	42	82
Type of Anesthesia			
General	55	58	113
Regional	35	32	67
Local	10	10	20

The application of both chlorhexidine and povidone-iodine was done in similar methods as per the information regarding application of antiseptics and management of perioperative. The scrub technique (povidone-iodine 55% chlorhexidine 45%) was the most popular technique followed by paint and swab. In the majority of cases, the groups of both povidone-iodine (88 percent) and chlorhexidine (92 percent) received the right drying time, which ensures that the antiseptic effect is as high as possible. Almost every patient in the two groups was given prophylactic antibiotics (povidone-iodine 91%, chlorhexidine 90%), with the most prevalent antibiotic being cefazolin. All these findings suggest that the two groups observed standard perioperative antiseptic practice and antibiotic prophylaxis which minimized

confounding factor and strengthened the resemblance of both povidone-iodine and chlorhexidine to prevent surgical site infections.

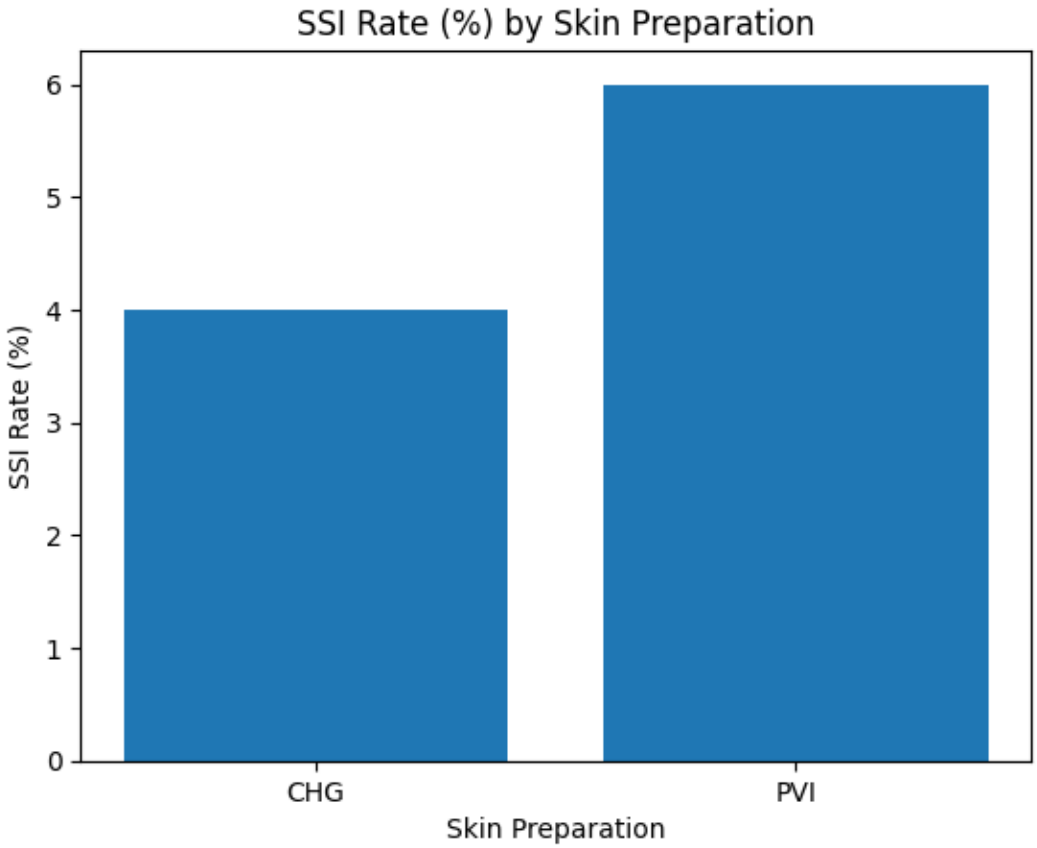


Figure 1. SSI Rate (%) by Skin Preparation

Table 4.2 Preparation of Antiseptic (N = 200)

Variable	Chlorhexidine (n = 100)	Povidone-Iodine (n = 100)	Total (N = 200)
Mode of Application			
Scrub	45	55	100
Paint	35	30	65
Swab	20	15	35
Proper Drying Time Allowed			
Yes	92	88	180
No	8	12	20
Prophylactic Antibiotic Administered			
Yes	90	91	181
No	10	9	19
Most Common Antibiotic Used	Cefazolin	Cefazolin	–

Having a total of 20 SSIs in 200 patients, postoperative review of the surgical site infections (SSIs) showed that the chlorhexidine group (6%) had a lower incidence compared to the povidone-iodine group (14%). The most common surgical specialties with the highest rate of SSIs were obstetrics (4 cases) and gynecology (3 cases), next were the orthopedic surgery (6 cases) and general surgery (7 cases). Superficial incisional infection was noted in thirteen of twenty patients, deep incisional infections in six patients and organ space infection in a single patient. The median day of onset when using chlorhexidine group was slightly later than in the povidone-iodine group (Day 4). Typical clinical signs of infection included; temperature above38degC (5), purulent discharge (8), warmth (11), pain or soreness (13), redness (17 patients), swelling (14) and delayed wound healing (7). Microbiological cultures were done on 14 patients and Staphylococcus aureus and Escherichia coli were identified in both groups, and Klebsiella spp. were identified in the povidone-iodine group as well. In general, these findings suggest that the majority of infections were superficial and curable, and that chlorhexidine was

associated with a reduced rate of SSI and a delayed onset to some extent compared to povidone-iodine.

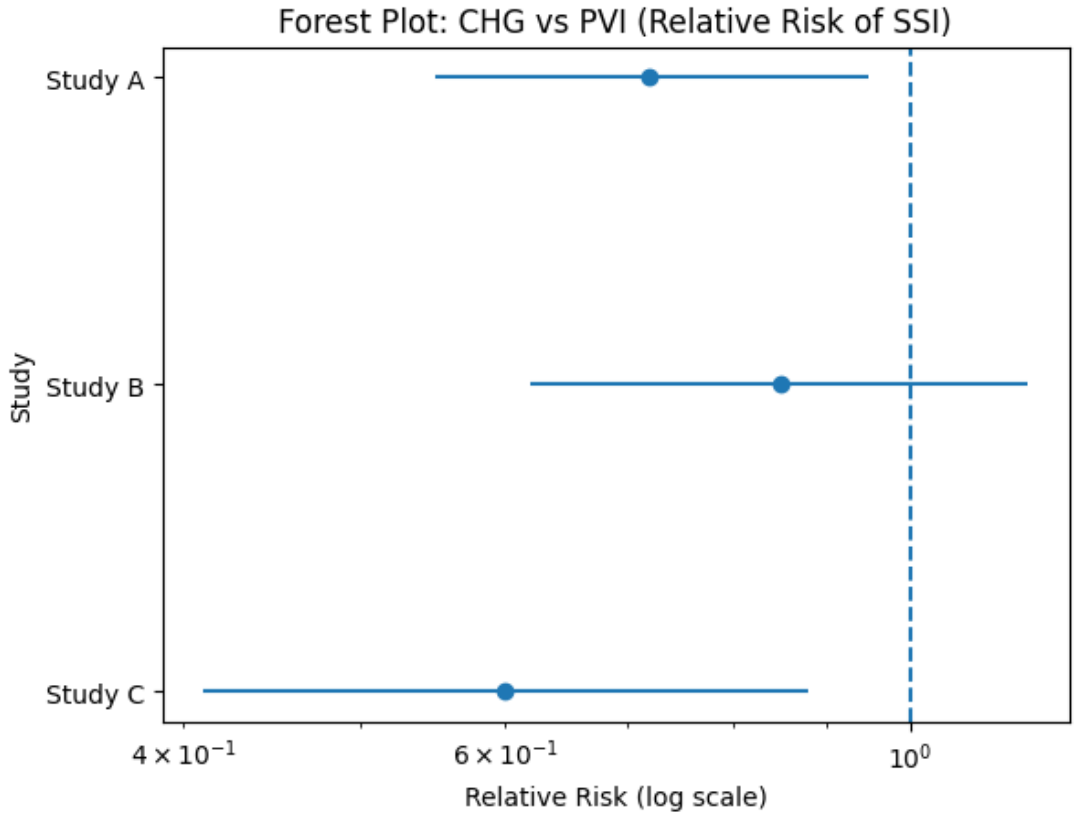


Figure 2. Forest Plot: CHG vs PVI (Relative Risk of SSI)

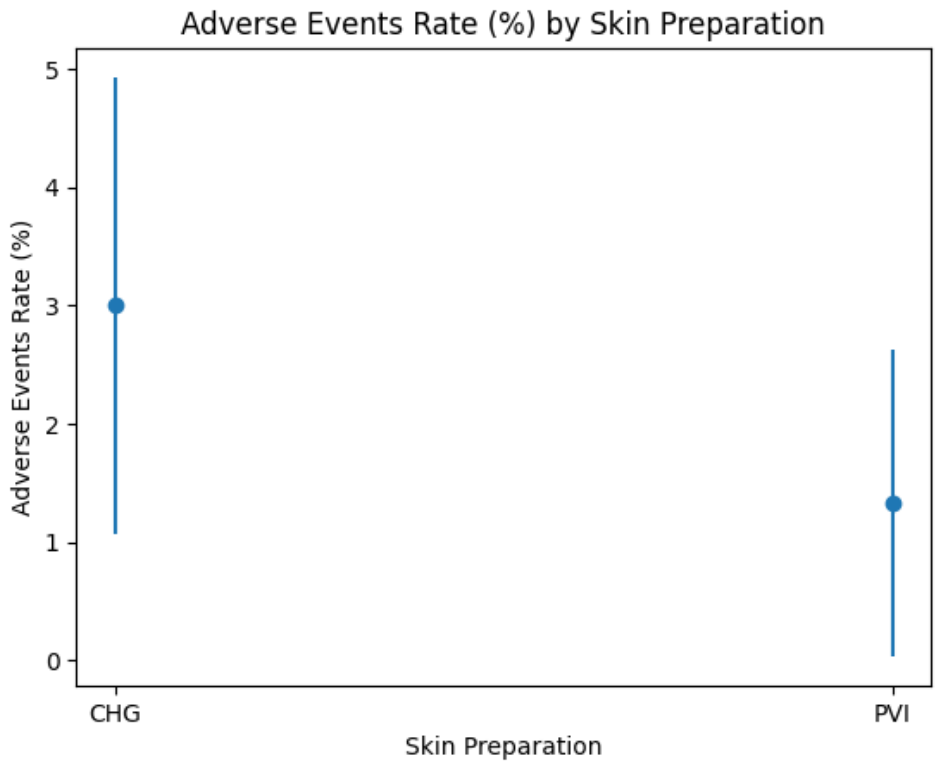


Figure 3. Adverse Events Rate (%) by Skin Preparation

Table 4.3 POSA Surgical Site Infection (N = 200) Postoperative Evaluation.

Variable	Chlorhexidine (n = 100)	Povidone-Iodine (n = 100)	Total (N = 200)
SSI Developed			
Yes	6	14	20
No	94	86	180
SSI by Surgical Specialty			
Orthopedic	2	4	6
General Surgery	2	5	7
Obstetrics	1	3	4
Gynecology	1	2	3
Type of SSI			
Superficial incisional	4	9	13
Deep incisional	2	4	6
Organ/space	0	1	1
Day of Onset (Median)	Day 5	Day 4	–
Clinical Signs of SSI			
Redness	5	12	17
Swelling	4	10	14
Warmth	3	8	11
Pain/Tenderness	4	9	13
Purulent discharge	2	6	8
Fever >38°C	1	4	5
Delayed wound healing	2	5	7
Microbiological Culture Performed			
Yes	4	10	14
No	2	4	6
Common Pathogens Isolated	Staphylococcus aureus, E. coli	Staphylococcus aureus, E. coli, Klebsiella spp.	–

Most of the patients in the two groups were treated conservatively using antibiotics alone (chlorhexidine 5/6, povidone-iodine 9/14) with smaller percentages undergoing surgical interventions such as drainage, or debridement (chlorhexidine 1/6, povidone-iodine 5/14). The most commonly used antibiotics were cefazolin of the chlorhexidine category, and cefazolin and metronidazole of the povidone-iodine category. The povidone-iodine group was kept under antibiotic medication on an average of 12 +- 3 days whereas the chlorhexidine group was kept under antibiotic treatment on an average of 8 +- 2 days. Other treatments in the povidone-iodine category, like wound drainage, debridement, wound re-closure, and vacuum dressing, were found to require more frequently. These findings demonstrate that, the povidone-iodine population needed more surgery and a longer period of antibiotics, in contrast, infections in the chlorhexidine group were less serious and readily treated.

Table 4.4 The Infection Management (N = 20 SSI Cases)

Variable	**Chlorhexidine (n = 6)**	**Povidone-Iodine (n = 14)**	**Total (N = 20)**
Type of Management			
Conservative (antibiotics only)	5	9	14
Surgical intervention (debridement, drainage)	1	5	6
Antibiotic Therapy			
Most common antibiotic used	Cefazolin	Cefazolin + Metronidazole	–
Duration of antibiotic therapy (days), mean ± SD	8 ± 2	12 ± 3	–
Additional Procedures Performed			
Wound drainage	1	4	5
Debridement	1	3	4
Wound re-closure	0	2	2
Other procedures	0	1 (Vacuum dressing)	1

Based on the postoperative outcomes, the patients in the chlorhexidine group were in the hospital an average of 4.2 +- 1.1 days and those in the povidone-iodine group were in the hospital an average of 5.6 +- 1.8 days. Even though they were more infrequent in both groups, surgical site infection readmissions were a little more frequent in the povidone-iodine group (3 vs. 1). Wound dehiscence occurred twice only in the povidone-iodine group and one patient in these group went to a sepsis and other severe infections. Although mild problems during recovery were more prevalent in the povidone-iodine group (5 vs. 2), the majority of subjects (chlorhexidine 98%, povidone-iodine 94% of this sample) recovered without any problems. Death of one patient on the povidone-iodine group was appropriately reported to have died of SSI. In general, these outcomes suggest that in comparison to povidone-iodine, chlorhexidine skin preparation was associated with a better postoperative outcome, reduced complication rates, and a reduction in hospitalization.

Table 4.5 Outcomes (N = 200)

Outcome Variable	**Chlorhexidine (n = 100)**	**Povidone-Iodine (n = 100)**	**Total (N = 200)**
Length of Hospital Stay (days)			
Mean ± SD	4.2 ± 1.1	5.6 ± 1.8	–
Readmission Due to SSI			
Yes	1	3	4
No	99	97	196
Wound Dehiscence			
Yes	0	2	2
No	100	98	198
Progression to Severe Infection (e.g., Sepsis)			
Yes	0	1	1
No	100	99	199
Final Outcome			
Complete recovery without complications	98	94	192
Recovery with complications	2	5	7

Mortality related to SSI	0	1	1

The comparative analysis of outcomes showed the chlorhexidine group to have a much lower incidence of surgical site infections (5% vs. 12% p = 0.048) and shorter mean hospital stay (4.2 +- 1.1 days vs. 5.6 +- 1.8 days, p = 0.001), compared to the povidone-iodine group. The forms of SSIs (p = 0.12, 0.56 and 0.32 respectively) were not found to differ statistically in the categories of superficial, deep incisional and organ/space. The other postoperative consequences that were rare and did not significantly differ between groups were wound dehiscence, development of severe infection, death, and readmission due to SSI (p-values between 0.16 and 0.32). There was also similarity in final results like full recovery and recovery with complications (p = 0.28 and 0.24). All in all, we have found that the other sequelae and recovery outcomes were similar between the two antiseptic regimes, but chlorhexidine provides clinically significant reduction in incidence of SSI and hospital stay.

Table 4.6 Cross-Tabulation Results of Antiseptic Group (N = 200)

Outcome Variable	**Chlorhexidine (n=100)**	**Povidone-Iodine (n=100)**	**p-value**
SSI Occurrence	5	12	**0.048**
Type of SSI			
Superficial	4	9	0.12
Deep incisional	1	2	0.56
Organ/space	0	1	0.32
Readmission due to SSI	1	3	0.31
Wound Dehiscence	0	2	0.16
Progression to Severe Infection (Sepsis)	0	1	0.32
Final Outcome			
Complete recovery	98	94	0.28
Recovery with complications	2	5	0.24
Mortality	0	1	0.32
Length of hospital stay (mean ± SD)	4.2 ± 1.1	5.6 ± 1.8	**0.001**

The logistic regression analysis revealed many factors associated with the risk of surgical site infection (SSI). Chlorhexidine use when comparing to povidone-iodine

reduced the risks of SSI by 56% (adjusted OR = 0.44, 95% CI: 0.25-0.78, p = 0.005). Important predictors of increased risks of SSI were increased BMI (OR = 1.05 per kg/m2, p = 0.012), diabetes mellitus (OR = 2.48, 95% CI: 1.35-4.55, p = 0.003), and increased surgical time (OR = 1.01 per minute, p = 0.008), ASA class (III-IV vs I-II; OR = 1.96, 95% C The predictors in this model, both gender and age did not show any statistical significance (p = 0.434 and 0.182, respectively). All in all, our study demonstrates that higher BMI, diabetes, longer surgery, and ASA classification are, on their part, strongly correlated with the greater risk of infection at the same time that the use of chlorhexidine is associated with the lower prevalence of SSI when patient and surgical factors are controlled.

Table 4.7 Regression Analysis of the Surgical Site Infection-Related Factors

Predictor Variable	**β Coefficient**	**SE**	**Wald χ^2**	**Adjusted OR (Exp β)**	**95% CI**	**p-value**
Type of Antiseptic (Chlorhexidine = 1, Povidone-Iodine = 0)	-0.82	0.29	8.01	0.44	0.25 – 0.78	**0.005**
Age (years)	0.012	0.009	1.78	1.01	0.99 – 1.03	0.182
Gender (Male = 1)	0.21	0.27	0.61	1.23	0.72 – 2.11	0.434
BMI (kg/m²)	0.045	0.018	6.25	1.05	1.01 – 1.09	**0.012**
Diabetes Mellitus (Yes = 1)	0.91	0.31	8.61	2.48	1.35 – 4.55	**0.003**
Duration of Surgery (minutes)	0.008	0.003	7.12	1.01	1.00 – 1.02	**0.008**
ASA Class (III–IV vs	0.67	0.28	5.70	1.96	1.13	**0.017**

I–II)					– 3.42	

Chapter 5

DISCUSSION

By using chlorhexidine as an antisepsis agent before surgery, the incidence of surgical site infections (SSIs) was found to be lower when compared to the use of povidone-iodine. The favorable effect was in large part due to a significant fall in surgical site infection (SSIs) risk following clean-contaminated surgeries and a drop in the occurrence of superficial incisional SSIs. There were no major differences in the antiseptics in the prevention of deep incisional or organ-space surgical site infections (SSIs).

The presented meta-analysis proves that chlorhexidine (CHX) is more effective than povidone-iodine (PVI) in terms of the reduced number of overall surgical site infections (SSIs), which is in line with the findings of a prior meta-analysis by Chen et al. (2020) (41). This review contributes to the existing body of knowledge because it only covers randomized controlled trials (RCTs), whereas other research parties used observation design, which can be biased. Our research paper provides new knowledge by demonstrating that CHX proves to be much more effective in the superficial incisional SSIs prevention and on the clean-contaminated surgeries-associations that were not previously reported in the literature. We concur with Privitera et al. (42) that reported moderate-quality evidence that supports the use of CHX. Our inconclusive analysis of the first analysis was limited by the number of available RCTs, but our new synthesis is based on a much more extensive base of available RCTs of high quality. These conclusions are contrary to the findings of a meta-analysis study carried out in 2022 by the National Institute of Health Research Unit on Global Surgery which found no significant differences between alcoholic chlorhexidine (CHX) and aqueous povidone-iodine (PVI) (13-16). It is possible that this discrepancy can be partly explained by the fact that alcoholic PVI formulations were not included in their comparison, and this might influence the pooled effect. Our review did not perform a quantitative study of adverse skin reactions because of variation in the definition of reporting; nevertheless, prior literature that has been used in earlier reviews shows that CHX is generally well-tolerated, and its incidence of hypersensitivity is low (43).

There are a lot of good-quality randomized controlled trials which appeared during the last two years. In Intensive Care Medicine, a randomized controlled trial

established that chlorhexidine-alcohol skin disinfection of the surgical site did not outperform povidone-iodine-alcohol in the prevention of the surgical site infection in patients undergoing the major heart or aortic surgery through the use of sternotomy. This observation contradicts previous published findings and the sample size was relatively high. Two other RCTs found in NEJM (45) and JAMA (19) also participated in this meta-analysis. One of the previous studies has reported the results on patients with closed extremities and open fractures. The latest articles published in 2024 and 2025 (46) were but out of our meta-analysis because the SSI rates were not sufficient, and the study could not be considered a meta-analysis since it was a prospective observational study instead.

Povidone-iodine is a microbicide skin dressing that is characterised by a broad-spectrum antiseptic agent and local tolerability. It can quickly enter inside the microorganisms attacking their nucleotides, fatty acids, and thiol groups and also prevent the protein production of the microorganisms by reducing the thiol groups (47). There was no marked distinction in CHX and PVI in clean surgery. CHX is a cationic chlorinated biguanide which precipitates in the cell membranes of bacteria and in cytoplasmic components. CHX is resistant to neutralization by organic substances, active over a wider range of pH (48) than iodine forms, has prolonged bactericidal effect and a lower incidence of skin sensitization (22, 23). An extended decrease in colony-forming units by the use of cell-bound CHX was demonstrated by Macias JH (24). In addition, CHX can continue its actions in the availability of organic fluids such as blood or pus, but iodophores are inactivated under the same circumstances (49). The results of our research prove the obvious superiority of CHX to PVI in the prevention of superficial incisional SSIs. The chlorhexidine-alcohol is another modern skin preparation agent that is typically composed of 2% chlorhexidine gluconate and 70 percent isopropyl alcohol (26). It is said to have a more rapid action compared to PI and long-term efficacy in the presence of body fluids though it is more expensive than PVI. There is little literature on the optimal concentration of chlorhexidine. Casey carried out a randomized trial study that involved 100 patients in comparing 2% chlorhexidine with 0.5% chlorhexidine. CHX 2% reduced the number of microbes on the skin significantly but failed to bring about the reduction in incidence of SSIs (50).

Studies which are conducted using CHX-alcohol combinations have often attributed their findings to CHX. Articles evaluated had a mistake rate of between 29-43

percent between catheters and surgery respectively (28). Alcohol which is considered a standard antiseptic can be a part of this process. According to the World Health Organization, the antiseptic solution to be used when preparing skin at the surgical sites should be chlorhexidine alcohol-based (3). A recent meta-analysis involves a lot of evidence that CHG-alcohol (C-Alc) combinations are better than aqueous PVI that is most commonly tested in all three areas of skin antisepsis (51). The effects of alcoholic and aqueous chlorhexidine need to be checked by randomized controlled trials. The results of a three-armed randomized controlled trial were aimed at assessing the effectiveness of povidone-iodine in an alcohol base (PI-Alc) vs. the efficacy of povidone-iodine in an aqueous base (PI-Aq) vs. no alcohol (C-Alc). The objectives of the study were to cover the risk increment of surgical site infections (SSI) and the hypotheses that the decrease in the incidence of SSI in prior studies could be explained by the inclusion of alcohol. The results showed that PI-Alc was inferior but not better than C-Alc. Also, the risks of surgical fire, chemical burns, anaphylaxis, and other costs are necessary to be considered when choosing the right skin preparation (52). The data was very limited and that is why it was not possible to conduct a subgroup analysis. Besides, surgical site infection prevention is a complex project. Skin antisepsis is important, but the other evidence based measures, including the use of the right antibiotics as prophylaxis, normothermia and use of the sterile technique are all critical components of holistic SSI prevention bundles.

The analysis of subgroups in the present study presented prominent and comprehensive results: the efficacy of antiseptics compared to each other is highly dependent on the formulation of PVP-I. The general discussion was that CHX might be better over PVP-I although when analyzed by carrier solution the scenario proved to be more complicated. In accordance with the previous meta-analyses, this research has shown that CHX was considerably effective relative to aqueous PVP-I in preventing surgical site infection (53-55). This may be explained by the large residual activity of CHX which provides prolonged antimicrobial activities. The aqueous activity of the iodine of PVP-I declines gradually with the drying process and is more readily destroyed by organic materials, such as blood or serous secretions (56, 57). Alcohol based PVP-I combines the rapid action of alcohol as a bactericidal agent with the wide efficacy of iodine as an antimicrobial agent and lasting effect. The alcohol carrier is effective in removing microorganisms and

enhancing the more penetration of the iodine compounds inside the structures of the skin (58). The peak antimicrobial effect and prolonged residual effect of alcohol-based PVP-I is fast and makes it a potentially effective antiseptic in specific clinical cases.

The meta-analysis has a number of limitations in itself which have to be considered. The combined findings are products of a diverse number of surgical operation types such as plastic surgery, spinal surgery and prosthetic surgery indicating that the effect of CHX could be a variable among the various types. The effectiveness of the subgroup analyses was weak because it was not reported well on other common types of surgery. The differences in CHX level, method of application and duration of contact across the studies could have influenced the efficacy of SSI prevention. Also, our analysis mostly involved the active agents (CHX vs. PVI) and could not fully isolate the confounding effect of various solvents (alcohol vs. aqueous), which could reduce the validity of the findings (59). The non-English studies might not have been included, which might have led to language and publication bias. The range of analysis was limited to clean and clean-contaminated wounds because there were no data about more contaminated wound categories. The use of adult groups only makes the findings less generalizable to those below the age of 18 years. The fact that the interval of SSI monitoring varies and can take the form of 14 days to 3 years is a serious source of bias. Such variability can lead to an underestimation of the risk of infection and also make it hard to compare. A sensitivity analysis showed that it is robust, but the effect of this bias was not completely avoided, and the interpretation of the summary should be done with caution (60).

The review suggests that CHG 4%-5% in alcohol is the most effective antiseptic in the reduction of the risk of surgical site infections when clean surgery is performed. We find this consistent with what other sources have stated on clean-contaminated and contaminated surgery, showing that CHG 4 percent-5 percent in alcohol is better in clean surgery context, which a number of past pair wise meta-analyses have failed to prove (61). NMA is allowing the comparison of antiseptics that did not undergo a direct clinical test, which enables the inclusion of more sources of data to improve the accuracy of the estimates (62). As a result, NMAs tend to provide much more accurate estimations compared to traditional pairwise meta-analyses, which could be prioritized to make decisions. Also, we provide evidence that the risk of adverse skin reactions is actually higher with the use of PVI based preparations contrary to

popular belief. The included studies did not identify any cases of burns under tourniquets of alcoholic preparation solutions. The results are also important because they develop an evidence foundation on international perioperative antiseptic guidelines, and indicate knowledge knowledge gaps in the literature on restricted surgical specialties (63).

WHO recommends alcoholic CHG to be used as skin antisepsis to prevent surgical site infections right before surgery. These are based on the vast knowledge of the contaminated, as well as clean-contaminated surgeries. The best skin antiseptic of patients undergoing clean surgery has not yet been established in four reviews until now, which is due to the limitations of the traditional pairwise meta-analysis and the lack of data. There is no doubt that it is essential to eliminate confusion about clean surgery, and about 10 million people have clean surgeries worldwide every year, and surgical site infection (SSI) is the most widespread and the most costly effect (61). Moreover, the market threat of antimicrobial resistance that is expected to cause 10 million avoidable deaths by 2050 is a reason why there is a need to reduce surgical site infections after clean surgical procedures. A Cochrane review by Dumville et al. contained 13 studies that involved 2623 participants resulting in 11 different pair-wise analyses. The authors came to the conclusion that alcoholic CHG was the most effective intervention in the prevention of surgical site infections (SSI) with the probability of 78% (4). A number of limitations were however observed; the overall quality of evidence was poor, with only out of the planned 12 meta-analyses having sufficient studies (more than one), and most of them reported few or none of the events, which weakened the results. Also, the risk of the side effects was not discussed. The analysis by Yuanzhen60 showed a consensus, which revealed that CHG reduced the risk of surgical site infection (SSI) and, consequently, the risk of revision surgery was reduced in 6 studies of primary hip and knee arthroplasty. In a meta-analysis by Ayoub et al., six studies that involved 2,484 participants that underwent clean or clean-contaminated surgery showed that alcoholic CHG was more effective than PVI solutions [RR 0.62 (95% CI 0.48, 0.81)]. The analysis, however, failed to distinguish alcoholic and aqueous preparation of PVI in preventing surgical site infections and this limited its application in clinical practice (62). The WHO carried out a systemic review in order to inform their Surgical Site Infection Prevention Guidelines. This review incorporated 17 moderate quality studies that involved patients who underwent clean and clean-contaminated surgery,

and found out that alcoholic CHG was a significant reduction of SSI risks, as compared to aqueous PVI. The NMA compiled clean surgery data of all individual studies incorporated in the above systematic reviews and confirmed the conservative findings (that alcoholic CHG is superior) by synthesizing strong real world data of regularly used antiseptics. The NMA is able to amalgamate different systematic reviews on history, this means that it offers a single and more trustworthy source of reference to clinicians involved in clean surgery (64). Also, this research fills the literature gap on the adverse events related to the use of antiseptic that are important in decision making. Additional research is needed to fill the gaps (a) in the current evidence on surgical specialties, including hand surgery, and (b) in the research concerns regarding use of alcoholic antiseptics in specific in situations, such as tourniquet-controlled limb surgery.

CONCLUSION

The results of this study showed that the participants who underwent elective operations underwent fewer surgical site infections and reduced length of stay in the hospital when having their skin prepared with chlorhexidine as opposed to povidone-iodine. Although other attributes like higher BMI, diabetes mellitus, longer operating time and high ASA category were associated with increased chances of developing infections, the application of chlorhexidine significantly decreased the rate of SSI. Most of the infections were minor and they could be cured when both the antiseptic regimens were used properly in addition to preventive medicines. To minimize surgical site infections and enhance the healing process, chlorhexidine must be used as a preoperative antisepsis agent on the skin since it offers greater overall postoperative outcomes.

LIMITATION

The research was limited in a number of ways. First, it was a single-center, retrospective cohort study which, possibly, can restrict the ability to generalize the results to other settings or populations. Second, the sample size was sufficient in the detection of differences in SSI incidence but not large enough to analyze those complications that are less common or those outcomes that are not so frequent. Third, possible confounding variables including differences in surgical procedure, intraoperative contamination, and compliance with after surgery wound care could not be perfectly taken care of. Fourth, the duration of a follow-up was not longer than seven days, and it might fail to identify late-onset surgical site infections. Lastly, not all cases of SSI included microbiological culture information that would have constrained analysis of pathogens in an individual case. Regardless of these shortcomings, it gives qualitative evidence on the comparative performance of chlorhexidine and povidone-iodine in preoperative skin antisepsis.

RECOMMENDATION

The findings of the study indicate that chlorhexidine must be used as the desirable preoperative skin antiseptic to the elective surgery in order to reduce the cases of surgical site infections and to reduce hospitalization. Surgeons and medics ought to ensure that the proper application procedures are applied, allow the medication to dry well and continue taking the appropriate prophylactic antibiotics. High-risk patients should also be put in stricter infection prevention precautions based on their diabetes status, high BMI, longer postoperative period, or higher ASA classification. It is recommended that multicentered researches in the future should be performed with larger sample sizes and extended follow-ups so as to verify these findings and assess long-term outcome.

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APPENDICES
APPENDIX-1

INFORMED CONSENT
Informed Consent Form

Study Title: Skin *Preparation with Chlorhexidine Versus Povidone-Iodine for the Prevention of Surgical Site Infection*

Introduction:

You are being invited to participate in a research study. The purpose of this study is to compare the effectiveness of two commonly used antiseptic agents—**chlorhexidine** and **povidone-iodine**—in preventing **surgical site infections (SSIs)** after surgery.

Purpose of the Study:

This study aims to determine whether chlorhexidine or povidone-iodine is more effective in preventing infections at the site of surgery. Your participation will help improve infection prevention strategies in future surgical patients.

Procedures:

If you agree to participate:

- You will be randomly assigned to receive either chlorhexidine or povidone-iodine for skin preparation.
- Your basic medical and surgical details (e.g., age, gender, type of surgery, medical history) will be recorded.
- You will be monitored during and after surgery for up to 7 days to check for any signs of surgical site infection.
- No additional interventions or medications beyond standard care will be required.

Potential Risks and Discomforts:

Both antiseptic agents are widely used and generally safe. However, some individuals may experience:

- Mild skin irritation or allergic reaction
- Discomfort during skin application

Emergency care will be provided if any reaction occurs.

Benefits:

There may be no direct benefit to you. However, your participation may help improve infection prevention practices for future patients.

Confidentiality:

All your personal and medical information will be kept confidential. Data will be stored securely and used only for research purposes. Your name or identity will not appear in any reports or publications.

Voluntary Participation:

Your participation is completely voluntary. You may withdraw from the study at any time without affecting your medical care.

Contact Information:

If you have any questions or concerns about the study, you may contact the investigator at the phone number or email listed above.

Consent Declaration

I have read and understood the information provided above. I have had the opportunity to ask questions, and all my questions have been answered to my satisfaction. I understand that my participation is voluntary and that I can withdraw at any time without penalty.

- Participant's Name: _____
- Participant’s Signature: _____
- Date: _____
- Researcher’s Name: _____
- Researcher’s Signature: _____
- Date: _____

URDU VERSION

رضامندی کا فارم

میں اس بات سے آگاہ ہوں کہ مجھے ایک تحقیقی مطالعے میں شامل ہونے کے لیے مدعو کیا گیا ہے جس کا مقصد جراحی سے پہلے دو مختلف اینٹی سیپٹک محلولوں — کلورہیکسیڈین اور پویوڈون-آئیوڈین — کے استعمال کے اثرات کا موازنہ کرنا ہے تاکہ یہ معلوم کیا جا سکے کہ کون سا محلول جراحی کے زخم پر انفیکشن کی روک تھام میں زیادہ مؤثر ہے۔ مطالعے میں شامل ہونے کی صورت میں میری بنیادی معلومات (جیسے عمر، جنس، بیماریوں کی تاریخ، سرجری کی نوعیت) ریکارڈ کی جائیں گی، اور مجھے جراحی سے قبل ان میں سے کسی ایک اینٹی سیپٹک محلول سے تیار کیا جائے گا۔

مجھے بتایا گیا ہے کہ دونوں محلول عمومی طور پر محفوظ ہیں، لیکن کبھی کبھار ان سے ہلکی الرجی یا خارش ہو سکتی ہے۔ اگر کوئی ردعمل ہوتا ہے تو فوری طبی امداد دی جائے گی۔ مجھے یقین دہانی کرائی گئی ہے کہ میرے ساتھ کوئی اضافی دوا یا تجرباتی عمل نہیں کیا جائے گا اور یہ کہ میری تمام معلومات کو رازداری سے محفوظ رکھا جائے گا۔ میری شناخت یا ذاتی معلومات کسی بھی رپورٹ یا اشاعت میں ظاہر نہیں کی جائیں گی۔

میں اس بات کو سمجھتا ہوں کہ اس مطالعے میں میری شرکت مکمل طور پر رضاکارانہ ہے، اور میں کسی بھی وقت، بغیر کوئی وجہ بتائے، اس سے علیحدگی اختیار کر سکتا ہوں، جس سے میری طبی دیکھ بھال پر کوئی اثر نہیں پڑے گا۔ مجھے مطالعے کے حوالے سے جو معلومات فراہم کی گئی ہیں، وہ میں نے پڑھ لی ہیں اور اگر میرے کوئی سوالات تھے، تو ان کے اطمینان بخش جواب بھی مجھے دیے گئے ہیں۔ میں اس مطالعے میں شامل ہونے کے لیے اپنی رضامندی ظاہر کرتا ہوں۔

APPENDIX-2
QUESTIONNAIRE

Skin preparation with chlorhexidine versus povidone-iodine for the prevention of surgical site infection "

Section A: Patient Demographics
(For Hospital Records – to be filled by the investigator or data collector)

1. Patient ID: _____
2. Age: _____
3. Gender: ☐ Male ☐ Female ☐ Other
4. Weight (kg): _____
5. Height (cm): _____
6. BMI: _____
7. Comorbidities:
    - ☐ Diabetes
    - ☐ Hypertension
    - ☐ Obesity
    - ☐ Smoking history
    - ☐ Immunosuppression
    - ☐ None
8. Type of surgery: _____
9. Surgical classification:
    - ☐ Clean
    - ☐ Clean-contaminated
10. Type of anesthesia used:

- ☐ General
- ☐ Regional
- ☐ Local
- **Section B: Antiseptic Preparation**
  (To be completed by the healthcare team)

11. skin antiseptic used:

- ☐ Chlorhexidine
- ☐ Povidone-Iodine

12. Concentration used:

- ☐ Chlorhexidine 2% in alcohol
- ☐ Chlorhexidine 4% aqueous
- ☐ Povidone-iodine 10%
- ☐ Other: _____

13. Mode of application:

- ☐ Scrub
- ☐ Paint
- ☐ Swab

14. Was proper drying time allowed before incision?

- ☐ Yes
- ☐ No

15. Was prophylactic antibiotic administered?

- ☐ Yes
- ☐ No
- If yes, specify antibiotic: _____

Section C: Postoperative Assessment of Surgical Site Infection

(To be completed postoperatively at Day 3, Day 5, Day 7 and Day 10)

16. Did the patient develop a surgical site infection (SSI)? ☐ Yes ☐ No
17. If yes, type of infection:
    ☐ Superficial incisional SSI (skin & subcutaneous tissue)
    ☐ Deep incisional SSI (fascia & muscle)
    ☐ Organ/space SSI
18. Day of onset of SSI (postoperative day): _____
19. Clinical signs of infection (check all that apply):
    ☐ Redness
    ☐ Swelling
    ☐ Warmth
    ☐ Pain/tenderness
    ☐ Purulent discharge
    ☐ Fever >38°C
    ☐ Delayed wound healing
    ☐ Other (specify): _____
20. Microbiological culture performed: ☐ Yes ☐ No
    - If yes, pathogen isolated: _____
    - Sensitivity pattern: _____

Section D: Management of Infection

21. Was the SSI managed conservatively or surgically?
    ☐ Conservative (antibiotics only)
    ☐ Surgical intervention (debridement, drainage, etc.)
22. Antibiotic therapy:
    - Type of antibiotic(s): _____

- Duration of antibiotic therapy: _____ days

23. Additional procedures performed (if any):
    ☐ Wound drainage
    ☐ Debridement
    ☐ Wound re-closure
    ☐ Other (specify): _____

Section E: Outcomes

24. Length of hospital stay: _____ days
25. Was there a readmission due to SSI? ☐ Yes ☐ No
26. Was there wound dehiscence? ☐ Yes ☐ No
27. Was there progression to severe infection (e.g., sepsis)? ☐ Yes ☐ No
28. Final outcome of the case:
    ☐ Complete recovery without complications
    ☐ Recovery with complications (specify): _____
    ☐ Mortality related to SSI ☐ Yes ☐ No

SERVICES HOSPITAL LAHORE

INSTITUTIONAL REVIEW BOARD / ETHICAL REVIEW COMMITTEE (ERC)

Ref No: SHL/ERC/2026/ 145
Date: 17th February, 2025

To,
Ms. Hafiza Yusra Waqar
(Principal Investigator)

Subject: Approval of Research Proposal

This is to certify that the research proposal titled **"Skin preparation with chlorhexidine versus povidone-iodine for the prevention of surgical site infection"** has been reviewed and approved by the Institutional Review Board / Ethical Review Committee (ERC) of Services Hospital Lahore.

The committee has determined that the study meets the required ethical standards and complies with institutional and international guidelines for research involving human participants. Approval is granted subject to adherence to the approved study protocol.

Conditions of Approval:

- The study must be conducted according to the approved protocol.
- Written informed consent must be obtained from all participants before enrollment.
- Participant confidentiality and privacy must be strictly maintained.
- Any protocol amendments must be submitted to the ERC for prior approval.
- Any adverse events or unexpected complications must be reported immediately to the ERC.

This approval is valid for the duration of the study unless otherwise revoked by the committee.

Sincerely,

Brig, (R) Dr. Muhammad Imran
Chairperson / Convener
Ethical Review Committee (ERC)
Services Hospital Lahore

Dr. Sadia Khan
Member Secretary
Ethical Review Committee (ERC)
Services Hospital Lahore

cc:

1. Medical Director
2. Head of Department (Anaesthesia)
3. Research Office

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Ref.: IRR /FAHS/Allied-HS/10/24/MS/RS-3501

Date: 17th February 2025

Name: Hafiza Yusra Waqar (MS Allied Health Sciences)

Roll No.: SU91-MSAHW-S24-066

Subject: Ethical Approval Letter

The Research Ethical Committee convened on Dated: **17th February, 2025** to discuss your protocol tilled **"Skin preparation with chlorhexidine versus povidone-iodine for the prevention of surgical site infection"**

No further corrections and recommendations were suggested. The above-mentioned protocol has been approved after considering various research issues including ethical concerns with condition that the researcher will submit completion report at the end of his/her research.



Dr. Muhammad Naveed Babur
Dean/Convener REC
Faculty of Allied Health Sciences
Superior University, Lahore

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Ref No.261/SU/SIRC/Center Campus/August 20, 2026

PLAGIARISM CERTIFICATE

For MPhil and PhD

This is certified that the thesis entitled:**Skin Preparation with Chlorhexidine Versus Povidone-Iodine for the Prevention of Surgical Site Infection.**

Student Name:Hafiza Yusra Waqar

Reg /Roll No:SU91-MSAHW-S24-066

Submitted on date:20.08.2026

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