Assessment of Hemostatic Efficacy and Osseous Wound Healing Using HemCon Dental Dressing

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Abstract

Introduction: Obtaining hemostasis in the surgical crypt during periradicular surgery is essential. It allows for improved visibility and contributes to a dry environment suitable for the placement of moisture-sensitive root-end filling material. Although current materials may not be moisture sensitive during setting, hemostasis is important for proper placement of root-end filling materials during apical surgery. A new hemostatic agent, HemCon dental dressing (Patterson Dental, St Paul, MN), may improve upon the efficacy of wound healing and hemostasis both in extent and time. The aim of this study was to evaluate the hemostatic effect of HemCon in osseous wound sites and evaluate the wound healing potential and percentage of new bone formation in osseous crypts treated with HemCon.

Methods: A split-mouth design was used with random allocation of sham and experimental sites in 12 rabbits. In experimental sites, either HemCon or 15.5% ferric sulfate was applied to osseous crypts created with a round bur. Hemostatic efficacy was evaluated using predetermined scores. Rabbits were sacrificed at 21 days, and tissues were harvested and prepared for histologic evaluation. A blinded pathologist scored samples relative to inflammation. The percentage of new bone deposition was calculated using NIS Elements software (Nikon Instruments Inc, Melville, NY).

Results: There was no statistically significant difference in hemostatic efficacy or wound healing between HemCon and ferric sulfate (P > .05). The HemCon group showed a significantly higher percentage of new bone deposition compared with the controls (P < .01).

Conclusions: HemCon shows promise as an adjunct to the endodontic surgical armamentarium. (J Endod 2011;37:807–811)

Key Words
Ferric sulfate, HemCon dental dressing, hemostasis, osseous crypt, periradicular surgery

Surgical root canal therapy should be considered when adequate nonsurgical endodontic therapy has been implemented and the patient is not responding positively to treatment (1, 2). The modern microsurgical approach using a specialized armamentarium including the dental operating microscope and microinstruments can achieve success rates in the 90th percentile (3–5). The key to this high rate of success is a meticulous approach to treatment in conjunction with an understanding of how to manage both soft and periradicular tissues (6). In order to achieve the precision required in periradicular surgery, visualization of the area is paramount. This is greatly influenced by the administration of local anesthetic, proper flap design, and size of the osteotomy (6–8). Although gaining adequate hemostasis in the soft tissues lays the foundation for a successful surgery, obtaining hemostasis in the osseous crypt is just as essential. Not only does it allow for increased visibility, but it also contributes to a dry environment suitable for the placement of moisture-sensitive root-end filling material. Together, the ability to control this environment can help to minimize the consequences associated with prolonged surgical time.

Currently, there are a number of hemostatic agents available that can be applied topically to aid in achieving a dry surgical crypt. Broadly classified, topical hemostatic agents can be either non-collagen or collagen based. Common non–collagen-based hemostatic agents include bone wax, vasoconstrictor-impregnated cotton pellets, ferric sulfate, thrombin, calcium sulfate, Gelfoam (Pfizer, Inc, New York, NY), and Surgicel (Ethicon, Inc, San Angelo, TX). Bone wax, which was developed in 1892, requires meticulous removal because of the potential for persistent inflammation when left in the crypt (6). Epinephrine-impregnated pellets have been shown to be the most effective when hemostasis is required, but there are risks in leaving cotton fibers in the tissues as well as direct cardiovascular impact (6, 8). Ferric sulfate has been used since the mid-19th century but requires use in limited quantities and must be completely removed from the surgical site before suture removal (6). Similar to bone wax, the risk of foreign-body reaction with ferric sulfate is a concern if the material is not thoroughly removed from the crypt. Thrombin can also be used as a topical agent but has poor handling characteristics and is expensive (6). Calcium sulfate, although primarily used as a scaffold to fill in bony defects, can be used as a hemostatic agent (9). This inexpensive putty-like material is biodegradable but only acts as a mechanical barrier to elicit hemostasis (10). Gelfoam and Spongostan (Ethicon, Inc, San Angelo, TX) can also be used, but both have the tendency to swell when placed, are difficult to manipulate, and can potentially obscure the operators view (10). Additionally, Surgicel, an oxy cellulose gauze, forms an artificial coagulum to provide hemostasis but must be completely removed because of the potential for foreign-body reaction (11). Collagen products can be used to obtain hemostasis in 2 to 5 minutes using multiple mechanisms of hemostasis such as mechanical tamponade, release of serotonin, activation of Hageman factor (factor XII), and stimulation of platelet adhesion (12). Collagen-based hemostatic agents include Avitene (Davol, Inc, Warwick, RI) and INSTAT (Ethicon, Inc, San Angelo, TX), which are two popular forms of microfibrillar collagen (10). The handling properties of these agents make them difficult to work with because of their high affinity for wet surfaces and how they readily adhere to instruments and gloves. In addition, these agents are expensive (15). Although all agents aforementioned could be used successfully in obtaining hemostasis locally within a bony crypt, there may be a new non–collagen-based agent,
HemCon dental dressing (Patterson Dental, St Paul, MN), with the potential to improve hemostasis in both extent and time. HemCon is manufactured from freeze dried chitosan and forms to a highly electropositive sponge-like material that binds to negatively charged red blood cells. As such, it results in the formation of a viscous clot to facilitate hemostasis (14). Malmquist et al (14) evaluated the use of HemCon in extraction sites and found that all extraction sites, including nine patients taking oral anticoagulant therapy treated with HemCon, achieved hemostasis in less than 1 minute versus control wounds at 9.53 minutes.

In comparison to traditional hemostatic agents in use today, another distinguishing factor of HemCon is that it possesses bactericidal properties. Kishen et al (15) investigated the incorporation of chitosan nanoparticles into a zinc oxide–based seal to investigate the antimicrobial effectiveness. It was found that the nanoparticles improved the antimicrobial effectiveness without affecting the characteristics of the sealer. Furthermore, the investigation conducted by Dai et al (16) involved the application of a HemCon bandage to full-thickness excision wounds in mice that had been infected with pathogenic bacteria such as Pseudomonas aeruginosa, Proteus mirabilis, and Staphylococcus aureus. HemCon was found to not only rapidly kill the bacteria and save the mice from developing fatal infections but also stimulate wound healing (16).

To date, HemCon has not been evaluated in periradicular surgical sites. Therefore, the purpose of this study was to evaluate the hemostatic effect and wound healing potential of HemCon in osseous surgical wound sites and to evaluate the percentage of new bone formation in osseous crypts.

Materials and Methods

Experimental Animals

To evaluate the wound healing potential of HemCon in comparison to the traditional use of ferric sulfate, a split-mouth design in rabbits, previously used by Jeansson et al (17), was applied. The experiments were conducted using 12 mature male New Zealand White rabbits (each approximately 3 kg in weight) obtained from Myrtle’s Rabbitry (Thomp- sons Station, TN).

Surgical Procedures

Anesthesia was obtained by an intramuscular injection of a combination of xylazine (10 mg/kg intramuscularly), ketamine (50 mg/kg intramuscularly), and atropine (0.20 mg/kg subcutaneously). After anesthesia was obtained, an incision was made along the alveolar crest intramuscularly), and atropine (0.20 mg/kg subcutaneously). After anesthesia was obtained, an incision was made along the alveolar crest and the surgical area was exposed. The alveolar cortical bone and an osseous defect (3 mm in diameter) was created using a round bur. A flap was elevated to allow access to the surgical site. The material was gently placed in the osseous defect. In group 1, the experimental site consisted of the gentle application of HemCon. In group 2, the experimental site consisted of the gentle application of HemCon, achieved hemostasis in less than 1 minute versus control wounds at 9.53 minutes.

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To assess the timeline of hemostasis achieved with HemCon and ferric sulfate in periradicular surgical sites, predetermined scores used by Vy et al (18) were applied. The adequacy of hemostasis was determined by the surgical operator at 30 seconds and then at 1, 2, 3, 4, and 5 minutes using scores of 0 (no hemorrhage control), 1 (slight but apparent intermittent bleeding that persisted after application of

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results

The results (Fig. 2) show that intermittent bleeding was obtained with a mean value of 1 minute (standard deviation [SD] ±0.55) for both HemCon and ferric sulfate, whereas complete hemostasis was
obtained with mean values of 2.17 (SD = 0.98) and 2.33 (SD = 0.52) minutes for HemCon and ferric sulfate, respectively. Although both experimental agents were significantly better in achieving hemostasis when compared with controls, statistical analysis revealed no statistically significant difference (P > .05) between HemCon and ferric sulfate in achieving either intermittent bleeding (score of 1) or complete hemostasis (score of 2).

In regards to osseous wound healing, scores for the 24 graded specimens ranged from 1 to 5 (Fig. 1A–F). In the HemCon experimental group (Fig. 3), 50% of specimens were categorized with a score of 1, 33.3% with a score of 2, and 16.6% with a score of 3. In the ferric sulfate group, 50% of the specimens were categorized with a score of 1, 33.3% with a score of 2, and 16.6% with a score of 5. For the control groups, the majority of the specimens (58.3%) were categorized with a score of 5.
The purpose of this investigation was to evaluate the hemostatic effect of HemCon in osseous wound sites and evaluate the wound healing potential and the percentage of new bone formation in osseous crypts. HemCon is manufactured from freeze-dried chitosan and molds to form a highly electropositive sponge-like material. This charge facilitates blood clot formation because it allows binding with red blood cells. Red blood cells are negatively charged and bind to the electropositive HemCon Bandage material, generating a rapidly forming extremely viscous clot that seals the wound site and causes hemostasis. In addition, the formation of other electropositive anion-binding sites plays a role in attracting other chemotactic factors involved in the clotting process.

Chitosan is a carbohydrate biopolymer extracted from N-acetylated chitin, a structural ingredient in the skeletons of crustaceans and the cell walls of fungi. It has been reported to be nontoxic and biodegradable when used in human and animal models and provides a nonprotein matrix for tissue growth. Chitosan activates macrophages and mononuclear cells and induces the production of various growth factors. In addition, it has received recent attention as an effective carrier system for the release of bioactive agents, particularly bone morphogenetic proteins and lead to bone regeneration. Chitosan is effective in the formation of other electropositive anion-binding sites plays a role in attracting other chemotactic factors involved in the clotting process.

The results (Fig. 4) show that the mean percentage of new bone formation was 23.8% (SD ±7.4) for controls, 32.4% (SD ±10.2) for ferric sulfate, and 46.1% (SD ±21.0) for HemCon. New bone formation was significantly higher in the HemCon group compared with controls (P < .01). There was no statistically significant difference between the control and ferric sulfate groups (P > .05) or between the ferric sulfate and HemCon groups (P > .05).

**Discussion**

The mean percentage of specimens representing histological scores: (1) = complete healing of surgical site filled with healthy cancellous bone, (2) = fibrosis with dense collagen with or without early bone formation, (3) = granulation tissue with or without chronic inflammation, (4) = acute inflammation with or without granulation tissue, (5) = abscess formation. No statistically significant difference between HemCon dental dressing, 15.5% ferric sulfate, or control groups (P > .05).
controls, statistical analysis revealed no statistically significant difference between the experimental groups in achieving either intermittent bleeding or complete hemostasis.

The results of this study showed that the majority of osseous wound healing scores ranked from complete healing with the surgical site filled with healthy cancellous bone (1) to granulation tissue filling the surgical site with or without chronic inflammation (3). Only one animal showed abscess formation (5), which occurred in both control and experimental sites in which ferric sulfate was applied as the experimental agent. This could have resulted from inadequate curettage of ferric sulfate ferric sulfate leading to a foreign-body reaction because of contamination during the surgical procedure or a compromised host (17). In five (20.8%) of the 24 graded specimens that were categorized as complete healing (1), a healing defect composed of fatty marrow in both experimental (ferric sulfate and HemCon) and control sites were noted to be present in the created defect, whereas one (4.2%) of the 24 samples (control site) showed the presence of skeletal muscle attachment into the created defect (Fig. 1G and H). These aforementioned tissues were noted in defects where healthy bone had also proliferated. The fact that no statistically significant difference was noted between HemCon and ferric sulfate in regards to osseous wound healing could have been attributed to the small sample size.

The assessment of new bone formation revealed that HemCon showed significantly more bone deposition within osseous crypts in comparison to controls ($P < .01$). This may be attributed to the fact that HemCon possesses antibacterial properties that may contribute to an environment more conducive to new bone deposition (16). On the other hand, 15.5% ferric sulfate showed no statistical significant difference in comparison to either controls or HemCon ($P > .05$). This may be attributed to its ability to elicit foreign-body reaction if any remnants remain in the osseous crypt, which could contribute to delayed bone formation.

In summary, no significant difference was noted between HemCon and ferric sulfate in regards to hemostatic efficacy or osseous wound healing. However, in terms of new bone deposition, HemCon produced a significantly greater percentage of bone fill than did controls. As such, HemCon shows promise as an adjunct to the endodontic surgical armamentarium.

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The authors deny any conflicts of interest related to this study.

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