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Department of Surgery and Ophthalmology

Comparative study of Povidone-Iodine and Chlorhexidine used in surgical procedures of dogs and cats.

(Review of literature)

THESIS

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Table of contents

Contents

List of abbreviations

CHX – Chlorhexidine

CG – Chlorhexidine Gluconate

CGI – Chlorhexidine Gluconate in Isopropanol

CD – Chlorhexidine Diacetate

PVP-I – Povidone Iodine

BZC – Benzalkonium Chloride

CET – Cetrimide

SC – Saline Control

SSI – Surgical Site Infection

CFU – Colony Forming Units

ANOVA – Analysis of Variance

MRSA – Methicillin Resistant Staphylococcus Aureus

MRSP – Methicillin Resistant Staphylococcus Pseudointermedius

CoPS – Coagulase-Positive Staphylococci

MSCoPS – Methicillin Susceptible Coagulase-Positive Staphylococci

MRCoPS – Methicillin Resistant Coagulase-Positive Staphylococci

BHI – Brain Heart Infusion

RODAC – Replicating Organism Detection and Counting

BGS – Bacterial Growth Score

MIC – Minimum Inhibitory Concentration

1. Abstract

Antiseptics used on skin and oral mucosa play a significant role perioperatively. They can influence the tissue regeneration period and prevent the development of infections on post-surgical wounds. The most common antiseptics used nowadays in Veterinary medicine are PVP-I and CHX. Each one of them has a different mechanism of action, duration of action, cytotoxic reactions, and antimicrobial spectrum, for example CHX acts against Methicillin-Resistant Staphylococcus Aureus within shorter exposure time than PVP-I. Veterinary surgeons are encouraged to be knowledgeable about the efficacy of asepsis protocols used in surgery and to take these factors into consideration in all situations. This study will conduct a literature review and compare the effectiveness of PVP-I and CHX.

2. Introduction

Antiseptics are chemical agents that have been used preoperatively since the 1840s, when a Hungarian medical doctor, Ignaz Semmelweis recorded a significant decrease in puerperal sepsis related with the use of suitable handwashing strategies at the 1st Clinic of Obstetrics and Gynecology in Vienna. Then, in the 1870s Lister used carbolic acid and exhibited superior infection control and a decrease in surgical morbidity and therefore, antiseptics earned more recognition and are now used in almost every surgical operation. Antisepsis is an essential component in limiting Surgical Site Infection (SSI), any infections that are developed at the operative wound within 30 days of the operation. They are used preoperatively as scrubbing to eliminate the skin flora physically and to inhibit and limit the number of microorganisms chemically. (Echols *et al.*, 2015)

Surface skin flora of dogs and cats typically includes Actinobacteria, Bacteroidetes, Firmicutes, Fusobacteria and Proteobacteria, and in a large number Corynebacteriaceae, Staphylococcae, Moraxellaceae and Mycoplasmataceae. (Zamarian *et al.*, 2020) However, in Surgical Site Infections (SSI) the most frequent bacteria involved is Staphylococcus Aureus and other bacteria such as Enterococcus, Escherichia Coli, group A Streptococci and Pseudomonas Aeruginosa. (Echols *et al.*, 2015)

Another prevention method of SSI is the aftercare of the surgical wound. Post-surgery wound treatment options are antibiotics and alternatively antiseptics which have a broader antimicrobial spectrum than antibiotics. This is because microorganisms have several modes of action that target different components of cell biology. (Bigliardi *et al.*, 2017)

Generally, the efficacy of a perfect antiseptic depends on its capability to penetrate biofilms and necrotic tissue, broad spectrum effect against microorganisms, minimal possibility for resistant strain development, good tolerability, and wound healing aid by suppressing pain, skin irritation, inflammation, and swelling. Ideal antiseptics used before and after the operation are the ones that have the greatest efficacy without harming healing tissues, as a side effect, and the ones that are effective for a longer time. Nowadays, according to these properties Povidone-Iodine (PVP-I) and Chlorhexidine (CHX) are the most frequent substances used in surgeries by veterinarians and medical doctors. (Bigliardi *et al.*, 2017)

This thesis aims to expand the knowledge for the decision of which of the two antiseptics, PVP-I and CHX, should be used in surgery based on their comparative study. This study was carried out using data of various research and experimental trials conducted by veterinarians, medical doctors, and scientists with the purpose of understanding the different efficacy of PVP-I and CHX.

3. Povidone-Iodine (PVP-I)

3.1 History

Iodine, a naturally occurring element, has been used to prevent infection and cure wounds for over 150 years. However, it was only with the invention of iodophors as this extremely effective microbicide could be used in a variety of medicinal purpose. Bernard Courtois, a chemist from Dijon, discovered the natural element iodine in 1811 and in 1880, after 69 years, its bactericidal efficacy was described for the first time by Davaine. Because of the extremely violet color vapors, it was named after the Greek word “ioeides”, which means "violet-colored." Nonetheless, despite having no real knowledge of the active component, use of its curative effect had been made previously. Wounded men were treated with extracts from seaweed, a plant rich in iodine from sea water, during Napoleon's Egyptian campaign. Iodine was typically utilized as iodoform and ethylic iodine tincture even though it had the drawbacks of having irritating and caustic properties on skin and mucosa. Later on, Iodophors were large-scale used because of the fact that they were developed and the detoxification of iodine took place by binding to macromolecules. (Fleischer and Reimer, 1997)

3.2 Morphological structure

PVP-I forms a complex with the synthetic carrier polymer povidone, 1-vinyl-2-pyrrolidinone polymer (Figure 1), and a halogen emitting compound. This agent influences key proteins and their nucleotides, fatty acids and generally the cell negatively. (Atiyeh, Dibo and Hayek, 2009)

Iodine is bonded to the synthetic polymer complex by hydrogen bonds in the water-soluble complex. Nevertheless, in the aqueous solution equilibrium is established by free iodine being liberated from the PVP-I complex.(Figure 2) (Bigliardi *et al.*, 2017)

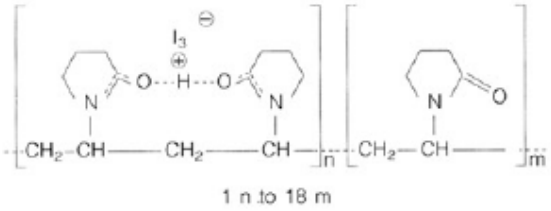

Figure 1. The poly(1-vinyl-2-pyrrolidone)-iodine complex, source by: (Fleischer and Reimer, 1997)

Figure 2: The chemical equilibrium of PVP-I in aqueous medium. (Fleischer and Reimer, 1997)

3.3 Mode and Mechanism of action

Principally, the mode and mechanism of action of PVP-I relies on the free iodine released. PVP-I has not only a bactericidal effect but also an effect on other pathogenic organisms called germicidal effect. The germicidal effect of PVP-I is set on by the concentration of free iodine and its oxidative potency (Figure 3). It has the ability to inhibit the essential cellular mechanisms of bacteria, destruct the cell structures and also denature and deactivate vital enzymes. (Bigliardi *et al.*, 2017)

Electron microscopic methods and biochemical tests were used in recent projects by Schreier et al. to illustrate molecular destruction pathways in various microorganisms and he came into conclusion that microorganism enzyme denaturation is caused by the interaction of PVP-I with the cell wall and the lipid membrane that leads to persistent pore formation.(Fleischer and Reimer, 1997)

In addition, PVP-I had the ability to decrease inflammation caused by the host itself and the pathogens. The effects against the inflammation caused by the host are that it has an antioxidant effect by regulating the redox potential, it suppresses inflammatory cells, decreases the plasmin initiation, increases the healing process by the initiation of white blood cells and inhibits metalloproteinase production. In the case of inflammation caused by the pathogen, PVP-I stops the assembly of exotoxins and bacterial enzymes produced by the pathogen. (Bigliardi *et al.*, 2017)

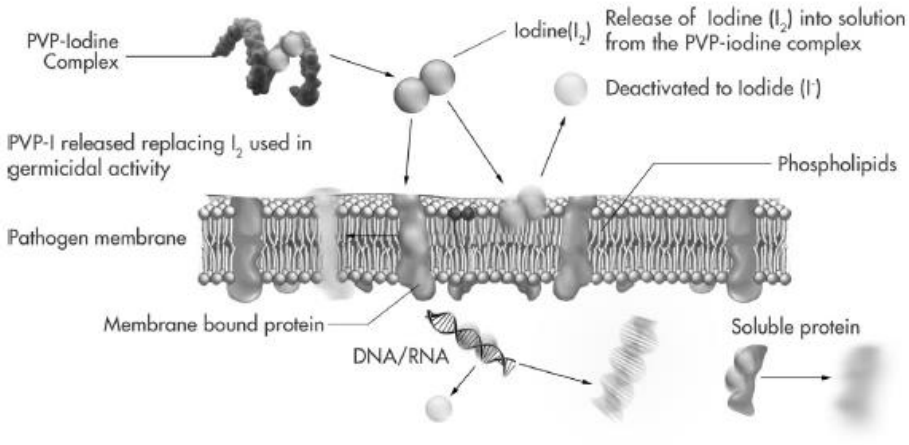

Figure 3: Mechanism of action of Povidone-Iodine in equilibrium free iodine. Free iodine ocidises vital pathogen structures. (Bigliardi *et al.*, 2017)

3.4 Antimicrobial spectrum

One of the few topical antimicrobials with a broad killing range is PVP-I. It acts against gram-positive and gram-negative bacteria, fungi, spores, viruses, protozoa, and amoebic cysts (Table 1 & 2). In comparison with CHX, it acts against Methicillin-Resistant Staphylococcus Aureus within shorter exposure time. (Bigliardi *et al.*, 2017)

Table 1: Microbicidal spectrum of iodine (Fleischer and Reimer, 1997)

Gram-negative bacteria	Viruses	Gram-positive bacteria
Aerobacter aerogenes	Influenzaviruses	*Bacillus* sp.
Bacteroides sp. *(oralis)*	Poliomyelitis viruses	*Clostridium* sp.
Citrobacter sp.	Herpesviruses	*Corynebacterium* sp.
Edwardsiella sp.	Vaccinia virus	*Diplococcus pneumoniae*
Escherichia coli	Rubella virus	*Diphtheroides* sp.
Haemophilus sp. *(vaginalis)*	HIV	*Micrococcus flavus*
Herellea sp.	Acid-fast bacteria	*Sarcina lutea*
Klebsiella sp.	*Mycobacterium* sp.	*Staphylococcus* sp.
Mimea polymorpha	Treponema	*Streptococcus* sp.
Neisseria gonorrhoeae	*Treponema pallidum*	Yeasts and other fungi
Proteus sp.	Protozoans	*Aspergillus* sp.
Pseudomonas sp.	*Entamoeba histolytica*	*Candida* sp.
Salmonella sp.	*Trichomonas vaginalis*	*Cryptococcus neoformans*
Serratia sp.		*Epidermophyton floccosum*
Shigella sp.		*Microsporum audouinii*
		Nocardia sp.

Table 2: Antimicrobial spectrum for different antiseptics (Bigliardi *et al.*, 2017)

Antiseptic	Vegetative bacteria			Spores	Fungi	Viruses
	Gram-positive	Gram-negative	Actinobacteria			
Povidone iodine 10%	BC +++, LS	BC +++, LS	BC ++	SC ++	FC +++, LS	VC ++, LS
Polihexanide	BC +++, LS	BC +++, LS	NA	NA	FC ++, IS	VC +, IS
Chlorhexidine	BC +++, LS	BC +++, IS	NA	NA	FC ++, IS	VC +, IS
Octenidine	BC ++, LS	BC ++, IS	NA	NA	FC ++, IS	VC +, IS
Ethanol 70%	BC +, LS	BC +, LS	BC +	NA	FC +, LS	VC +

+: Weak; ++: Medium; +++: High.
BC: Bactericidal; FC: Fungicidal; IS: Incomplete spectrum; LS: Large spectrum; NA: No activity; SC: Sporicidal; VC: Virucidal.

3.5 Adverse effects

PVP-I used in pre-operative surgery for long time or even in high concentrations, can cause systemic toxicity, ioderma-like reaction and skin burns. (Echols *et al.*, 2015) Furthermore, its' commercial product (e.g., Betadine) label states that it should not be used by allergic patients, patients that undergo radio-iodine therapy or patients that have thyroid disturbances. (Bigliardi *et al.*, 2017)

3.6 Clinical applications

PVP-I is widely used as a preventative as well as therapeutically in wounds. Firstly, it is used for mucosal antisepsis and for skin and hand disinfectant, which implies that it can also be used pre-operatively. It's great ability on reducing SSI confirms that it is one of the first clinical options in sensitive surgeries such as breast and spinal surgery, total joint arthroplasty and intraperitoneal flushing during laparotomy. (Bigliardi *et al.*, 2017) Moreover, clinical studies carried out by Rahn's work group and other scientists have shown that prior to oral cavity surgeries, radio chemotherapy and uro-catheterization, diluted PVP-I is also used. This is because it is efficient for prevention of bacteremia rate occurring after surgery and its ability to heal damaged mucosa. These studies also demonstrated its high systemic tolerance over a prolonged period of daily hygienic administrations on the mucosa. (Fleischer and Reimer, 1997)

In therapeutic use, PVP-I is an important and useful agent as well. It is applied on acute and post-operative wounds along with chronic and burn wounds to promote early onset of epithelization and diminish bacterial counts. Likewise, several clinical trials took place and revealed that PVP-I's fast healing rate aids for the treatment of leg ulcers, diabetic foot ulcers and pressure ulcers. In these trials PVP-I solution was applied on a daily basis locally and it has been observed that it decreased the microbial burden, inflammation and hence pain reception. (Bigliardi *et al.*, 2017) In addition, when PVP-I is utilized at correct dilutions it can also be used for the eye and body cavities. For example, on the treatment of eye infections, pleural empyema, mediastinal infections and the prophylaxis against ophthalmia neonatorum. (Fleischer and Reimer, 1997)

4. Chlorhexidine (CHX)

4.1 History and Morphological structure

CHX is one of the most frequent antiseptics used for skin and mucous membrane sepsis since its' description in 1954. (McBain *et al.*, 2003)

Its chemical structure consists of two symmetrical biguanides with 4-chlorophenyl rings bonded by a hexamethylene chain (Figure 4) and on both phenolic rings, it owes singular chlorine atoms which makes it a strong cationic and alkalic molecule. Additionally, CHX is not soluble in water but salts such as gluconate, acetate, diacetate and hydrochloride makes it water soluble. (Karpiński and Szkaradkiewicz, 2015)

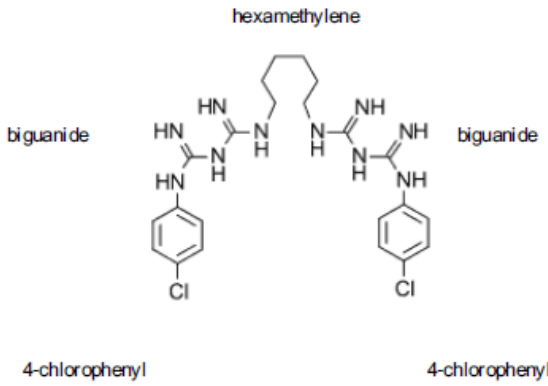

Figure 4: Structure of Chlorhexidine [1:6 di(4-chlorophenyl-diguanido) hexane].(Lim and Kam, 2008)

4.2 Mode and Mechanism of action

CXH is concentration dependent, and it acts as both bacteriostatic and bactericidal in different concentration amounts. This implies that it prevents bacterial growth (= bacteriostatic) at low concentrations and it kills bacteria (= bactericidal) completely at higher concentrations. (Karpiński and Szkaradkiewicz, 2015)

At low concentrations, it inhibits bacterial growth by passing through the cell wall of the bacteria and damaging its' cytoplasmic membrane. (Lim and Kam, 2008) This results in the escape of cytoplasmic components such as potassium, phosphorus, and other low molecular weight compounds. In higher doses, CHX induces the death of the bacteria through cytolysis. Intracellular components are being lose, cytoplasmic

proteins are coagulated and cell protein structures are modified. (Karpiński and Szkaradkiewicz, 2015)

Apart from bacteriostatic and bactericidal effect it acts also against fungi and viruses, this it is a fungistatic, fungicidal and viricidal antiseptic as well. (Lim and Kam, 2008)

4.3 Antimicrobial Spectrum

CHX acts against viruses, bacteria, fungi, and tubercle bacilli. (Table 5-7) However, its bactericidal effectiveness is stronger against Gram-positive bacteria and poorer against Gram-negative bacteria. (Table 2) It has no effectivity against bacterial spores, unless high temperatures, and it has little effect against fungi and tubercle bacilli. (Atiyeh, Dibo and Hayek, 2009)

Table 3: Bacteriostatic activity of chlorhexidine. (Lim and Kam, 2008)

Organism	Mean MIC (mg/l)	Range (mg/l)
Gram-positive cocci		
Staphylococcus aureus	1.6	1-4
Staphylococcus epidermidis	1.8	0.25-8
Streptococcus faecalis	38	32-64
Streptococcus mutans	2.5	
Streptococcus pneumoniae	11	8-16
Streptococcus pyogenes	3	1-8
Streptococcus viridans	25	2-32
Gram-positive bacilli		
Bacillus subtilis	1	
Clostridium welchii	14	4-32
Corynebacterium spp	1.6	0.5-8
Lactobacillus casei	128	
Listeria monocytogenes	4	
Gram-negative bacteria		
Acinetobacter anitratus	32	16-64
Acinetobacter lwoffi	0.5	
Bacteroides fragilis	34	8-64
Campylobacter pyloridis	17	8-32
Enterobacter cloacae	45	16-64
Escherichia coli	4	2-32
Haemophilus influenzae	5	2-8
Klebsiella oxytoca	32	
Klebsiella pneumoniae	64	82-128
Proteus mirabilis	115	64>128
Proteus vulgaris	57	32-128
Pseudomonas aeruginosa	20	
Salmonella typhimurium	13	

MIC – minimum inhibitory concentration.

Table 4: Bactericidal activity of chlorhexidine (Lim and Kam, 2008)

Organism	Mean log reduction in 0.05% chlorhexidine after 20 seconds	Mean log reduction in 0.05% chlorhexidine after 1 minute	Mean log reduction in 0.05% chlorhexidine after 10 minutes
Gram-positive cocci			
Staphylococcus aureus	0.4	0.7	2.5
Staphylococcus epidermidis	2.2	3.4	>5.1
Streptococcus faecalis	0.4	0.4	1.1
Streptococcus pneumoniae	0.8	1.5	>3.5

Table 4: Bactericidal activity of Chlorhexidine (continued)

Organism	Mean log reduction in 0.05% chlorhexidine after 20 seconds	Mean log reduction in 0.05% chlorhexidine after 1 minute	Mean log reduction in 0.05% chlorhexidine after 10 minutes
Streptococcus pyogenes	1.2	1.8	>3.7
Streptococcus viridans	0.4	0.8	2.3
Gram-positive bacilli			
Bacillus subtilis	0.5	0.5	0.3
Clostridium welchii	2.1	3.1	>4.8
Corynebacterium spp	1.1	1.4	3.7
Lactobacillus casei	0.2	0.2	4.1
Listeria monocytogenes	0.6	2.2	4.8
Gram-negative bacteria			
Acinetobacter anitratus	1.4	2.6	>5.3
Bacteroides distastonis	0.9	2.7	>4.9
Bacteroides fragilis	3.0	4.2	5.2
Campylobacter pyloridis		2.8	>4.0
Escherichia coli	3.2	5.0	>6.4
Haemophilus influenzae	>4.1	>4.1	>4.1
Klebsiella aerogenes	2.7	3.9	>5.9
Klebsiella pneumoniae	3.0	4.8	>6.2
Proteus mirabilis	0.8	0.9	2.9
Proteus vulgaris	0.8	1.0	4.1
Pseudomonas aeruginosa	1.7	2.7	4.9
Salmonella typhimurium	2.0	3.7	>6.0

Table 5: Fungistatic activity of Chlorhexidine (Lim and Kam, 2008)

Organism	Mean MIC (mg/l)
Mould/fungi	
Aspergillus fumigatus	32
Aspergillus niger	16
Penicillium notatum	16
Yeasts	
Candida albicans	9
Dermatophytes	
Epidermophyton floccosum	4
Microsporum canis	4
Microsporum fulvum	6
Microsporum gypseum	6
Trichophyton equinum	4
Trichophyton interdigitale	3
Trichophyton mentagrophytes	3
Trichophyton quinkeanum	3
Trichophyton rubrum	3
Trichophyton tonsurans	3

MIC – minimum inhibitory concentration.

Table 6: Fungicidal activity of Chlorhexidine. (Lim and Kam, 2008)

Organism	Mean log reduction in 0.05% chlorhexidine after 20 seconds	Mean log reduction in 0.05% chlorhexidine after 1 minute	Mean log reduction in 0.05% chlorhexidine after 10 minutes
Mould /fungi			
Aspergillus fumigatus	0.7	1.2	2.4
Aspergillus niger	0.7	1.2	3.0
Penicillium notatum	0.6	2.0	3.5
Rhizopus sp	0.4	0.4	0.5
Scopulariopsis spp	0.6	1.1	2.3
Yeasts			
Candida albicans	2.8	>4.1	>4.2
Candida guillermondii	3.5	>4.3	>4.3
Candida parapsilosis	2.1	3.4	>4.2
Candida pseudotropicalis	3.6	>4.4	>4.4
Cryptococcus neoformans	4.0	>4.2	>4.2
Prototheca zopfii	3.3	>3.6	>3.6
Saccharomyces cerevissia	3.7	>3.7	>3.7
Torulopsis glabrata	1.3	2.2	>4.4
Dermatophytes			
Epidermophyton floccosum	0.7	0.5	>1.8
Microsporum canis	0.4	1.0	>2.0
Microsporum fulvum	0.2	0.6	>2.4
Microsporum gypseum	0.1	0.3	2.0
Trichophyton equinum	0.5	1.1	>2.1
Trichophyton interdigitale	0.4	0.9	>2.4
Trichophyton mentagrophytes	1.3	>2.1	>2.1
Trichophyton quinkeanum	0.2	0.9	>2.8
Trichophyton rubrum	0.3	0.6	>2.4
Trichophyton tonsurans	0.4	0.3	1.6

Table 7: Virucidal activity of Chlorhexidine (Lim and Kam, 2008)

Virus	Family	Activity	Chlorhexidine (%)
Respiratory syncytial virus	Paramyxovirus	+	0.25
Herpes hominis/simplex	Herpesvirus	+	0.25
Polio virus type 2	Enterovirus	-	0.02
Adenovirus type 2	Adenovirus	-	0.02
Equine infectious anaemia virus	Retrovirus	+	2.0
Variola virus (smallpox)	Poxvirus	+	2.0
Herpes simplex virus type 1/type 2	Herpesvirus	+	0.02
Equine influenza virus	Orthomyxovirus	+	0.001
Hog cholera virus	Togavirus	+	0.001
Bovine viral diarrhoea	Paramyxovirus	+	0.001
Parainfluenza virus	Paramyxovirus	+	0.001

Table 7: Virucidal activity of Chlorhexidine (Continued)

Virus	Family	Activity	Chlorhexidine (%)
Transmissible gastroenteritis virus	Coronavirus	+	0.001
Rabies virus	Rhabdovirus	+	0.001
Canine distemper virus	Paramyxovirus	+	0.01
Infectious bronchitis virus	Coronavirus	+	0.01
Newcastle virus	Paramyxovirus	+	0.01
Pseudo rabies virus	Herpesvirus	+	0.01
Cytomegalovirus	Herpesvirus	+	0.1
Coxsackie virus	Picornavirus	-	0.4
Echo virus	Picornavirus	-	0.4
Human rota virus	Reovirus	-	1.5
Human immunodeficiency virus type I	Retrovirus	+	0.2

4.4 Adverse effects

According to many research and studies, CHX adverse effects are limited to the skin or oral mucosa. However, contact with the eyes, middle ear and meninges must be avoided. Animal and human studies have come into conclusion that it causes a permanent destruction of the corneal epithelium and later on, to the corneal opacity. (Echols *et al.*, 2015) This is the reason that in ophthalmological surgeries, the preparation around the skin of the eye, contains lower concentrations of CHX. (Lim and Kam, 2008)

Another adverse effect of CHX is proven by its use on an animal. The investigation was carried on cats and the results have shown that CHX has been related to the loss of hearing and sensory neurons of the middle ear. (Echols *et al.*, 2015)

In response to topical use, skin reactions may occur. Danish skin clinic studied the prevalence of contact dermatitis associated with Chlorhexidine-gluconate (CG) sterilization and confirmed it using patch testing technique. Likewise, many different case reports, from different countries, showed positive anaphylactic and acute hypersensitivity reactions to CHX. Lastly, in some cases CHX is used as a pre-operative antiseptic in a solution mixed with alcohol. In such a case, diathermy burns can be caused due to the alcohol. (Lim and Kam, 2008)

4.5 Clinical Applications

Persistent hand microorganisms in the superficial skin layers have been linked to nosocomial infection. The flora that resides in the skin's deeper layers is less likely to pose a threat. Therefore, antiseptic techniques are used to reduce the number of microorganisms. Iodine, alcohol, and CHX are the most frequently utilized antiseptic agents. The onset action of alcohol is the quickest, followed by CHX and finally PVP-I. However, CHX has the highest residual antibacterial action. CHX and alcohol formulations are frequently combined for the quick onset of alcohol and the long-lasting effects of CHX. Another benefit of CHX in alcohol is its antimicrobial properties in the blood and therefore it is used to prevent catheter-related bloodstream infections before venipuncture. (Lim and Kam, 2008)

In addition, surgical skin preparation prior to skin incision with CHX was linked with lower SSI rates and it lowers the newborn mortality when it is applied to the umbilical cord. Consequently, it is used frequently in obstetrics and gynecology and likewise, CHX can be administered to prevent infection after a caesarean surgery. (Karpiński and Szkaradkiewicz, 2015) The most widespread use of CHX has indeed been in oral hygiene and dentistry of humans. CHX appears in the form of oral rinses, aerosols and spray formulations, dental varnishes, toothpastes and gels for cleaning teeth, and dental floss. The use of CHX in mouthwashes reduces gingival irritation and plaque formation significantly. Moreover, the use of CHX varnish can help with gingivitis by lowering plaque formation and bleeding levels. Therefore, the use of CHX both pre- and post-operatively has a considerable prophylactic impact on oral surgeries. An example is the removal of lower third molars because it can cause alveolar osteitis and CHX can prevent it. CHX can also help with the treatment of halitosis by lowering the amounts of anaerobic bacteria.(Karpiński and Szkaradkiewicz, 2015)

Several human studies showed that severe oral mucositis, oral candidiasis, dental caries, xerostomia, gingivitis, cellulitis, and osteoradionecrosis have all been linked to intensive chemotherapy and radiation regimens. The use of CHX mouth rinse as an oral prophylaxis can benefit the patients that undergo intensive chemoradiotherapy because CHX decreases the number of oral microbes and the possible complications. Due to these effects, it also applies for the patients receiving bone marrow transplants.

5. Comparative data analysis of Pre and Post operative use of antiseptics on the surgical site

A comparative study has been carried out by Melekwe et al. (2018) at the Faculty of Veterinary Medicine University of Benin in Nigeria. The purpose of this study was to see if performing immediate asepsis preoperatively would reduce the microbes present on the skin and to compare the efficacy of Chlorhexidine Gluconate (CG), Cetrimide (CET) and PVP-I as aseptic agents used, for preparation of the skin, before surgery in dogs. In this research 6 male and 9 female dogs were used. All 15 dogs had approximately the same amount of weight and they were provided with ad libitum water and the same amount and quality of food once daily. During the study, the dogs were shaved on both sides of the abdomen, received the same amount of premedication, got anesthetized again with the same amount of medication and then they were scrubbed with "pre-surgical scrub solutions" with the same movement and quality of sponge for 5 minutes. Different scrubbing solutions were used on the right side and on the left side of the dog. On the right side, dogs were washed using 0.3% CG + 3% CET and on the Left side 10% of PVP-I was used. Then samples with swabs on both sides of each dog before and after (0, 30, 60, 90 minutes) the pre-surgical asepsis were taken, diluted with a tenfold serial dilution, and placed on nutrient agar plates for incubation. The nutrient agar plates were incubated for 3-5 days at 37 degrees Celsius to give the appropriate time for bacteria to grow and calculate the decline of bacteria correctly. Results were obtained by calculating the Colony Forming Units (CFU) of bacteria in nutrient agar plates by using ANOVA mixed design. According to the results observed, Malekwe et al. (2018) came into conclusion that both the use of CG and PVP-I can effectively decrease the SSI causing microbial presence of the skin, right away after the asepsis of the skin for 90 minutes (Table 8). However, the administration of CG and CET resulted in a greater reduction in mean bacteria count at 90 minutes than PVP-I, even though it is not statistically noteworthy. (Melekwe *et al.*, 2018)

Table 8: Mean bacteria counts pre and post scrubbing with CHX gluconate + Cetrimide and PVP-I.(Melekwe *et al.*, 2018)

Disinfectant	Time period (min)	Mean	SE	95% CI	
				From	To
Chlorhexdiine	Before	318,000	60988.159	189868.632	446131.368
	0	2431	457.551	1469.721	3392.279
	30	1695	336.495	988.049	2401.951
	60	1295	247.142	775.773	1814.227
	90	722	150.990	404.781	1039.219
Povidone-iodine	Before	348,000	60988.151	219868.632	476131.368
	0	2670	457.551	1708.721	3631.279
	30	2090	336.495	1383.049	2796.951
	60	1546	247.142	1026.773	2065.227
	90	981	150.990	663.781	1298.219

Another comparative study conducted by Belo et al. 2018, in University of Lisbon, Portugal aimed to evaluate the microbiological potency of alcoholic solution 2% CHX (Desinclor 2%) and the aqueous solution of 7.5% PVP-I (Braunol) used for prophylaxis during the skin preparation of a surgery to prevent SSI. In addition, this research also aimed to also study the efficacy of the two preoperative aseptic solutions, specifically, against methicillin resistant bacteria. This study included 46 dogs of around the same age and weight that were presented for various types of surgery. Half of them were chosen randomly for the 2% CHX evaluation and the other 23 for the 7.5% PVP-I evaluation. Evaluation of all dogs was carried out before and after (at 24 hours and at 30 days) skin asepsis with the according solution used, by the collection of skin swab samples and ANOVA test. Initial suspension of the pre-asepsis swabs collected were plated on an MRSA agar, for the quantification of MRSA species, and diluted suspensions were plated on Brain Heart Infusion (BHI), a general nutrient rich culture medium. Firstly, the results of the MRSA agar have revealed that, during pre-asepsis only 18 out of 46 dogs had MRSA bacterial growth on their skin surface. On the contrary, post-asepsis swabs did not present MRSA bacteria after asepsis protocols neither with 7.5% PVP-I nor 2% CHX with alcohol. (Figure 5) Secondly, the BHI agar pre-asepsis swabs showed bacterial presence, but post-asepsis results showed that bacterial number was lessened for both solutions used. This means that 7.5% PVP-I and 2% CHX alcoholic solution have alike antimicrobial effect against MRSA and other bacteria, which is essential for the prevention of SSI during or after the surgery. (Belo *et al.*, 2018)

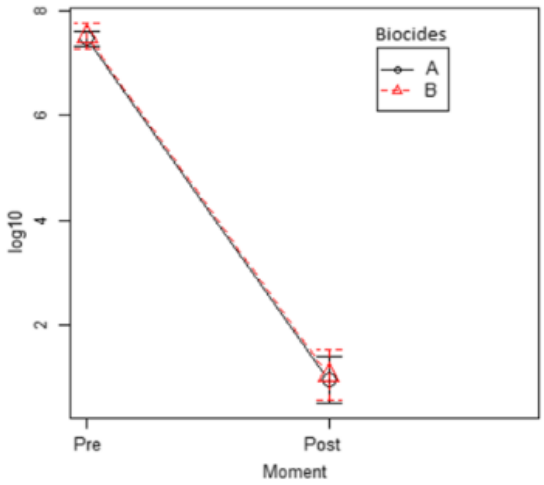

Figure 5: Log reduction of the bacterial number before and after asepsis using PVP-I (A) and CHX (B).(Belo *et al.*, 2018)

Additionally, a study that took place in North Carolina State University College of Veterinary Medicine, compared three skin preparation techniques in 100 dogs to see their side effects on the skin and to understand their ability to reduce bacterial growth. Osuna, DeYoung and Walker in 1990 have randomly used one of the three following aseptic solutions: PVP-I, 4% CG with saline rinse and CG with 70% isopropyl alcohol rinse for surgery skin preparation. The dogs were separated into 3 groups and every group was cleansed in the preparation room and into the operation room three times respectively. The first group consisted of 35 dogs that have undergone of a skin-asepsis using PVP-I in the preparation room and using 70% isopropyl alcohol in the operating room. The second group with 31 dogs were scrubbed with 4% GC in the preparation room and sterile saline solution in the operating room. Lastly the remaining 34 dogs were cleansed with again 4% CG solution in the preparation room but this time 70% Isopropyl alcohol in the operating room. In every group, three cultures with RODAC plates were taken from the skin to understand the effect on microbial growth of each technique. After the cleansing scrub in the preparation room, the sterile scrub in the operating room and after the surgery. One of the results obtained by this clinical trial is that all three pre-asepsis protocols had an equivalent effect on the inhibition of bacterial growth at any period of samples taken. (Figure 6) Another result though, when comparing the percentages of cultures with no growth (negative cultures) and those with high colony counts (>5 CFUs), have shown statistically significant variations between the three preparation techniques. Less negative

cultures with no bacterial growth were presented by the PVP-I application compared to CG and saline rinse and therefore, when "GC with alcohol results in significantly fewer negative postoperative cultures may be very important" as Osuna, DeYoung and Walker, 1990 state. (Figure 7 & 8)(Osuna, DeYOUNG and Walker, 1990b)

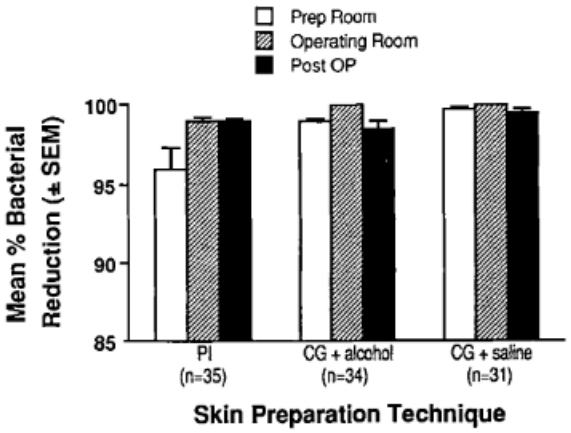

Figure 6: Mean percentages of antimicrobial decrease after the use of PVP-I, CG + alcohol rinse and CG + saline rinse in preparation room (cleansing scrub), operating room (sterile scrub) and post operation.(Osuna, DeYOUNG and Walker, 1990b)

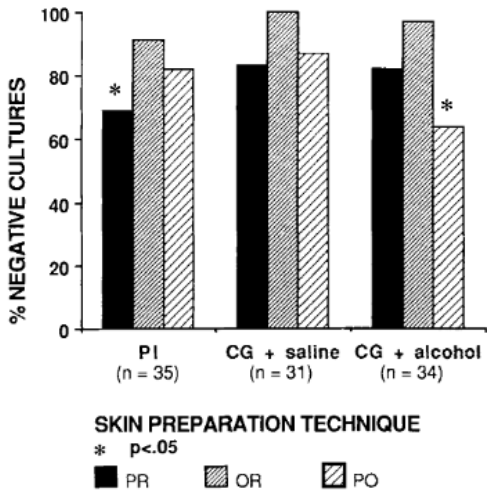

Figure 7: Negative cultures (no bacterial growth) mean percentages after the pre-asepsis of the skin using PVP-I, CG + saline and CG + alcohol in preparation room (PR), operating room (OR) and post operation (PO).(Osuna, DeYOUNG and Walker, 1990b)

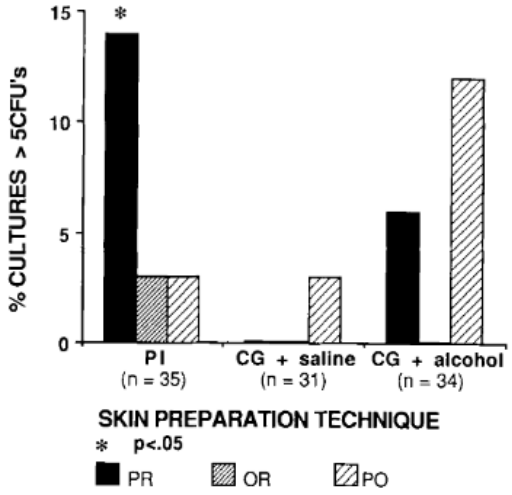

Figure 8: Peak of bacterial numbers (>5 CFUs) presented in percentage after the pre-asepsis of the skin using PVP-I, CG + saline and CG + alcohol in preparation room (PR), operating room (OR) and post operation (PO)(Osuna, DeYOUNG and Walker, 1990b)

A different approach was carried by Maillard, Messenger and Veillon in 1998 at the University of Wales in Cardiff. Three different tests were executed to study the antimicrobial efficacy of 2% PVP-I, 2% CHX diacetate, 1% Benzalkonium-chloride (BZC) and 1% CET against Pseudomonas aeruginosa, Staphylococcus Aureus and Escherichia coli. The tests were Suspension test, Glass-carrier test and an Ex-Vivo test. In the suspension test, the three bacteria were placed in a nutrient broth separately and suspended with sterile water, while after they were mixed again separately with the suitable disinfectant at different time frames (30 seconds, 1 and 10 minutes). The bacterial number of the broth was then calculated by "drop counting method" and expressed as CFU/Ml. In Glass-carrier test bacteria were also suspended with sterile water but this time in a glass bottle called Fisher and this time, before adding the sample of the disinfectant (in 30 seconds, 1 and 10 minutes) , it was "dried under a laminar flow cabinet". It was again evaluated by the "drop counting method". The third test used Ex-vivo test was carried out using a piece of actual skin from dead dogs or cats that were stored in optimal conditions. Pseudomonas aeruginosa, Staphylococcus aureus and Escherichia coli were implanted on the skin sample, dried and then the appropriate disinfectant was applied in 30 seconds, 1 and 10 minutes. All the tests were evaluated with "drop counting method", used a control sample and the same amount of bacterial suspension and biocide solution each time. It is noticed that PVP-I does not have a remarkable variation

between the three tests on its ability to inhibit S. aureus through the first minute, yet 9 minutes later it exhibited a more than 4 log drop in titer when assessed using the glass and suspension tests, but only a 2.5 log reduction in titer when evaluated using the ex-vivo test. (Figure 9a) Furthermore, PVP-I showed no discernible effect (Figure 10a) and its effect against Escherichia coli, even though it shows a reduction, are not reliable due to the high standard deviation that might have an impact on the results. Overall, PVP-I has shown strong antibacterial efficacy against all three pathogens tested in the investigation as Maillard, Messenger and Veillon, 1998 mention. Regarding Staphylococcus aureus reduction, 2% CHX, 1% BZC and 1% CET did not have an outstanding difference when comparing glass-carrier and suspension test, however they could be differentiated from an ex-vivo test because the ex-vivo test shows a limited inhibition in bacterial titer. (Figures 9b-d) CHX shows to have a good inhibitory effect on Pseudomonas aeruginosa, but it is to be noted that in this study when its activity in suspension test and glass-carrier test is compared with the ex-vivo test on the actual skin, it is shown that in the latter test it has less inhibitory effect on bacteria. (Figure 10b) This results against Pseudomonas Aeruginosa also occur for BZC and CET. (Figures 10c, 10d) Lastly, BZC and CET were the only biocides that did not show antimicrobial effect. (Maillard, Messager and Veillon, 1998)

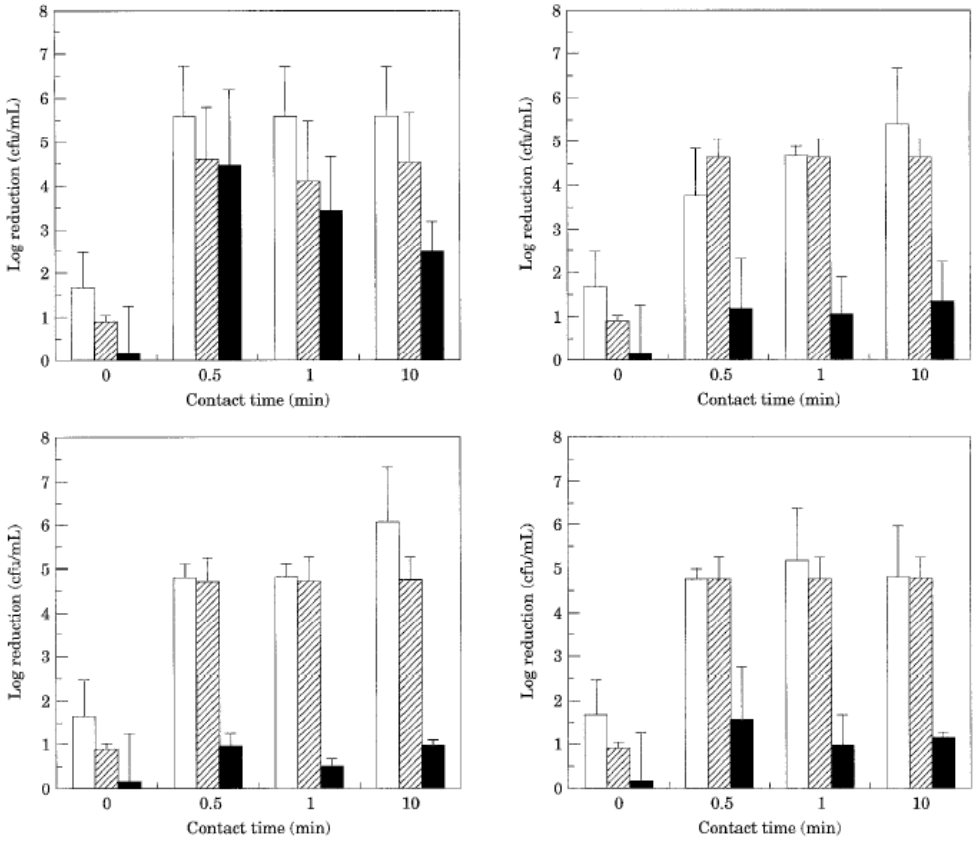

Figure 9a: Inhibitory effect of PVP-I (2%) against S.aureus from (□) glass-carrier, (▨) suspension and (■) ex-vivo test.

Figure 9b: Inhibitory effect of CHX diacetate (2%) against S.aureus from (□) glass-carrier, (▨) suspension and (■) ex-vivo test.

Figure 9c: Inhibitory effect of BZC (1%) against S.aureus from (□) glass-carrier, (▨) suspension and (■) ex-vivo test.

Figure 9d: Inhibitory effect of CET (1%) against S.aureus from (□) glass-carrier, (▨) suspension and (■) ex-vivo test.

(Maillard, Messager and Veillon, 1998)

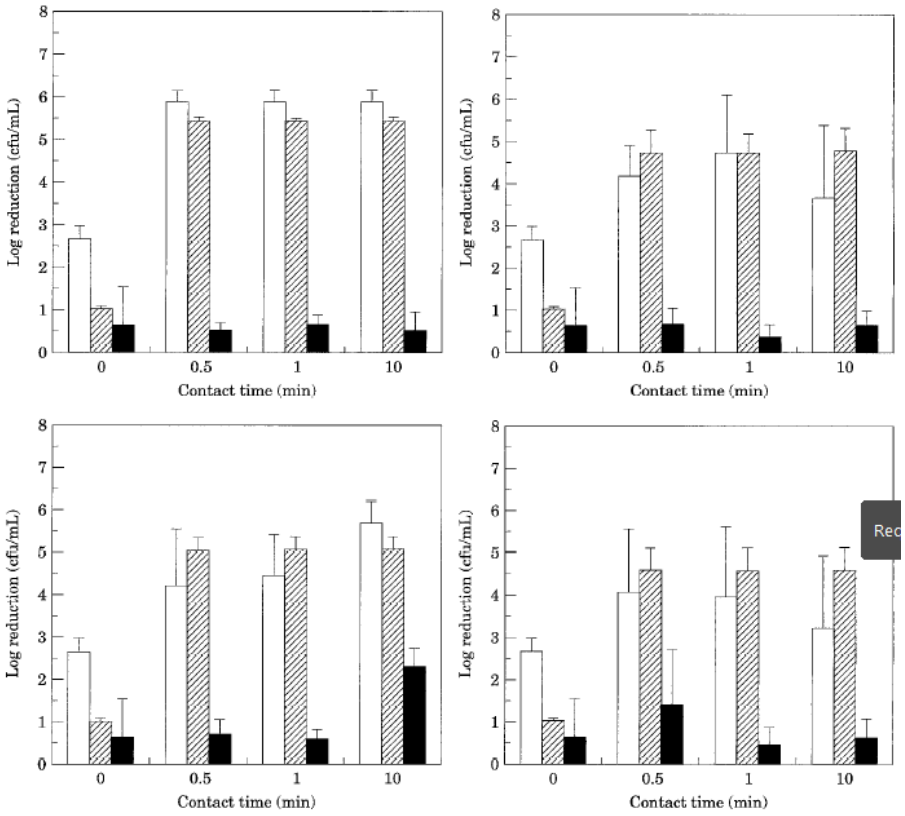

Figure 10a: Inhibitory effect of PVP-I (2%) against Ps. Aeruginosa from (□) glass-carrier, (▨) suspension and (■) ex-vivo test.

Figure 10b: Inhibitory effect of CHX diacetate (2%) against Ps. Aeruginosa from (□) glass-carrier, (▨) suspension and (■) ex-vivo test.

Figure 10c: Inhibitory effect of BZC (1%) against Ps. Aeruginosa from (□) glass-carrier, (▨) suspension and (■) ex-vivo test.

Figure 10d: Inhibitory effect of CET (1%) against Ps. Aeruginosa from (□) glass-carrier, (▨) suspension and (■) ex-vivo test.

(Maillard, Messager and Veillon, 1998)

One more in vitro comparative study was taken place in Thailand by Fungwithaya and Prapasarakul in 2016. The purpose of this study was to evaluate the time needed to kill canine CoPS using PVP-I and Chlorhexidine Gluconate in Isopropanol (CGI). Twenty CoPS were split into five MRSP and five isolates of MSCoPS, S. pseudintermedius, S. aureus, and S. schleiferi subspecies coagulants. Broth microdilution was used to test bactericidal effectiveness at concentrations of 0.1%, 1%, and 10% PI and 0.5%, 1%, and 2% CGI for 15s, 30s, 45s, 1 minute, 3 minutes, and 5 minutes, respectively. While susceptibility values did not change between strains, conclusion was made according to the fastest bactericidal effects. With respect to PVP-I, using 10% concentration, it took 3 minutes to kill S. schleiferi subspecies coagulans and S. Pseudointermedius but 1 minute to kill MRSP and S. aureus. To terminate all CoPS within shorter time, 45 seconds in this case, less concentration of PVP-I was needed (0.1% and 1%), with high bactericidal effect. This is called "the dilution phenomenon" explained by Rackur in 1985.However, in this study 1% and 2% of CGI seems to have a greater and faster bactericidal activity since all CoPS are killed within 15 seconds. (Fungwithaya and Prapasarakul, 2016)

Osuna, DeYoung and Walker, 1990b have done a second comparative trial on dogs aiming to understand the differences of antibacterial efficacy and the reactions of the skin promoted by three surgical preparation techniques. PVP-I with 70% isopropyl alcohol rinse, 4% CG with a saline rinse, or 4% CG with a 70% isopropyl alcohol rinse were used to prepare premeasured, clipped sections of skin on both sides of 30 adult dogs. RODAC plates were used to count skin bacteria and grow them for identification before, shortly after, and one hour after skin preparation. Analysis of variance and chi-square were used to determine the percentages of bacterial decrease immediately and at hour 1, as well as the percentages of negative cultures, cultures with more than five CFUs, and skin responses. The results showed that all three pre-asepsis protocols significantly reduced the amount of skin bacteria for at least 1 hour, with no significant difference between them. (Figure 11) Negative cultures percentages have shown also very similar results between the three antiseptics used, however one important matter was observed; Acute contact dermatitis that lasted several hours occurred in approximately half of the PVP-I-treated regions.(Figure 12) (Osuna, DeYoung and Walker, 1990a)

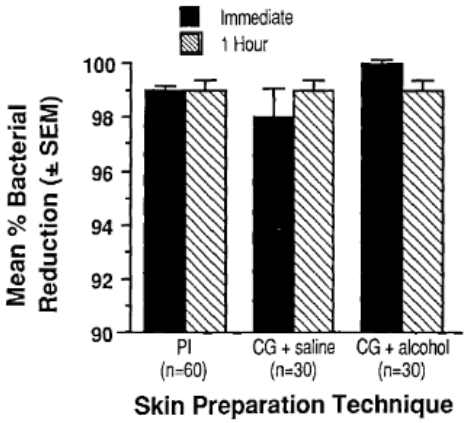

Figure 11: Mean percentages of skin bacteria decrease immediately and one hour after preoperative skin preparation with PVP-I, CG with saline rinse (CG + saline), and CG with alcohol rinse (CG + alcohol).(Osuna, DeYOUNG and Walker, 1990a)

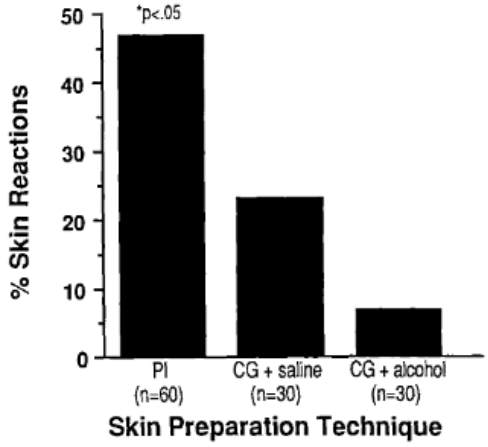

Figure 12: Preoperative skin preparation with PVP-I, CG with saline rinse (CG + saline), and CG with alcohol rinse (CG + alcohol): frequency of skin responses noted.(Osuna, DeYOUNG and Walker, 1990a)

To limit the danger of microbial infection, antiseptic flushing of the canine prepuce and its exclusion from the operative field are indicated prior to abdominal surgery. In this comparative study researchers cultured 60 healthy dogs' preputial cavities before and after flushing with 0.05% CD, 1% PVP-I, or 0.9% SC, aiming to examine and compare the adverse reactions and antimicrobial efficacy of the two antiseptics within the preputial cavity. Samples were collected and prepared under optimal and equal conditions and both

antiseptics, before use, were diluted in sterile buffered 0.9% saline as appropriate. In addition, preputial and penile mucosa were inspected five minutes after sample collection for signs of tissue responses such as wheals, erythema, and "weeping" of serum. Bacterial growth results were analyzed by a semiquantitative scoring using a “quadrant streak method”, the comparative decrease of Bacterial growth score (BGS) by Wilcoxon rank-sum test and the compared proportions of pre-flush and post-flush samples by x^2 analysis and Fisher’s exact test. According to the results of this study, there was a substantial decrease in post-flush BGS and none of the samples elevated BGS in any of the three groups. Nevertheless, when the three solutions were tested, there were no distinct changes in any of the variables tested between PVP-I and SC. On the other hand, except the fact that only one dog revealed diffuse erythema of the penile and preputial mucosa, when compared to PVP-I, CD resulted in a considerable drop in positive post-flush cultures. (Table 9) Neihaus et al., 2011 conclusion according to their findings that a 2 minute flush with 0.05% CD is advised to be used to prepare the preputial cavity before surgery. (Neihaus *et al.*, 2011)

Table 9: Summary of preputial flushing results with 0.9% SC, 0.05% CD, 1% PVP-I (Neihaus *et al.*, 2011)

	SC	CD	PI
Positive growth preflush	14/20 (70%)	13/20 (65%)	12/20 (60%)
Positive growth postflush*	11/14 (79%)	1/13 (8%)	7/12 (58%)
Reduction of ≥1 BGS*	8/14 (57%)	12/13 (92%)	6/12 (50%)
Postflush BGS >1*	6/14 (43%)	0/13 (0%)	4/12 (33%)
Median BGS preflush(range)	2.0 (0–4)	2.0 (0–4)	2.0 (0–4)
Median BGS postflush (range)	1.0 (0–4)	0 (0–1)	1.0 (0–3)
Adverse reactions	0/20 (0%)	1/20 (5%)	5/20 (25%)

Antiseptics are frequently used to irrigate infected wounds. The optimum wound antiseptic should be potent enough to kill germs while without damaging healing tissues. The goal of this research is to assess the cytotoxicity of CD and PVP-I at therapeutically relevant concentrations in canine embryonic fibroblasts, as well as the bactericidal activity against Staphylococcus aureus. Sanchez, Nusbaum, et al in 1988 cultured fibroblasts or S. aureus and subjected them to 0.5, 0.05, 0.03, 0.013, 0.006, 0.005, and 0.0005% CD, 5.0, 1 .0, 0.5, 0.3, 0.1, and 0.05% PVP-I, or sterile SC for 30 minutes. Later, Fibroblasts were trypsinized and counted to determine survival, and S. aureus colonies were counted on BHI agar. Both groups' numbers were represented as a percentage of the total number of viable cells in

buffered SC cultures. The analysis showed that when the concentrations of CHX and PVP-I increased, the mean % survival of fibroblasts and Staphylococcus aureus reduced. CHX concentrations of 0.05% completely inhibited Staphylococcus aureus, however it was also toxic to fibroblasts. Only dilutions of CHX of 0.006% or below permitted fibroblasts to survive. (Figure 13a) In addition PVP-I have killed bacteria completely at the concentration of 1% and allowed the survival of fibroblasts at the concentrations of 0.3% and less. (Figure 13b) In conclusion, at bactericidal doses, both antiseptics tested were fatal to canine fibroblasts. (Sanchez, Nusbaum, et al., 1988)

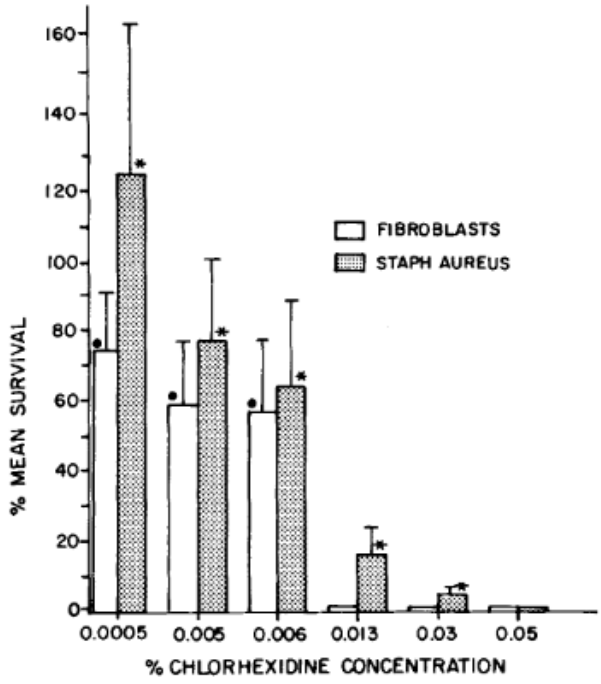

Figure 13a: After 30 minutes of CHX exposure, fibroblast and Staphylococcus aureus survival was represented as a percentage of SC. Asterisks indicate concentrations of CHX that allow S. aureus to survive. Dots indicate CHX concentrations that allow considerable fibroblast survival. The standard deviation is indicated by vertical lines above the bars.(Sanchez, Nusbaum, *et al.*, 1988)

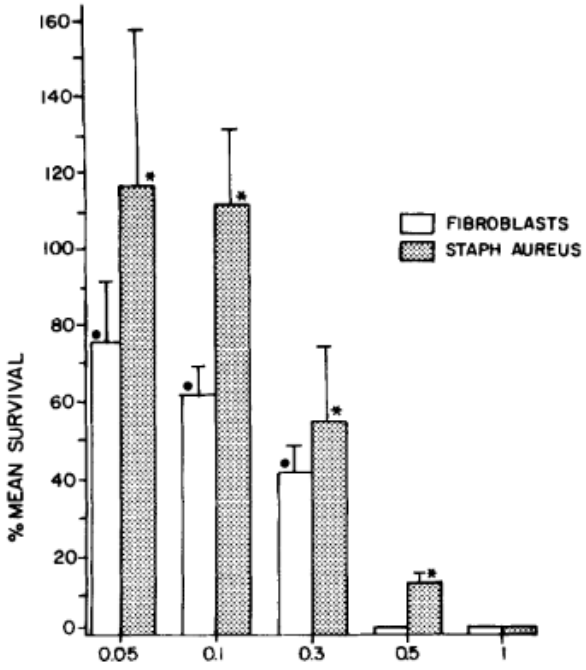

Figure 13b: After 30 minutes of PVP-I exposure, fibroblast and Staphylococcus aureus survival was represented as a percentage of SC. Asterisks indicate concentrations of PVP-I that allow S. aureus to survive. Dots indicate PVP-I concentrations that allow considerable fibroblast survival. The standard deviation is indicated by vertical lines above the bars.(Sanchez, Nusbaum, *et al.*, 1988)

Another experimental trial done by Sanchez, Swaim, et al. in 1988 compared the effects of 0.1% and 1% PVP-I and 0.1% and 1% CD according to their wound healing process rate and bactericidal activity (wound contamination). In this in-vitro trial, three thick squares of skin were cut from each dog, cultured, and rinsed once daily for 14 days using antiseptic solutions or SC. Bacterial cultures were taken from each incision before and after irrigation to assess the healing process. The effects of the treatments on mean percentages of nonhealing wounds and tissue regeneration, as well as microbial contamination, were examined using "Duncan's multiple range test" for analysis of variance of the means. According to culture contamination results, CD 0.05% outperformed PVP-I and SC in terms of bactericidal activity, and both CD concentrations exhibited residual effects 6 hours after irrigation. PVP-I and SC demonstrated no detectable bactericidal action. Neither antiseptic, however, proved completely efficient in preventing wound infection. In wounds treated with CD and PVP-I, the recovered wound area and contraction were comparable. On days 7 and 14, wounds treated with CD had more recovered wound area and greater contraction than SC treated wounds. Both CD irrigations demonstrated bactericidal effect and were more advantageous to wound healing than SC irrigations alone. (Figure 14) (Sanchez, Swaim, *et al.*, 1988)

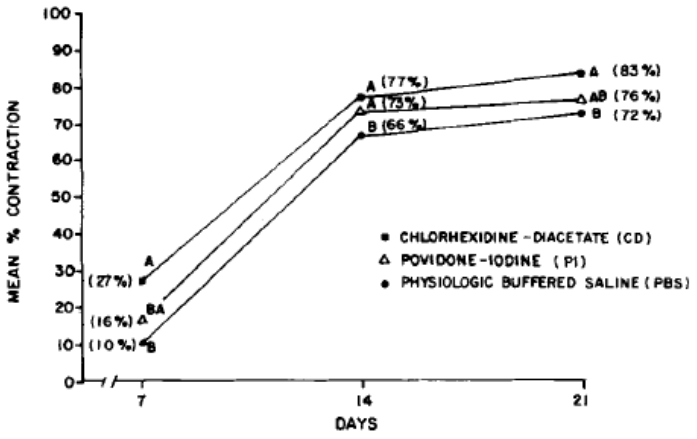

Figure 14: Mean percentage wound contraction for each test agent is compared. Duncan's multiple range test is referenced by capital letters; various letters on the same day are notably different.(Sanchez, Swaim, *et al.*, 1988)

6. Comparative data analysis of Pre and Post operative use of antiseptics in Oral surgeries

Because the bacterial count in the oral cavity is higher in dogs than on the skin surface, it is critical to choose an effective antiseptic that will significantly reduce the amount of intraoral pathogenic microorganisms, reducing the frequency of postoperative complications, particularly postoperative infections after intraoral procedures. Few publications in veterinary medicine have investigated at the antiseptic efficiency of CG and PVP-I in the oral cavity of dogs. One of the objectives of this study was to evaluate the fundamental aerobic bacterial microflora in the canine mouth as well as the antiseptic efficiency of 0.4% CD and 1% PVP-I on mandibular gingival mucous membrane. There were 45 dogs in total, separated into three groups. The first group was flushed 0.4% CG, the second group 1% PVP-I, and the third group SC. Swabs were collected from the mandibular gingiva before and after antiseptic solution treatment. A semiquantitative approach, like fisher's and chi-squared test, was used to assess the number of bacteria, and bacterial colonies were identified following colonization of individual colonies on blood agar. According to the identification of bacteria present after the gingival rinse β-hemolytic streptococcus species, Enterococcus species, Klebsiella species, Leuconostoc species and Pasteurella multicida were normally present in the canine oral microflora. Furthermore, as compared to the control group, both CG and PVP-I demonstrated a statistically significant decrease in bacterial colony growth. There were no significant variations in the efficiency of the two tested antiseptics in suppressing bacterial colony formation, and the number of positive swabs collected after washing with CG and PVP-I was similar. Based on the findings, a 2 minute flush with 0.4% CG or 1% PVP-I is advised for presurgical oral cavity preparation in dogs. (Dameski P, Habrun B, Vučković M, Matičić D, Musulin A, Kompes G, Vnuk D, 2019)

Another comparative evaluation was conducted in a hospital in India. The purpose of this study was to assess and compare the effectiveness of two topical antiseptic agents in preventing post-surgical bacteremia after mandibular third molar surgery. Thirty patients with Class 1, Position B mesioangular impacted mandibular third molars and not any systemic diseases noted in history were randomly chosen and placed into three groups of ten individuals each. Group I was treated with sterile water, Group II with 5% PVP-I and Group III with 0.2% CHX. Each patient was instructed to rinse his or her mouth for 1 minute with 15ml of the mouth washing solution appropriate. The blood samples were then obtained before and immediately after surgery, and microbiological investigations were performed on

them. Bacterial growth was calculated with the use of a magnifying lens, expressed as CFU, and their identification was detected using the conventional method of gram staining and biochemical testing. After 7 days of culture, all the surgical blood samples were negative for bacterial growth. There were 30 patients in total, with 12 having postoperative bacteremia. Six patients (60%) in group I, whereas 2 (20%) patients in group II and 4 in group III. (Table 10) Therefore, as compared to sterile water irrigation, the use of PVP-I and CHX prior to oral surgical operations reduces the risk of bacteremia. When compared to CHX and sterile water, PVP-I significantly decreases the incidence of bacteremia and the quantity of bacteria. (A *et al.*, 2017)

Table 10: Presence of bacteriemia after surgical procedure using Sterile water (Group I), 5% PVP-I (Group II) and 0.2% CHX (Group III).(A *et al.*, 2017)

Group	Postsurgical	Total cases	% of growth
Group I	6	10	60
Group II	2	10	20
Group III	4	10	40

Addy and Wright in 1978 performed clinical and laboratory studies aiming to analyze and compare the antimicrobial effect of 1% PVP-I and 0.2% CG mouth rinses on salivary microbiota in vitro. Particularly to examine the period during which both antiseptics had an impact on salivary flora. Bacterial MIC of PVP-I and CG was determined by “tube dilution method”. Each antiseptic’s same amount of dilution in different tubes was mixed with a drop of a bacteria’s culture and inspected for bacterial development according to the turbidity of the solution. In the second clinical study, 10 people participated to measure salivary gland bacterial levels before and after a single 1-minute rinse with 1% PVP-I mouthwash, 0.2% CG, or Sterile water. Saliva samples were collected, mixed, diluted, and then placed on blood agar plates. The colonies that formed were counted using a "Galenkamp illuminated colony counter". The number of bacteria in millions per milliliter of saliva was calculated based on these counts. The duration of residual antibacterial activity in the saliva after rinsing was determined by a third study. Saliva samples were again collected from patients after expectoration with mouthwash and inoculated with "Oxford staphylococcus". Bacterial

growth was recorded, and diameter was measured in millimeters. The data were statistically analyzed using the "Student's t-test". After a single rinse with PVP-I, total salivary aerobes and anaerobes dropped instantly in the group of ten individuals, followed by a restoration to normal levels 1 hour post washing. A comparable but higher drop in salivary bacterial counts was detected with CG, which remained present up to 7 hours after washing. (Table 11) In addition, Saliva samples taken from patients 2 minutes after washing with PVP-I inhibited the development of a test organism in vitro, while antibacterial activity was detectable in saliva samples up to 3-hour sampling interval following CH. (Table 12) In terms of MIC, PVP-I has a substantially higher MIC against various standard test organisms than CG. According to the findings, PVP-I has only an acute antibacterial impact as a mouthwash and, unlike CG, is not kept at antibacterial levels within the oral cavity following expectoration. (Table 13)(Addy and Wright, 1978)

Table 11: Salivary bacterial count X 10«/ml after a single washing with PVP-I, CHX, and water.(Addy and Wright, 1978)

	Povidone iodine		Chlorhexidine		Water	
	Aerobes	Anaerobes	Aerobes	Anaerobes	Aerobes	Anaerobes
0	28.1 (11.1)	56.4 (33.7)	33.1 (19.7)	46.7 (29.2)	34.4 (34.2)	41.1 (30.6)
2 min	19.1 (11.6)	30.5 (15.0)	3.4 (6.0)	4.0 (9.3)	37.8 (29.3)	59.8 (37.1)
30 min	17.7 (18.4)	28.8 (23.6)	7.3 (8.6)	11.0 (12.6)	29.5 (25.3)	46.0 (27.0)
1 h	26.9 (30.2)	45.6 (30.7)	8.1 (7.4)	12.1 (12.9)	39.6 (21.8)	57.3 (35.1)
2 h	23.0 (15.0)	44.7 (20.9)	4.5 (3.2)	6.3 (4.4)	42.4 (18.9)	50.75(13.4)
5 h	31.2 (12.2)	53.5 (20.5)	4.6 (3.8)	7.2 (4.1)	42.4 (22.4)	57.5 (28.2)
7 h	33.4 (16.6)	58.4 (25.6)	7.2 (5.8)	9.3 (7.1)	45.3 (30.6)	59.5 (33.6)
24 h	37.0 (25.6)	53.4 (35.7)	28.5 (21.2)	38.0 (26.9)	49.5 (34.9)	45.5 (31.2)

Aerobes *(Aerobier, aérobies)*, anaerobes *(Anaerobier, anaérobies)*, water *(Wasser, eau)*.

Table 12: Results of antibacterial efficacy against Oxford staphylococcus following the rinse with PVP-I and CG. (Inhibitory zone + 10 mm well diameter) n denotes the number of subjects.(Addy and Wright, 1978)

1 % Povidone iodine		2 min	30 min	1 h	2 h	3 h	5 h	7 h
	Mean (s. d.)	10.5	0	0	0	0	0	0
	n	1	0	0	0	0	0	0
Chlorhexidine gluconate	Mean (s. d.)	19.3 (2.4)	16.1 (2.7)	15.9 (2.3)	14.0 (2.9)	12.0 (1.4)	0	0
	n	10	10	10	9	4	0	0

Table 13: MIC (itg/ml) of PVP-I and CG for tested bacteria.(Addy and Wright, 1978)

Test organisms	Oxford staph. (NCTC 6571)	*E. coli* (NCTC 10418)	*Strep. mutans.* (NCTC 10922)	*Strep. viridans.* (NCTC 10712)	*C. albicans.* (LSTHM 3153)
Povidone iodine	1250–2500	1250–2500	625–2500	313–1250	1250–2500
Chlorhexidine gluconate	0.48–1.95	1.95–3.9	0.24–0.48	0.24–0.48	7.8–15.6

Test organism *(Testorganismen, micro-organismes expérimentaux).*

7. Conclusion

Detrimental clinical scenario, regarding post-surgical complications, might be experienced in SSI by invading microorganisms caused by poor perioperative preparation or post-surgical care. Therefore, the choice of antiseptic represents a major challenge for the surgeon, and the development, implementation, and regular use of appropriate infection control techniques has necessitated a significant effort on the part of health professionals and industry. There is no doubt that CHX and PVP-I are the most common antiseptics used in veterinary medicine. However, there is no consensus on which antiseptic is the most effective. This thesis research was based upon data from numerous studies and experimental trials carried out by veterinarians, medical practitioners, and scientists. All have shown different results of the two antiseptics regarding their antibiotic spectrum, duration of action, side effects and wound healing ability.

In dogs and cats underwent surgery, CHX and PVP-I appear to have comparable efficacy in reducing the overall load of cutaneous and oral microorganisms, including MRSA species, and avoiding SSI. Yet, neither antiseptic is 100% effective for preventing wound infection. CHX, on the other hand, in comparison to PVP-I, has demonstrated a greater effect on microbial decrease as well as a faster bactericidal, wound healing and contraction effect. This means that CHX requires significantly less time to eliminate all bacteria present on the skin or oral cavity and promotes faster tissue regeneration. In addition, CHX has a prolonged duration of action, especially when mixed with alcohol. With respect to cytotoxic reactions, PVP-I can sometimes promote undesirable skin reactions such as acute contact dermatitis and erythema. As a result, when PVP-I is used on patients, it must be administered with caution.

To conclude, every practice, regardless of size, must create strict asepsis protocols before, during and after surgery targeted at reducing the risk of surgical wound infection. It is also suggested that veterinarians must be aware and informed about the efficacy of each antiseptic to be used perioperatively to avoid any further risk on the animal's health.

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