THE ROLE OF ANTISEPTICS IN SURGERY

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ABSTRACT
Surgical site infection (SSIs) are one of the most frequent causes of nosocomial infections which not only increase the stay in the hospitals but also burden the patient financially. Skin acts as a barrier in the invasion of microbes from environment but on injury, the major source of infections could be normal flora on the skin. Antiseptic agents (ASAs) are applied on the skin as well as on the mucous membrane of minimize the chances of infection. ASAs should have a prolonged action to be more beneficial. A number of factors are involved in the prevention of SSIs. It has been established that the use of sterile antiseptics not only reduces the source of infections but also improves patient’s condition. A number of ASAs alone or as admixtures are commercially available and provide complete or partial eradication of microbes. ASAs like alcohols, chlorohexadione, iodine/iodophor, xylenol, triclosan and octenidine are still commonly used developed countries.

INTRODUCTION
Surgery has developed as an important part of worldwide healthcare system. According to debas et al, approximately 11% of the 1.5 billion disabilities have been treatable by surgery, and globally around 234 million surgeries are performed annually. Surgical site infections (SSIs) are one of the major causes of morbidity and mortality which not only overburden the cost of the debased therapy but also irritate the patients due to their overstay in the hospital. Although a number of preoperative measures have been taken, still the SSIs are the third most common cause of nosocomial infection. The rate of SSIs even in the advanced countries like USA, Australia, and Brazil is 2.8%, 7.9%, and 10%, respectively. Various researchers and authoritative guidelines like those of CDC, WHO, and NICE have been established to emphasize the importance of antiseptic agents (ASAs) in the reduction of SSIs. Despite the use of ASAs, a large number of risk factors such as age, blood transfusion, colonization, diabetics, duration of operation, surgical attire, hypovolemic, malnutrition, immunosuppressant drugs, obesity, oxygen supply, pre-operative stay, shaving, smoking, hypothermia, vasoconstriction, air supply, and low serum albumin have been involved in SSIs. The major extrinsic source of microbial contamination may be by hand, gloves, air supply, and surgical instruments. Microorganisms may develop resistance or became less susceptible to ASAs and the patients may suffer from allergic reactions (e.g., from iodine preparations). Several factors play an important role in the effectiveness of antiseptic solutions in scrubbing, such as the duration of the scrub, scrubbing technique, the condition of the hands, and the techniques used for drying. Contaminated ASSs may cause infections either on handwashing and/or on application as disinfectant on the skin of patients. Runge (1834) first discovered and described the structure and properties of carboxylic acid as an antiseptic agent. Lister, an English surgeon, was a pioneer for using phenol (carboxylic acid) as an antiseptic solution to prevent spreading of infections and its related complications. The most recommended antiseptic solutions contain chlorhexidine gluconate, chloroxylenol (para-chloro-metaxylenol), alcohol, iodine/iodophor as well as 70% isopropyl alcohol, chloroform medicated soap, all exhibiting good antibacterial susceptibility.

COMBINATIONS OF ANTISEPTICS
Antiseptic solutions are used alone and in combinations
mainly admixture of antiseptic solutions to produce synergistic effect. Another advantage of the combination of antiseptics is that it reduces the chances of microbial resistance. In USA, marketed ASAs usually contain combinations of antiseptics such as chlorohexadine and cetrimide, iodophors/iodine\textsuperscript{14,15} and naturally occurring agents such as honey are also used in the prevention of SSIs\textsuperscript{13}. Commercially available combinations of ASAs are Chloraprep, DuraPrep solution, Betadine\textsuperscript{9} Octenisept, Lavasept, Prontosan, Braunol, Hibiclens or Savlon Betaisodona\textsuperscript{8} Hibitane and Hibiscrub\textsuperscript{10}. A strong anti-bacterial effect has been shown with low concentration by Lavasept, Prontosan, and Octenisept as compared to povidone-iodine\textsuperscript{8}.

The major property of an antiseptic solution is its bactericidal and the residual effect for prolonged period either on skin or on mucous membrane\textsuperscript{10}. Antiseptics should leave a water soluble layer on the skin that upholds the antimicrobial property more than 48 hours and even resists wash-off by blood products and normal saline solutions e.g., Iodine Povacrylex [mixture of iodine (0.7%) and isopropyl alcohol (74% w/w)]. The adhesive property of ASSs facilitates the decontamination for open surgeries such as retroperitoneal lymph node dissection, radical prostatectomy, and cystoprostatectomy\textsuperscript{9}. A gentle pressure should be applied on patient’s skin to increase the antibacterial efficacy of ASAs e.g., alcohol reduces markedly bacterial count when friction is applied as compared to that without friction application of ASAs on the skin\textsuperscript{12}. One of the basic properties of antiseptic solution is to remove microbes as much as possible without irritating and damaging the skin or mucous membrane\textsuperscript{10}. ASAs must be applied on patient’s skin in concentric circles from the area of incision \textsuperscript{14,16}. They should be fast acting, broad spectrum and have consistent effect\textsuperscript{17,18}. Aqueous based ASAs are usually preferred for cervical and vaginal surgeries like minilaparotomy or endometrial biopsy using 2-4% chlorhexadine gluconate or povidone-iodine\textsuperscript{10}. The use of ASAs has reduced the economic burden on patients by more than £600 in UK\textsuperscript{13}.

**HAND SANITIZATION**

The most important challenge is the safety of the patient is to control the invasion of microbes. Surgical gloves have been punctured during the operations; therefore, there is a need for proper hand wash to prevent transfer of normal flora on skin of the hand to the patient\textsuperscript{19}. WHO has established first guidelines on hand hygiene\textsuperscript{1}. The resident bacterial counts on hands have been markedly reduced by surgical hands scrub prior to surgery\textsuperscript{20}. Scrubbed hand should be kept up away from body and dried by sterile towels before putting on sterile gloves and gowns\textsuperscript{11}. Larson has documented the alcohol based antiseptic solutions and that hand wash reduces a large number of bacteria and fungi\textsuperscript{13}. The microbes usually reside in nails, deep crevices, and hair follicles and can be removed by detergent solutions and water, and antiseptic solutions such as alcohol, chlorhexidine and povidoneiodine\textsuperscript{20}. According to Hingst\textsuperscript{21}, the bacterial counts are reduced by scrubbing for at least 2 minutes and it is as effective as the conventional 10- minute scrub. By the help of brush, there should be proper cleaning beneath the finger nails\textsuperscript{15,16,22}.

**SOURCE OF INFECTIONS**

The universal source of the pathogens is the human body itself. Skin is the best barrier to prevent invasion of microorganisms. Bacteria are commonly found as normal flora not only on skin but also in nose, mouth, and respiratory tract\textsuperscript{10}. Microbial counts are high in number especially in the axilla, groin, perineal region, anus, and vagina. Each sponge of ASAs should be discarded after a single use. Nearly currently, no available ASAs are ideal for every condition and eradicate all microbes\textsuperscript{24}. By the appliance of iodine-alcohol, coagulase negative staphylococci have been isolated even after three applications\textsuperscript{25}. Some transient microbes can also be removed but many resident bacteria and even most vegetative microbes and viruses including all transient microorganisms are killed by anti-septic solutions\textsuperscript{10}. Multi-drug resistance microbes are also found in various surgeries, like Staphylococcus epidermidis,
Staphylococcus aureus, and even methicillin-resistant Staphylococcus aureus (MRSA) and some fungi such as Candida spp., Aspergillus niger, Histoplasma capsulatum, Blastomyces dermatitidis, Cryptococcus neoformans, Coccidioides immitis, and dermatophytes. A wide number of microorganisms are especially encountered in genitourinary surgery including Enterococcus, Staphylococcus species, and Gram-negative rods. Staphylococcus aureus is the most common single isolate in chronic wounds especially in foot ulcer, 76% in some hospitals, MRSA and vancomycin-resistant Staphylococcus aureus (VRSA) have become common and cause increased resistance to traditional antiseptics.

STORAGE OF ANTISEPTIC SOLUTIONS
The main problem arising during the storage of ASSs is the prevention from evaporation and contamination. ASSs may be contaminated by some virulent microorganisms like Pseudomonas aeruginosa, Staphylococcus epidermidis, Staphylococcus aureus, gram-negative bacilli, and some endospores. There must be some precautionary measurements taken for ASSs such as not to remove the top lid of containers; always pour ASSs from bulk container to small and reusable container; before refilling of ASSs in small container it should be washed with soap and clean water and if necessary rinse with boiled water; do not use cotton buds or guaze in ASSs; should be stored in cool and dark place; avoid the direct exposure of sunlight or excessive heat; when bottle is opened, solution should be used within one week (prolonged storage increases the chances of contamination); turbid or cloudy solutions should not be used. Contaminated Povidone-iodine and poloxamer-iodine solutions may cause pseudobacteraemia and peritonitis due to the presence of Bacillus cepacia, P. cepacia or P. aeruginosa.

ANTISEPTIC AGENTS
The most commonly used antiseptic agents are as follows:

OCTENIDINE
Octenidine is an effective, safe bispyridine ASA, it not only kills Gram-negative and Gram-positive bacteria but also has significant effect on fungi. It also exhibits its action on herpes simplex virus, hepatitis B virus, and even HIV. It is usually applied in a highly effective concentration of 0.1% with no toxic effect. A useful antiseptic agent can be applied on male genital tract and mucous membrane of female. Due to its unpleasant effect, it has limited application in the oral cavity.

Triclosan
It has extensively been used for more than three decades in surgical scrubs, handwashes, and consumer products. It is less effective against Gram-negative, fungi and mycobacteria as compared to Gram-positive, even resistant strains of some antibiotics can be killed by 1% concentration. It has high efficacy against influenza A virus, herpes simplex virus and HIV. Triclosan solution has prolonged residual effect against transient and resident flora with nontoxic effects. It has killing effect on MRSA but some strains have reduced its susceptibility.

Chloroxylenol
Para-chlorometaxylenol (chloroxylenol) also possesses the same properties as that of triclosan. It can be neutralized by nonionic surfactants. Chloroxylenol is available in various concentration from 0.5-3.75% e.g., Dettol.

Iodine/Iodophor
Iodine is extensively used as a broad spectrum antiseptic agent on mucous membrane, wounds, and skin. It is available in both alcohol based (tincture of iodine) and water based iodophor (povidone iodine) solutions. Due to its availability in both sort of preparations, antiseptic of choice in surgeries like retroperitoneal lymph node dissection, radical prostatectomy, cystoprostatectomy and transurethral surgery. The most extensively used iodophore is povidone-iodine which is generally
available in preparations contain 1–10% povidone–iodine, equivalent to 0.1–1.0% of available iodine\textsuperscript{35}. Iodophors can be safely applied on the mucous membrane and on all surface of skin, contain iodine complexed with a solubilizing agent that allows for the release of free iodine\textsuperscript{9}. Iodine usually kills microbes by its action on amino acids and fatty acids, destroying cell structures and enzymes and DNA\textsuperscript{36}. Its prolonged contact may inactivate certain fungi and bacteria spores\textsuperscript{37}.

Alcohol based iodine solutions have shorter application and drying times\textsuperscript{9}. Iodophors are a better substitute of aqueous iodine and tincture of iodine as antiseptics\textsuperscript{12}. Major disadvantages related to iodophors are allergic reactions and is inactivated by blood or serum proteins. If the patient is treated for a longer period on a larger surface area, it may increase the serum iodine (and iodide). In case with hyperthyroidism, other disinfectants are used as antiseptic agents\textsuperscript{35}. It is better to check the hypersensitivity reactions before using antiseptics contain iodine. Povidone-iodine is commercially available at 1:2 – 1:100 to eliminate S. aureus and Mycobacterium chelonae more rapidly than the strong solutions\textsuperscript{12}. In contaminated povidone-iodine antiseptic solution B. cepacia has found to stay alive for up to 68 weeks\textsuperscript{38}. On exposure to concentrated solutions, S.aureus can survive for 2 minutes but on exposure of 1:100 dilution it cannot survive for 15 seconds\textsuperscript{12}.

Chlorhexidine
During the past four decades, chlorhexidine (a bisbiguanide) has generally been used as an antiseptic agent in surgery because of its efficacy and safety profile\textsuperscript{39,40}. It has also been used as a hand sanitizer and for the prevention and treatment of mouth disease (e.g. in mouthwash, plaque control, oral hygiene) but is bitter in taste and should be masked\textsuperscript{49}. Chlorhexidine has been coated on intravenous catheters to prevent from phlebitis and blood stream infection\textsuperscript{41}. It is available in both aqueous and alcoholic solutions as chlorhexidine gluconate and digluconate. It cannot be applied on genital organ like iodine\textsuperscript{9}. Its bactericidal activity is by destroying the bacterial cell membrane, causing coagulation of cell contents and leak out of cellular contents from cell\textsuperscript{40}. Chlorhexidine gluconate (CHG) has several benefits over iodophor such as higher antibacterial activity and prolonged residual action up to 6 hours. It is not inactivated by blood products like that of povidone-iodine\textsuperscript{42-44}. CHG should not be used for a long-term due to its severe hypersensitivity, and even anaphylaxis\textsuperscript{45,46}. It cannot be easily washed if absorbed by cotton or other fibers\textsuperscript{39}. CHG has been popularly used as hand scrubber and as disinfectant in the surgery of patient\textsuperscript{47}. It has been commonly formulated as 4% aqueous solution\textsuperscript{17}. CHG should be used with precautions since it is inactivated by soap and shampoos. It is irritant to eye and otoxic\textsuperscript{48}. It exhibit bactericidal and fungicidal effect but is also effective against influenza virus, herpes simplex virus, HIV, coxsackievirus, poliovirus, and rotavirus\textsuperscript{39}. CHG possesses low activity against spores of bacteria and fungi. Moreover, Mycobacteria cannot be killed but inhibited by CHG. Its activity can be reduced under acidic and basic environment and by anionic and nonionic soap, detergents, and moisturizers\textsuperscript{12}. Chlorhexidine solution has shown resistance against Proteus mirabilis, S. marcescens, S. aureus, P.aeruginosa, after prolonged use\textsuperscript{49,50}.

Alcohol
For a long period, alcohol (ethyl alcohol 60-95% and isopropyl alcohol 50-91.3%) is used as a nontoxic, non staining, quick, sustained, and durable and non allergic comparatively inexpensive broader spectrum antimicrobial agent\textsuperscript{11}. Alcohol is treated as a gold standard anti-septic in Europe\textsuperscript{52} due to its superior activity not only on Gram-negative and Gram-positive bacteria but also on viruses and resistant microbes like Methaillin Resistant Staphylococeus aureus (MRSA) and Vancomycin Resistant Enterococci (VRE), Mycobacterium tuberculosis and fungi\textsuperscript{52,53}. Alcohols destroy microorganisms by the damage of specific cellular functions and denaturation or coagulation of proteins, such as enzymatic proteins\textsuperscript{54}. CHG or iodophor solutions also contain alcohol for
a durable, sustainable effect for a long period after evaporation\textsuperscript{10}.
Alcohols (ethyl alcohol and isopropyl alcohol (IPA)) have broad spectrum of coverage against bacteria. Alcohol coagulates the enzymatic proteins which may impair the biological activity of microorganism and possess viriscidal and fungicidal effect. Its antimicrobial activity is enhanced by a dilution of 60-90\%\textsuperscript{12}. Ethyl alcohol (70-80\%) shows antibacterial activity against S. aureus, Streptococcus pyogenes, Enterobacteriaceae and P. aeruginosa. Isopropyl alcohol (IPA) exhibits greater antibacterial activity compared to ethyl alcohol. It is highly effective against fungi like Cryptococcus neoformans, Coccidioides immitis, Candida spp., Blastomyces dermatitidis, Aspergillus niger, Histoplasma capsulatum, and dermatophytes and mycobacteria, including Mycobacterium tuberculosis, and even the resistant VRE\textsuperscript{55}. Influenza virus, herpes simplex virus, and adenovirus can be inactivated by IPA and ethyl alcohol\textsuperscript{37}. Alcohols enhance the residual time and antibacterial activity. ASA like chlorhexidine is less active compared to alcoholic chlorhexadine\textsuperscript{56,57}. The major problem encountered with alcohols is when dry on the surface, they may cause irritation. They cannot penetrate protein rich material\textsuperscript{12} and are prone to flammability. A few cases of fire from alcohol-based skin preparations in the operation rooms have been reported\textsuperscript{58}. Droplets of alcohol may possibly produce explosive vapours\textsuperscript{9}.

**CONCLUSION**

Antiseptic agents (ASAs) are not only extensively used to reduce the chances of surgical site infections (SSIs) but are also applied as hand sanitizer. It has been concluded that there does not exist any single ideal antiseptic solution, which provides coverage against all causative pathogens of SSIs. Mainly the combinations of antiseptic solutions exhibit synergistic effect against pathogens. Only few ASAs possess activity against virus, fungi, and spores. ASAs may cause irritation and hypersensitivity; moreover, they may be contaminated by virulent pathogens. Currently used antiseptic solutions may cause cytotoxicity. It has been recommended in several guidelines that the sensitivity of ASAs should be checked before application.

**REFERENCES**


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