The importance of skin preparation

BY ANNA BAKER

With both aesthetic procedures and antibiotic resistance on the rise, good skin disinfection to reduce the risk of infection is more vital than ever. **Anna Baker** takes us through the evidence behind commonly used skin preparation formulations for aesthetic injectable treatments.

The global number of aesthetic procedures performed continues to rise exponentially [1]. The recent data from The American Society for Aesthetic Plastic Surgery (2017) confirms an overall 5.1% increase in the number of aesthetic procedures undertaken, in comparison to those performed in 2016; as well as a 40.6% increase over the past five years. Furthermore, non-surgical procedures increased by 4.2% in 2017, compared to 2016. As a consequence, a growing incidence of associated complications are described [2]. Furthermore, data from the US Food and Drug Administration (FDA) in 2017, indicates a three-fold rise in adverse reactions from 2008 to 2011, compared with 2005 to 2007 [3].

Alhede et al. reported on a murine study showing that pseudomonas, staphylococcus, and propionibacterium were all cultured following administration of hyaluronic acid, polyacrylamide gel, poly-L-lactic acid and calcium hydroxyapatite microspheres into the dermal pocket [4]. Furthermore, their findings also demonstrated that once biofilm was established, treatment with high dose antibiotics was unable to eradicate the infection. Antibiotic resistance is one of the most significant threats to patient safety in Europe, fuelled by overuse of antibiotics and inappropriate prescribing [5]. These cumulative factors emphasise a growing need and awareness of utilising adequate precautions to reduce the risk of associated complications, and attention to appropriate skin disinfection during all stages of a non-surgical procedure is key [6].

Chan et al. propose that the desirable traits of a good skin decontaminant are that it can effectively remove the contaminant of interest, is readily available, acts rapidly, does not enhance percutaneous penetration / absorption of the contaminant, can be readily removed without residue, and does not damage the skin [7]. This paper will explore some of the commonly used skin preparation formulations used for aesthetic injectable treatments.

Chlorhexidine

Chlorhexidine is a divalent, cationic biguanide antiseptic agent that that was first described in 1954 [8]. Chlorhexidine exists as a gluconate, acetate and hydrochloride salts [9]. It has a wide spectrum of activity encompassing gram-positive and gram-negative bacteria, yeasts, dermatophytes, fungi and some lipophilic viruses [7,10] but is ineffective against bacterial spores [11]. Chlorhexidine at low concentrations is bacteriostatic, whereas at higher concentrations it can be rapidly bactericidal [8]. Chlorhexidine acts by binding to the negatively charged bacterial cell wall and affecting the osmotic equilibrium of the cell [12]. Chlorhexidine effectively reduces numbers of bacterial skin flora, and is available for use in aqueous form, combined 70% alcohol and has been used in preparations for hand cleansing, both general and pre-surgical, for more than 50 years [13].

Alongside a broad range of activity, a key advantage of chlorhexidine when used as a skin disinfectant, was its 'residual activity' [14]. Furthermore, Aly and Maibach propose that in comparison to povidone iodine, chlorhexidine can produce a greater reduction in the skin flora, as well as exerting a longer residual activity [14], although, irritation of the skin and allergic reactions such as dermatitis, are more commonly reported at higher concentrations [15].

Historically, chlorhexidine has been one of the most frequently used antiseptic agents, yet, there are a small number of reports within the literature of bacterial resistance to biocides, antibiotic resistance effects of biocides, as well as potential for reduced susceptibility to chlorhexidine in staphylocci [16,17]. Bacteria may be described as insusceptible, phenotypically tolerant, tolerant or resistant to antiseptics [17]. Consistent with antibiotics, resistance to antiseptics can be intrinsic or acquired. Intrinsic resistance, or insusceptibility, to chlorhexidine is demonstrated by bacterial spores and mycobacteria [17]. In both cases the outer layers of the cell form an impermeable barrier to the ingress of the molecules [11]. There are inconsistences in the literature when attempting to define a consensus definition of 'chlorhexidine resistance,' as well as in defining a robust and standardised method for the detection of reduced susceptibility and / or resistance to in-use concentrations of chlorhexidine [17]. These are challenging concepts to quantify owing to the gaps and inconsistencies in the literature with scope for further research.

In contrast, the Medicines and Healthcare products Regulatory Agency (MHRA) issued a warning in 2012 for the use of chlorhexidine in light of a risk of anaphylactic reaction due to chlorhexidine allergy [18]. A subsequent warning was published in 2017 by the US FDA reiterating a similar concern, reporting 52 cases of worldwide anaphylaxis due to chlorhexidine gluconate [19]. In addition, in the 46 years between January 1969 and June 2015, the FDA reports 43 cases worldwide. These statistics reinforce the need for a comprehensive medical consultation, which includes details regarding known sensitivities and allergies.

Isopropyl alcohol

Alcohols are classified into primary, secondary and tertiary alcohols, on the basis of the number of carbon atoms linked to the carbon atom that bears the hydroxyl group [20]. Isopropyl alcohol, or isopropanolol, is a secondary alcohol, a structured isomer of propranolol, that can be produced by combining water and propene [21]. It is a clear and flammable liquid that has a moderate evaporation

rate and is widely used as an industrial solvent, and cleaning fluid, and is present in many products, such as lacquers, inks, and thinners, as well as household products [20]. In the EU, it is approved for use in cosmetics as a solvent, an antifoaming agent, a perfuming agent, and a viscosity controller. In light of its antimicrobial activity (which includes multidrug-resistant pathogens, mycobacterium tuberculosis, and a variety of fungi), isopropyl alcohol is accepted as a preservative, and as an antiseptic in the clinical environment [22.]

Alcohol is fast and short acting, with broad-spectrum antimicrobial activity, and is relatively inexpensive [23]. It is believed that alcohols cause membrane damage and rapid denaturation of proteins, with subsequent interference with metabolism and cell lysis [11]. Alcohol-based solutions that contain chlorhexidine gluconate or iodophores are reported to exert a sustained and durable antimicrobial activity that can persist after alcohol evaporation [11]. In addition, alcohol-based solutions can cause irritation if applied to mucous membranes [23]. Isopropyl alcohol remains a popular choice for skin preparation for aesthetic injectable treatments, yet, there are reports within the literature of skin sensitivity and dermatitis following use [24].

Iodine formulations

Iodophore-based formulations such as povidone iodine have remained popular after decades of use for antisepsis and wound healing applications owing to their favourable efficacy and tolerability [25]. In povidone iodine, iodine forms a complex with the synthetic carrier polymer povidone, which itself has no microbicidal activity [26]. In an aqueous medium, free iodine is released into solution from the povidone iodine complex, with more free iodine being released from the povidone iodine reservoir as iodine-consuming germicidal activity ensues [27]. Povidone iodine is one of the few topical antimicrobials shown to be effective against bacteria, several viruses, fungi, spores, protozoa, and amoebic cysts [28]. In conventional antimicrobial testing, povidone iodine has been shown to kill a variety of bacterial strains known to commonly cause nosocomial infections, including methicillin-resistant *Staphylococcus aureus* (MRSA) and other antibiotic-resistant strains within 20-30 seconds of exposure [29].

The microbicidal activity of iodine appears to involve the inhibition of vital bacterial cellular mechanisms and structures, and oxidises nucleotides fatty / amino acids in bacterial cell membranes, in addition to cytosolic enzymes involved in the respiratory chain, causing them to become denatured and deactivated [25]. In addition, the combination of alcohol and iodine has demonstrated good effectiveness, in comparison to alcohol alone, which may be a result of the immediate germicidal action of alcohol and the residual activity of iodine [30]. Data on the systemic absorption of antiseptics is limited and iodine seems to be absorbed from the skin, but more significantly from mucosa [25], although, this may be determined by the condition of the skin barrier at the site of application [31].

Iodine based formulations are highly effective for surgical procedures owing to their broad antimicrobial properties, yet the residual, and temporary discolouration of skin following application may be challenging in terms of practicality for practitioners administering aesthetic injectable treatments.

Chlorine based and Hypochlorous solutions

Sodium hypochlorite was the first antiseptic used to prevent infection, as demonstrated in the 19th century by the pioneering work of Ignaz Semmelweis, who used it to disinfect hands, lowering the incidence and mortality of puerperal fever [32]. In the 20th century, 0.5% sodium hypochlorite (Dakin's solution) was used to treat traumatic injuries during the First World War [11]. Subsequently, it became widely used, yet its medical use as an antiseptic has been limited due to its instability, which necessitated the addition of large quantities of stabilisers [32]. In addition, Eusol (an acronym for Edinburgh university solution of lime) was one of several hypochlorite solutions that was used in the management of open wounds left to heal by secondary intention [33]. Eusol consisted of a chlorinated lime (calcium hypochlorite) and boric acid solution containing between 0.25% weight / volume of available chlorine with a pH between 7.5 and 8.5 [33]. Dakin's solution has a higher pH and is based on sodium hypochlorite but contains no boric acid [33].

The production of an electrolyte solution of sodium hypochlorite, stable at approximately pH 10 was developed for patients receiving dialysis and to irrigate wounds and burns [34]. More recently, Selkon et al. reported preliminary findings from their study to demonstrate an appreciable reduction in the bacterial burden in chronic venous leg ulcers that had not healed with conventional treatment, with 10 out of 30 subjects achieving a 44% ulcer reduction after three weeks of standard treatment with hypochlorous acid [35]. Furthermore, Robson et al. concur that stabilised hypochlorous acid has rapid and broad-spectrum antimicrobial activity against clinically relevant microorganisms in vitro and in vivo, as long as the narrow effective pH range is maintained [36].

In vivo, hypochlorous acid is produced in the intracellular matrix in response to phagocytosis of pathogens by neutrophils and plays an important role in the destruction of pathogens. The hypochlorous technology has been developed further by Clinical Health Technologies to formulate a solution which has a skin neutral pH which the manufacturer claims to deliver a 6 log reduction within seconds, with a highly oxidising action which is not subject to antimicrobial resistance. Clinisept+ is a stable, non-toxic, non-mutagenic, and non-irritant to skin, eyes and mucosa with non-cytotoxic properties to new skin cells and is designed for topical use, pre and post treatment. Hypochlorous has been well described to possess anti-bacterial, anti-sporicidal, anti-fungal and anti-virucidal properties [35] and is well positioned as a current, strong contender to meet the demands of a safe, versatile and effective skin preparation to be used through all stages of aesthetic injectable treatments.

Conclusion

A significant body of literature acknowledges that adequate skin preparation, pre and post treatment, extends beyond the selection of the most appropriate skin cleansing formulation. The aesthetic practitioner needs to give consideration to a number of other factors, for example, the clinical environment, as well as the use of sterile dressing packs, and a detailed consultation, outlining medical history as well as previous injectable treatments. Negating these important considerations places the patient at risk of developing complications, irrespective of which skin preparation has been used. It is likely that the exponential rise in the number of procedures performed in the aesthetic sector will continue to rise, which will continually reinforce the importance of 'getting the basics right' in terms of good skin practice. There is a considerable body of literature underpinning the skin preparations discussed, underpinned by National Institute for Health & Care Excellence (NICE) guidelines which are focused principally on surgical procedures requiring skin disinfection. With this in mind, the clinician is encouraged to adopt a critical approach in justifying rationale for choice of formulation(s), for cosmetic non-surgical procedures.

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