



# International Journal of Medical and All Body Health Research



International Journal of Medical and all body Health Research

ISSN: 2582-8940

Received: 03-09-2021; Accepted: 18-09-2021

www.allmedicaljournal.com

Volume 2; Issue 5; September-October 2021; Page No. 20-23

## Use of Chlorhexidine gluconate in wound healing and its potential formation of granulation tissue

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### Abstract

**Background:** According to the literature described, antiseptics are chemical agents whose function is to inhibit or destroy the growth of microorganisms in living tissues, among the most widely used antiseptics is chlorhexidine gluconate, which is widely used in hospitals due to its characteristics and properties. different applications, which make a powerful agent to prevent infection at the wound site.

**Methodology:** A narrative review was carried out in which databases such as pubmed, science direct, scielo, academic Google, among others, were used to search for articles, these were taken from indexed journals in first and second

languages. As keywords, the descriptors DECS and MeSH, antiseptics, chlorhexidine gluconate, wounds, infection were used.

**Results:** Several studies have demonstrated the effectiveness of chlorhexidine gluconate, in preventing infections in wounds, and various application techniques have been used, such as compresses impregnated with the antiseptic, washing in the preoperative site before the incision, showers or baths, among others. All demonstrating the high efficiency in reducing bacterial colonies.

**Keywords:** Chlorhexidine gluconate, antiseptics, wounds, infection

### Introduction

Antiseptics are chemical agents that destroy or inhibit the growth of microorganisms in living tissues in a non-selective way. The main objective of antiseptics is to reduce the colonization of microorganisms, avoiding the infection of open wounds. Among the most widely used antiseptics is chlorhexidine gluconate (CHG) <sup>[1]</sup>. Which has been available for more than 50 years and is considered an important component to be safe and effective and largely for the reduction of associated infections in medical care <sup>[2]</sup>.

CHG is a cationic bisbiguanide developed in England in 1954. The base form is minimally soluble in water, but the salt form, digluconate, is much more soluble. Its antimicrobial activity is attributed to its binding to the cytoplasmic membrane, altering the osmotic balance and causing precipitation of cell contents <sup>[3-4]</sup>.

### Methodology

A narrative review was carried out, the search for articles was carried out using databases such as pubmed, science direct, scielo, academic google, among others; Indexed journals were used in the first and second languages, that is, English and Spanish. The keywords DECS and MeSH, chlorhexidine gluconate, antiseptics, wounds, infection were used as keywords. With the aforementioned terms, a total of 30 related articles were found, of which 14 were used for the development of this writing. The inclusion criteria used were that they allow the reading of the full text, were related to the subject studied and that they were not less than the year 2017; As exclusion criteria, it was found that it did not allow a complete reading and that its theme was not in accordance with what was needed.

## Results

### Chlorhexidine Gluconate

There are varieties of chlorhexidine salts, but the most used in the hospital environment is chlorhexidine gluconate, due to its solubility characteristics, allowing it to be combined with alcohol, increasing its activity. It is stable at room

temperature and needs to be protected from light. In the presence of alkaline pH and anionic soaps / detergents, its activity decreases. It should not be mixed with other non-alcoholic antiseptics, as it could precipitate <sup>[5]</sup>. CHG has different clinical applications from oral hygiene to skin preparation in the preoperative surgical bed <sup>[6]</sup>.

**Table 1:** Composition of chlorhexidine gluconate

| Chlorhexidine gluconate | It belongs to the biguanide family                                                                                                                                                                                                               |
|-------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                         | <b>-Stability:</b> It needs to be protected from light. It is not deactivated in the presence of organic matter.                                                                                                                                 |
|                         | <b>Compatibility:</b> It is compatible with cationic derivatives, but it is incompatible with anionic surfactants, some non-ionic compounds and some colorants.                                                                                  |
|                         | <b>Mechanisms of action:</b> It acts on the cytoplasmic membrane with a maximum effect in 20 s and a subsequent residual effect, preventing microbial growth for about 29 h.                                                                     |
|                         | <b>Aspect of activity:</b> It is bactericidal on gram-positive and gram-negative bacteria, some strains of <i>Proteus</i> spp. And <i>Pseudomonas</i> spp, yeast and mold.                                                                       |
|                         | <b>Antiviral action:</b> Includes HIV, herpes simplex, cytomegalovirus and influenza. It does not act on mycobacteria and spores.                                                                                                                |
|                         | <b>Toxicity and other effects:</b> It presents few allergic reactions and little irritation to the skin and mucous membranes. It should not be applied to the CNS, meninges or the middle ear due to its neuro ototoxicity, leading to deafness. |

Chlorhexidine is used at different concentrations: 4% aqueous solution with detergent base for the patient's body wash and pre-surgical hand washing, 1% aqueous solution on wounds, 0.5-2% alcoholic solution (ethyl or isopropyl

alcohol 70%) for skin disinfection in preoperative procedures <sup>[5]</sup>. Depending on the concentration in which it is, this will be the way of its use, table 2.

**Table 2:** Recommendations for clinical use

| 2% or 4% soap solution                        | Use: surgical hand washing, skin preparation prior to invasive procedure, inpatient baths.           |
|-----------------------------------------------|------------------------------------------------------------------------------------------------------|
| Chlorhexidine in alcoholic base at 0.5% or 2% | Use: Skin preparation prior to invasive procedures: venipuncture, installation of vascular catheters |
| Chlorhexidine 1% and alcohol 61%              | Usage: surgical hand washing                                                                         |
| 2% aqueous based dyed chlorhexidine           | Use: Preparation of the skin prior to surgeries                                                      |
| Chlorhexidine in aqueous base 2%              | Use: Preparation of the skin prior to surgeries                                                      |
| 0.12% oral solution or 0.2% gel               | Use: dental surgeries, toilets in the oral cavity in patients undergoing mechanical ventilation.     |
| Gel or sponge dressing with 2% chlorhexidine  | Usage: Venous Catheter Coverage, External Fixator Insertion Site Coverage <sup>[8]</sup>             |

### Use of Antiseptics in Wounds

Antiseptics are used on open wounds for the prevention and treatment of infection, thus improving healing. The proper use of antiseptics helps greatly to reduce the consumption of antibiotics, due to the increase that is being seen in bacterial resistance to antibiotics, arousing great interest in the scientific community in antiseptics and dressings

impregnated with them <sup>[9]</sup>.

Wounds are classified into different groups and in turn into subgroups, we find surgical wounds that are distributed in class I-IV (Table 3), wounds according to the evolution of the scarring process, dividing into acute and chronic, and according to the mechanism of action (table 4) <sup>[9-10]</sup>.

**Table 3:** Classification of surgical wounds

| Class                            | Infection Risk | Examples                                                                      |
|----------------------------------|----------------|-------------------------------------------------------------------------------|
| CLASS I: clean wound:            | <2%            | Laparotomy, breast resection, vascular interventions.                         |
| CLASS II: clean wound:/ polluted | <10%           | Elective cholecystectomy, small bowel resection, laryngectomy.                |
| CLASS III: contaminated wound:   | 20%            | Appendicular phlegmon, gangrenous cholecystitis.                              |
| CLASS IV: dirty / infected wound | >40%           | Infected traumatic wounds, accumulation of pus like abscesses <sup>[10]</sup> |

**Table 4:** Classification of wounds according to their mechanism of action

| A. Traumatic                                                                                                                                                                                                                                                                                                                                        | B. Surgical                                                                                                                 |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>Produced as a result of trauma or assault.</li> <li>Incises: provoked with a Sharp object</li> <li>Blunt: caused by blunt object</li> <li>Sharps - caused by long, sharp objects</li> <li>Abrasions: caused by friction, behaving like burns</li> <li>By bite: they have a high risk of infection</li> </ul> | Produced in a sanitary environment, with previous field cleaning and with disinfected sanitary instruments <sup>[5]</sup> . |

Different measures have been adopted for wound healing, highlighting the use of antiseptics as optimal therapeutic measures in reducing infections, among the uses given to antiseptics such as CHG we find antiseptic showers or baths. A study involving more than 700 patients in which they received two antiseptic baths with chlorhexidine, mainly demonstrating a reduction of up to 9 times the bacterial colonies, while soap medicated with povidone iodine or triclocarban reduced the colony count by 1.3 and 1.9 times [12]. Due to the great reduction of bacteria strains by the CHG, these measures have been adopted in the intensive care unit (ICU), performing daily baths with CHG and incorporating the use of mouthwash twice a day, becoming a standard of care primary [11-12]. In a prospective study, Ostrander *et al* evaluated 125 consecutive patients undergoing foot and ankle surgery using random antiseptics in patients (0.7% iodine and 74% isopropyl alcohol; 3.0% chloroxylonol or 2% of chlorhexidine gluconate and 70% isopropyl alcohol), quantitative samples were obtained from 3 sites. CHG was found to be the most effective agent for killing bacteria [13]. Another effective application of chlorhexidine to prevent surgical site infections, especially *Staphylococcus aureus*, is the decolonization of asymptomatic carriers, who present a higher risk of infections due to this pathogen. Bode *et al.* carried out a prospective, randomized, double-blind clinical study involving 808 patients who were to undergo surgery.

One group was treated with a combination of mupirocin and chlorhexidine, while the other was treated with placebo. The mupirocin and chlorhexidine group had lower rates of deep incision infections than the placebo group [3].

### Discussion

Different studies such as that by Hamill *et al.*, Which speak of corneal abrasion models in rabbits, showed that irrigation with 2% and 4% chlorhexidine gluconate decreased the re-epithelialization rate, but this did not happen with concentrations from 1%. In another similar study by Platt and Bucknall, but in infected guinea pig wounds, irrigation with chlorhexidine gluconate completely prevented sepsis and did not slow the wound healing rate [14].

In a retrospective observational study, they analyzed patients with defects in skin coverage, both adults and pediatric, of both sexes, admitted to the trauma and orthopedic service of the Regional Hospital of Comodoro Rivadavia, Chubut, Argentina, since July 1, 2017 until December 21, 2018. The longest granulation time that was observed was in patients who presented symptoms of wound infection, so the infectious picture could have been treated simultaneously to accelerate and achieve adequate tissue granulation. The wound that required the longest granulation time was that produced by an active fistula due to leg osteomyelitis resulting from an open fracture [14].



**Fig 1:** Patient presents traumatic amputation injury A. Foot injury from vehicular accident with amputation of hallux. B. Day 9 post-treatment with 20% chlorhexidine digluconate in a condition to receive epithelialization, graft or skin flap treatment, or a referral to a plastic surgeon. Image taken from [14].

### Conclusion

Chlorhexidine gluconate, used in a correct way could help prevent many infections at the wound site, helping not only to heal potentially fatal wounds but also allowing the formation of new tissue in a faster way, this being optimal. Antiseptic has proven to have a great advantage compared to others such as povidone iodine or triclocarban, and when used properly, the massive consumption of antibiotics could be reduced.

Currently there are not enough studies to make comparisons of studies and further demonstrate the effectiveness of this antiseptic in terms of the formation of granulation tissue, but it is believed that this antiseptic may be related to the formation of tissue.

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