CLINICAL INSIGHTS

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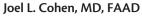
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Integrating HOCl into Wound Care: A New Paradigm for Patient Management



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re- and post-operative management of surgical wounds is important to prevent infection and dehiscence, minimize scar formation, and reduce the risk for other complications. Suboptimal wound healing can induce physical symptoms of itching, stiffness, scar contracture, tenderness, and pain, in addition to psychosocial effects caused by scarring, including diminished self-esteem, stigmatization, disruption of daily activities, anxiety, and depression.¹

A consideration of current practices in wound healing suggests a need for new strategies for optimized pre- and post-procedural management.²⁻⁵ There is growing evidence to suggest the utility of topically applied hypochlorous acid (HOCI). Naturally produced by the innate immune system, HOCI has known anti-microbial properties that also break down biofilm. It has also been shown to be anti-pruritic, anti-inflammatory, and increase oxygenation to wound sites.^{6,7,8}

PHYSIOLOGIC WOUND HEALING

While several systemic factors influence healing, the local skin environment is known to be critically important to wound closure and long-term cosmesis. Physiologic wound healing is characterized by a balance between new tissue biosynthesis and degradation of the existing extracellular matrix via apoptosis. 9,10 Scar formation may result when the

underlying regulatory mechanisms are impaired, often as a result of disruption of oxygenation and introduction of microbes.¹¹

Topical preparations play a central role in pre- and postoperative wound management, to both facilitate wound cleansing and to reduce the risk of infections, and to support the natural healing process. Despite their popularity, use of topical antibiotic ointments remains controversial.¹² Studies suggest that between 1.5 and 9.1 percent of individuals are allergic to bacitracin and between 7.2 and 13.1 percent are allergic to neomycin.^{13,14} Topical antiseptics may be detrimental to wound healing, especially if they are cytotoxic to keratinocytes and fibroblasts.¹⁵ Chlorhexidine solution, specifically, has been found to be toxic to the middle ear and is associated with irreversible cornea damage with minimal exposure.¹⁶

A NEW APPROACH

A new paradigm for periprocedural skin management is indicated—one based on HOCI-based formulations.

Available by prescription or for in-office dispensing, a line of products containing HOCl-based Microcyn Technology may be used both as surgical prep and for postprocedural wound management. Its unique antimicrobial, anti-inflammatory, and healing properties aid in scar management.

Skin preparation. HOCI damages the integrity of the bacterial cell membrane by increasing its permeability. As such, its potency is non-specific. HOCI is active against numerous bacterial, viral, and fungal pathogens, including Staphylococcus aureus, Pseudomonas aeruginosa, and Candida albicans. Pseudts from an in vivo study of skin inoculated with S. aureus, showed that topically applied hypochlorous acid gel reduced the bacterial count by ≥99 percent.

In one study to assess the antimicrobial effects of Microcyn-based formulations for use as a pre-operative skin

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	Physician Dispensed	Uses
Skin preparation and healing	Solution	Intended for the cleansing, irrigation, moistening, debridement, and removal of foreign material including microorganisms and debris from exudating wounds, acute and chronic dermal lesions.
Post- procedure; scar reduction	Scar Gel	Intended for the management of old and new hypertrophic and keloid scars resulting from burns, general surgical procedures, and trauma wounds.

Mycrocyn Technology (Stabilized HOCI)

- · Eradicate microorganisms
- Reduce inflammation via inhibition of mast cell degranulation
- · Reduce itch and pain
- Increase oxygenation of wound sites to improve healing
- · Break down biofilms

preparation, the product had similar antimicrobial activity as Hibiclens at all time points (30 seconds; 10 minutes; six hours)

Supporting wound healing. When a Microcyn technology plus antibiotics regimen was compared to Betadine plus antibiotics in the management of diabetic foot ulcers, Microcyn was associated with a statistically significantly greater reduction in microbial load. Average healing time for the Microcyn arm was 43 days, compared to 55 days for the Betadine arm. HOCl has also been shown to increase oxygenation at wound sites. Increases in TCPO2 (transcutaneous pressure oxygen) play a role in regranulation, which may account for speedier healing.

Managing symptoms. HOCl also has significant antiinflammatory activity via inhibition of nuclear factor kB kinase (NF-kB), which regulates activation of NF-kB, an activator of pro-inflammatory genes. ¹⁸ It appears likely that HOCl also functions to stabilize local mast cell activity. It also reduces the activity of histamine, leukotriene B4 (LTB4), and interleukin 2 (IL-2), all of which are known mediators of itch. ¹⁹

In one study of topically applied HOCl, a 28 percent reduction in investigator-assessed irritation was evident as early as day one, with a 46 percent reduction by day three. Fifty percent of subjects reported improvement in itching

at day one, and 85 percent had improvement at day three. Reducing the urge to itch abates a potential mechanism for mechanical disruption of the skin.

Scar reduction. A recent analysis determined the efficacy of topical HOCl in preventing and treating hypertrophic and keloid scars and in relieving associated pruritus and pain. The inclusion of this modified silicone-based polymer to the formulation is believed to help support tissue remodeling. Unlike many silicone-based products, Celacyn Scar Gel and Regenacyn Scar Gel can be applied directly to the wound site in the immediate post-op period.

In a randomized, double-blind study comparing the efficacy, safety, and tolerability of Microcyn-based scar gel with a comparator device, trends suggested that Microcyn slightly outperformed the competitor and provided a statistically significant improvement in scars at day 112 compared to baseline.

A new paradigm. A recent analysis of the data regarding the use of HOCI for wound management concludes that the agent is safe and effective with minimal reported side effects. In fact, the authors urge that use of topical HOCI formulations be "strongly considered as a post-surgical/procedural wound healing agent."

- 1. Van Loey NE, Bremer M, Faber AW, et al. Itching following burns: epidemiology and predictors. Br J Dermatol. 2008;158:95–100.
- 2. Del Rosso JQ. Wound care in the dermatology office: where are we in 2011? J Am Acad Dermatol. 2011 Mar;64(3 Suppl):51-7.
- 3. Drucker CR. Update on topical antibiotics in dermatology. Dermatol Ther. 2012 Jan-Feb;25(1):6-11.
- 4. Ruiz ES, Ingram A, Landriscina A, Tian J, Kirsner RS, Friedman A. Identifying an Education Gap in Wound Care Training in United States Dermatology. J Drugs Dermatol. 2015 Jul;14(7):716-20.
- 5. Elston DM. Topical antibiotics in dermatology: emerging patterns of resistance. Dermatol Clin. 2009 Jan;27(1):25-31.
- 6. Robson MC, Payne WG, Ko F, Mentis M, Donati G, Shafii SM, Culverhouse S, Wang L, Khosrovi B, Najafi R, Cooper DM, Bassiri M. Hypochlorous Acid: Its Role in Decreasing Tissue Bacterial Bioburden and Overcoming the Inhibition of Infection on Wound Healing. J Burns Wounds. 2007 Apr 11;6:e6.
- Sakarya S, Gunay N, Karakulak M, Ozturk B, Ertugrul B. Hypochlorous Acid: an ideal wound care agent with powerful microbicidal, antibiofilm, and wound healing potency. Wounds. 2014 Dec;26(12):342-50.
- 8. Leung TH, Zhang LF, Wang J, Ning S, Knox SJ, Kim SK. Topical hypochlorite ameliorates NF- B-mediated skin diseases in mice. J Clin Invest. 2013 Dec;123(12):5361-70.
- 9. Guo S, Dipietro LA. Factors affecting wound healing. J Dent Res. 2010 Mar;89(3):219-29.
- 10. Sandulache VC, Parekh A, Li-Korotky H, et al. Prostaglandin E2 inhi-bition of keloid fibroblast migration, contraction, and transforming growth factor (TGF)-beta1-induced collagen synthesis. Wound Repair Regen. 2007;15:122-133.
- 11. Gauglitz GG, Korting HC, Pavicic T, et al. Hypertrophic scarring and keloids: pathomechanisms and current and emerging treatment strategies. Mol Med. 2011;17:113-125.
- 12. Del Rosso JQ, Kim GK. Topical antibiotics: therapeutic value or ecologic mischief? Dermatol Ther. 2009 Sep-0ct-27(5):398-406
- 13. Alavi A, Sibbald RG, Ladizinski B, Saraiya A, Lee KC, Skotnicki-Grant S, Maibach H. Wound-Related Allergic/Irritant Contact Dermatitis. Adv Skin Wound Care. 2016 Jun;29(6):278–86.
- 14. Gehrig KA, Warshaw EM. Allergic contact dermatitis to topical antibiotics: Epidemiology, responsible allergens, and management. J Am Acad Dermatol. 2008 Jan;58(1):1–21.
- 15. Thomas GW, Rael LT, Bar-Or R, Shimonkevitz R, Mains CW, Slone DS, Craun ML, Bar-Or D. Mechanisms of delayed wound healing by commonly used antiseptics. J Trauma. 2009 Jan;66(1):82-90; discussion 90-1.
- 16. Steinsapir KD, Woodward JA. Chlorhexidine Keratitis: Safety of Chlorhexidine as a Facial Antiseptic. Dermatol Surg. 2017 lan:43(1):1-6
- 17. Sakarya S, Gunay N, Karakulak M, Ozturk B, Ertugrul B. Hypochlorous Acid: an ideal wound care agent with powerful microbicidal, antibiofilm, and wound healing potency. Wounds. 2014 Dec;26(12):342-50.
- 18. Leung TH, Zhang LF, Wang J, Ning S, Knox SJ, Kim SK. Topical hypochlorite ameliorates NF- B-mediated skin diseases in mice. J Clin Invest. 2013 Dec;123(12):5361-70.
- 19. Van Loey NE, Bremer M, Faber AW, et al. Itching following burns: epidemiology and predictors. Br J Dermatol. 2008;158:95-100.