

Ivan Bristow

Feb 21, 2019

<https://www.foot.expert/post/2019/02/19/hclo>

Goodbye Chlorhexidine?

Introduction

Over twenty years ago, when I was working at the Dermatology Department in Oxford, through a colleague, I was introduced to Dr Joseph Selkon, a respected Consultant Microbiologist, who at that time was just about to retire but was researching a chemical so interesting that he didn't want to. What was it? An antiseptic which was alleged to be potentially antimicrobial but non-toxic to humans – the holy grail of antiseptics? Fast forward to 2019, and I have recently been re-introduced to the chemical, now as a marketed product resulting from Dr Selkon's (and others) research. Having used this in practice, I can potentially see this as one of the rare products which could make a difference in daily podiatry practice. Every day as podiatrists we are constantly battling against cross infection undertaking procedures from autoclaving to cleaning. Every patient we treat too, must undergo skin preparation with the trusty pink chlorhexidine spray or for nail surgery, povidone-iodine. These have been very much the staple of podiatry practice for many years but is that about to change?

History

Very little in this world is original; often it's a case of new light through old windows and this is certainly the case with this story. In 1915, Dakin published a paper in the British Medical Journal suggesting the use of a hypochlorite solution as a means of cleaning wounds. Sodium hypochlorite is commonly found in household bleach, and although highly effective at destroying microbes, the solution is strongly alkaline and highly irritant to tissue and so is seldom used clinically now (and only in a very dilute form). However, over the decades, recognising its potential effectiveness, researchers have continued to develop a solution with the same antimicrobial potency, but which was less toxic. Within the chemistry of hypochlorite, there was an answer - hypochlorous acid (chemical formula HClO).

Hypochlorous acid (HClO)

Hypochlorous acid is actually a weak acid but has rapid bactericidal, viricidal, fungicidal and sporicidal properties. The substance is a strong oxidiser consequently it can rapidly penetrate microbial cell walls whilst leaving larger and more robust human cells unaffected. In fact, the immune system itself harnesses exactly the same chemical when fighting infection. Neutrophils and other phagocytic cells arriving at the site infection are known to release HClO to destroy pathogens – known as the “respiratory burst”. Released superoxide rapidly turns to form hydrogen peroxide (H₂O₂). The enzyme myeloperoxidase then uses hydrogen peroxide (H₂O₂) to oxidize chloride ions to hypochlorous acid (HClO) (1). The effect of the HClO release is the rapid destruction of microbes.

Clinically, a substance which was “natural” to the body sounded appealing but HClO possesses other positive benefits being non-irritant, non-flammable and non-toxic to host tissues. With these advantages it is clear to see why research persisted to give this clinical utility. However, the translation from the laboratory to the clinic was not straightforward. Natural HClO is highly unstable so developing a stable form of HClO with a high purity has proven difficult but has been finally achieved. In June 2017, Clinisept+® was launched in the UK. The product stands alone in manufacturing as a highly stabilised form of hypochlorous acid which has a high purity of the chemical within it and a two-year shelf life. The product is ideal for use on the skin with a working pH of 5.2 to pH 5.8 it complements the skin’s natural pH of 5.5. A skin-neutral pH means that it is unlikely to cause any irritation and reduce inflammation associated with infection.

So is this better than chlorhexidine & povidone iodine?

Currently in our clinics, skin preparation is carried out using the infamous pink spray of Chlorhexidine Gluconate Spray (which is most commonly used as 0.5% Chlorhexidine in a 70% alcoholic vehicle). Chlorhexidine has known antibacterial properties. It is most effective against gram positive organisms but has a reduced effect on gram-negative bacteria and fungi. In addition, it is not particularly sporicidal (2). Allergy and rarely anaphylaxis have been reported in some patients (3, 4). In addition, research has shown how it may delay wound healing (5) and some outbreaks of resistant organisms have been reported (6). Povidone-Iodine comes in various formulations and has the trademark brown stain when applied to the skin. It has a broader spectrum of activity than chlorhexidine against a range of organisms (7). True povidone-iodine allergy is rare although it may cause stinging and irritant dermatitis in some patients when used topically (8).

The toxicity and irritancy of hypochlorous acid has been shown to be minimal and literature investigating its antimicrobial properties highlight its rapid killing of microbes. One laboratory study tested the chemical against a range of bacteria and fungi and showed 99% of microbes were killed within two minutes of application (9). In a further study assessing its efficacy for skin disinfection compared against povidone-iodine and chlorhexidine, it was shown to have an immediate effect in destroying methicillin-resistant *S. aureus* - much faster than the two other chemicals. Against a range of other microbes in these tests, its speed of action was equal or superior to the other two antiseptics (10). Other work has shown how it is an effective treatment against biofilms (11). Reassuringly, the rapid oxidising action of the chemical also means resistance to hypochlorous acid is extremely unlikely.

So, in terms of the competition, Clinisept+® can offer broad spectrum antimicrobial cover to bacteria, fungi and virus and sporicidal cover is a bonus. The product is a clear, colourless solution. It has a slight smell of chlorine but nothing like your local swimming pool. The liquid is non-sticky and being non-toxic to tissues it is not likely to slow healing or cause irritation. In fact, much of the feedback to date has discussed how, unlike other antiseptics, it appears to calm inflamed areas with no stinging (unlike an alcoholic solution) or staining that we see with povidone-iodine. Clinisept+® is also able to be used in more sensitive areas such as the eyes and mouth.

Potential Podiatric Applications

The introduction of such a product could have a range of possibilities in podiatry. Firstly, as a replacement for our usual skin disinfectants which are used pre- and post-op on patients undergoing treatment. The non-irritant aspect of the product potentially means when spraying it will not cause any irritation to the eyes or respiratory system should it inadvertently stray - unlike chlorhexidine that can particularly as it is an alcoholic solution. In addition, it does not sting like traditional alcoholic solutions - all the patients we have used this on to date have reported no stinging – even on open wounds.

Secondly, we frequently see superficial infections of the skin. Where it may prove invaluable is in the treatment of interdigital infections such as erythrasma. Having a topical spray product, which can be used in clinic and safely at home, interdigital hygiene should become a straightforward process without the usual stinging of surgical spirit or other astringents currently used. Maintaining webspace is an important factor in preventing secondary infection such as cellulitis (12). Other superficial bacterial infections such as pitted keratolysis could also be treated.

As a treatment for cleaning ulcers, hypochlorous acid has really made its mark. Studies have been undertaken and reviewed in the treatment of diabetic foot ulcers. A review by David Armstrong and colleagues highlighted its antimicrobial efficiency with minimal cytotoxicity and concluded there was strong evidence in supporting its use in diabetic foot ulcers (13). Along similar lines following nail surgery, cleansing of the wound by the podiatrist and patient alike could be undertaken using the product to decontaminate the area and promote healing at home and in the clinic. Its effects on fungi, and particularly the dermatophytes is particularly interesting. Studies have shown its fungal killing abilities along with its sporicidal properties. To this end, I am currently undertaking work to assess its potential and will be reporting this soon, as this could have an impact on the management of this common, stubborn foot infection.

The Product

The product for podiatry currently comes in two presentations. “Prep & Procedure” is a 500ml bottle containing 250 parts per million hypochlorous acid and is intended for use as a pre-procedural skin disinfectant. The second is “Aftercare” a 100ml bottle containing the same concentration of hypochlorous acid but it differs only in that it has a spray applicator. The product is simple to use, it is applied as a spray or via a cotton swab soaked in the solution placed on the area to be treated. This product can be used in clinic and sold or supplied to patients for home use as well. The product should be available in the coming weeks from Canonbury and other podiatry suppliers.

Declaration

The author has independently written this article with no financial support from any company involved in the manufacture, distribution or retail of this product.

References

1. McKenna SM, Davies KJ. The inhibition of bacterial growth by hypochlorous acid. Possible role in the bactericidal activity of phagocytes. *The Biochemical journal*. 1988;254(3):685-92.
2. Karpinski TM, Szkaradkiewicz AK. Chlorhexidine--pharmaco-biological activity and application. *Eur Rev Med Pharmacol Sci*. 2015;19(7):1321-6.
3. Guleri A, Kumar A, Morgan RJM, Hartley M, Roberts DH. Anaphylaxis to Chlorhexidine-Coated Central Venous Catheters: A Case Series and Review of the Literature. *Surgical Infections*. 2012;13(3):171-4.
4. Sharp G, Green S, Rose M. Chlorhexidine-induced anaphylaxis in surgical patients: a review of the literature. *ANZ J Surg*. 2016;86(4):237-43.
5. Niedner R, Schöpf E. Inhibition of wound healing by antiseptics. *Br J Dermatol*. 1986;115(s31):41-4.
6. Kampf G. Acquired resistance to chlorhexidine – is it time to establish an ‘antiseptic stewardship’ initiative? *J Hosp Infect*. 2016;94(3):213-27.
7. Reimer K, Wichelhaus TA, Schafer V, Rudolph P, Kramer A, Wutzler P, et al. Antimicrobial effectiveness of povidone-iodine and consequences for new application areas. *Dermatology*. 2002;204 Suppl 1:114-20.
8. Wykoff CC, Flynn HW, Jr., Han DP. Allergy to Povidone Iodine and Cephalosporins: The Clinical Dilemma in Ophthalmic Use. *Am J Ophthalmol*. 2011;151(1):4-6.
9. Wang L, Bassiri M, Najafi R, Najafi K, Yang J, Khosrovi B, et al. Hypochlorous acid as a potential wound care agent: part I. Stabilized hypochlorous acid: a component of the inorganic armamentarium of innate immunity. *Journal of burns and wounds*. 2007;6:e5.

10. Anagnostopoulos AG, Rong A, Miller D, Tran AQ, Head T, Lee MC, et al. 0.01% Hypochlorous Acid as an Alternative Skin Antiseptic: An In Vitro Comparison. *Dermatol Surg*. 2018;44(12):1489-93.

11. Del Rosso JQ, Bhatia N. Status Report on Topical Hypochlorous Acid: Clinical Relevance of Specific Formulations, Potential Modes of Action, and Study Outcomes. *The Journal of clinical and aesthetic dermatology*. 2018;11(11):36-9.

12. Dupuy A, Benchikhi H, Roujeau J-C, Bernard P, Vaillant L, Chosidow O, et al. Risk factors for erysipelas of the leg (cellulitis): case-control study. *Brit Med J*. 1999;318(7198):1591-4.

13. Armstrong DG, Bohn G, Glat P, Kavros SJ, Kirsner R, Snyder R, et al. Expert Recommendations for the Use of Hypochlorous Solution: Science and Clinical Application. *Ostomy Wound Manage*. 2015;61(5):S2-s19.