Topical Treatments for Hydrofluoric Acid Dermal Burns

Further Assessment of Efficacy Using an Experimental Pig Model

Brendan J. Dunn, MS
Michael A. MacKinnon, MD
Norman F. Knowlden, MS
Donald J. Billmaier, MD
Michael J. Derelanko, PhD
George M. Rusch, PhD
Dennis J. Naas, BS
Robert R. Dahlgren, DVM, PhD

Several topical treatments for hydrofluoric acid dermal burns (Zephiran®, calcium acetate and magnesium hydroxide antacid soaks, and calcium gluconate gel) were assessed for efficacy in a pig model. Gross appearance and histopathology of treated and untreated burn sites were evaluated. For superficial burns, Zephiran was most effective; calcium acetate, magnesium hydroxide antacid, and calcium gluconate gel were less effective. For deep burns, gross observations showed that calcium acetate and Zephiran were most efficacious, whereas histopathology indicated comparable efficacy of Zephiran, calcium acetate, and calcium gluconate gel for all skin layers. Magnesium hydroxide antacid demonstrated efficacy only for the subdermis. The clinically beneficial effects of both Zephiran and calcium gluconate gel were affirmed. Although results suggest that calcium acetate and magnesium-containing antacids may be beneficial for human hydrofluoric acid dermal burns, these are not established clinical treatments.

The anesthetized pig model has been reported previously to show good applicability for assessing the efficacy of treatments for dermal lesions caused by hydrofluoric acid (HF) exposure.[1] Our earlier research assessed six clinically applicable treatments by subjectively scoring and statistically analyzing gross and histopathological data obtained from treated and untreated control lesions. Iced topical Zephiran® soaks and 10% calcium acetate soaks at room temperature were found to be highly effective in reducing tissue damage; 2.5% calcium gluconate gel, intra- and interdermal injection of 5% calcium gluconate solution, and iced Hyamine® 1622 (Lonza Inc., Fairlawn, NJ) soaks were effective; and intra- and interdermal injection of 10% calcium gluconate solution was ineffective. Calcium gluconate gel (2.5%), iced Zephiran soaks and iced Hyamine soaks were most effective in reducing superficial dermal damage, whereas both the injection of 5% calcium gluconate solution and topical 10% calcium acetate soaks were beneficial to the deeper tissues of the skin, the dermis and subdermis.

The purpose of this investigation was (1) to verify the reproducibility of the anesthetized pig model for evaluating therapies for HF dermal burns, (2) to further investigate topical application of calcium acetate soaks as a potential treatment for HF dermal burns, (3) to evaluate a magnesium hydroxide antacid as a potential treatment for HF dermal burns,

From AlliedSignal Inc., Morristown, New Jersey (Mr Dunn, Dr MacKinnon, Mr Knowlden, Dr Billmaier, Dr Derelanko, and Dr Rusch), and WIL Research Laboratories, Inc., Ashland, Ohio (Mr Naas and Dr Dahlgren).

Address correspondence to: Brendan J. Dunn, MS, Senior Toxicologist, AlliedSignal Inc., 101 Columbia Road, Morristown, NJ 07962-1139.

1076-2752//0-0507$3.00/0

and (4) to evaluate the efficacy of each treatment with superficial and deep burns. Superficial and deep burns were produced by exposing the skin to 38% HF for 7 minutes and 12 minutes, respectively. The frequently used topical treatments, iced Zephiran soaks and 2.5% calcium gluconate gel applications, were both reassessed to verify that each treatment effectively reduces tissue damage in all three layers of the skin. The potential of topical 10% calcium acetate soaks to effectively reduce dermal damage was also verified. In contrast to the previous investigation,[1] which evaluated room-temperature calcium acetate soaks, iced soaks were evaluated in this study. Iced soaks are thought to be preferable to room-temperature soaks because the cold appears to relieve pain and probably reduces absorption and penetration of fluoride ions (F^-) by constricting blood vessels in the dermal tissues, thereby reducing tissue damage. Additionally, the efficacy of the magnesium hydroxide antacid, Phillips'® Milk of Magnesia, was investigated for two reasons: (1) it is known that magnesium salts and antacids interfere with the absorption of ingested fluoride,[2] and (2) research studies demonstrate that the antacid, Mylanta II®, effectively reduces dermal tissue damage in rabbits exposed to HF.[3,4] Burkhart et al[4] confirmed that topical calcium gluconate gel therapy is an effective treatment of dermal HF burns and found no statistically significant differences between the effectiveness of equimolar amounts of calcium gluconate, magnesium gluconate, and magnesium hydroxide antacid (Mylanta II®) when each was mixed in KY® lubricating jelly and applied by massage to skin sites of rabbits exposed to 48% HF. These findings suggested that the magnesium-containing antacids are just as effective as calcium gluconate in the treatment of HF dermal burns. It is hypothesized that the magnesium salts in the antacid effectively bind F^-, thus the F^- is not available to complex with tissue calcium.

Methods

Chemicals

Aqueous HF (38%) was supplied by AlliedSignal Inc. (Geismar, LA). A commercial preparation of calcium gluconate gel (2.5% wt/vol; H-F Antidote Gel) was obtained from Industrial Pharmaceutical Service Ltd. (Altrincham, United Kingdom). Zephiran® chloride (benzalkonium chloride concentrate, 17% wt/vol) was obtained from Winthrop-Breon Laboratories (New York, NY) and formulated at WIL Research Laboratories as a 1:750 dilution in sterile water (USP). Calcium acetate was purchased from Fisher Scientific Co (Fairlawn, NJ) and formulated at WIL Research Laboratories Inc. as a 1:10 dilution in sterile water. Phillips'® Milk of Magnesia was obtained from The Chas. H. Phillips Co., Division of Sterling Drug Inc., (New York, NY) and used as received.

Animals

Twenty male adolescent white pigs were purchased from Oberholtzer Farms (Ashland, OH) and acclimated for a minimum of 7 days. On the day of study initiation, body weights ranged from 8.7 to 11.4 kg. Animals were housed individually in stainless steel flush cages with grate bottoms in an environmentally controlled room with a 12-hour light/dark photoperiod cycle. Air-handling units provided approximately ten fresh air changes per hour. A basal ration of Buckeye Porkmaker® pig feed (Buckeye Feed Mills, Inc., Dalton, OH) was provided on schedule and water was available ad libitum.

Animal Preparation

Approximately 48 hours before HF exposure, the hair on the back of each animal was clipped with an Oster® electric small-animal clipper (Oster Professional Products, McMinnville, TN) equipped with a No. 40 (surgical) blade. Immediately after the hair-clipping procedure, the clipped area was swabbed with Prepodyne® Surgical Scrub (West Agro Inc., Kansas City, MO) to prevent possible skin infection. Approximately 18 hours before HF exposure, the remaining hair stubble on the dorsal surface was removed with a depilatory (Neet® Lotion Hair Remover, Whitehall Laboratories, Inc., New York, NY).

Just before HF exposure, each pig was anesthetized to allow dosing and treatment to be conducted in a safe, precise, controlled, and humane manner. Atropine sulfate and fentanyl-droperidol were administered by intramuscular injection (IM) at dose levels of 0.04 mg/kg and 68.5 μL/kg, respectively. With onset of sedation (10 to 15 minutes), ketamine was administered intramuscularly at a dose level of 11 mg/kg to induce anesthesia. Surgical anesthesia was attained in 5 to 10 minutes and lasted approximately 30 to 45 minutes. Maintenance of surgical anesthesia was achieved with supplemental IM administration of ketamine and/or Innovar-Vet® at dose levels of approximately 4.4 mg/kg and 17 to 30 μL/kg, respectively.

Because of a limited supply of ketamine and Innovar-Vet®, three of the animals on study were anesthetized with an alternative drug, Telazol® (Elkins-Sinn Inc., Cherry Hill, NJ). Atropine sulfate was administered in conjunction with Telazol® in the same manner as described for the ketamine and Innovar-Vet® regimen. Initially, Telazol® was administered by IM injections ranging between 0.10 and 0.15 mL/kg, and anesthesia was maintained with supplemental IM injections at 0.05 mL/kg. We would not expect that the change in anesthetic had an effect on the outcome of the study.

HF Exposure

All animals were exposed to HF similarly. Before HF administration, application sites were delineated and labeled with an indelible ink felt-tip

marker. Eight dermal sites, four on each side of and parallel to the spinal column, were each topically exposed to a volume of 0.4 mL of 38% wt/vol HF by using an occlusive dermal delivery system, a 25-mm Hill Top Chamber® (Hill Top Research, Inc., Cincinnati, OH). On each side of the back, the transverse plane was used to separate sites of application anteriorly and posteriorly. One chamber was applied anteriorly and a second chamber was applied posteriorly for a 12-minute period. Five minutes later, a third chamber was applied anteriorly and a fourth chamber was applied posteriorly for a 7-minute exposure period. A strip of dermal tape was applied to the top of each of the four chambers on each flank so that when the 12-minute exposure period ended, the chambers could be removed simultaneously from each experimental animal by lifting the tape with attached chambers.

Treatment

Immediately after exposure, all eight dermal sites on each animal were rinsed with running, temperature-controlled (23 ± 1°C) tap water for exactly 1.5 minutes at a rate of approximately 9.0 L/minute. Uniform rinsing of all sites was achieved by administering the water with a hose fitted with a spray head.

Treatment of HF-exposed sites was initiated 2 minutes after completion of the water rinse. Each treatment was administered to a group of four pigs. In each treatment group, the four dermal lesions on the right side of two pigs received treatment, those on the left side remained untreated (controls), and the four dermal lesions on the left side of the other two pigs received treatment while those on the right side served as untreated controls. This was done to compensate for any potential site-to-site variation in responsiveness. Four treatments were evaluated.

Calcium Gluconate Gel. A sufficient amount of gel to completely cover the HF-exposed dermal site was gently massaged into the skin for 1 minute, every 15 minutes, or 4 hours. A double layer of surgical gloves was used to avoid contact with any residual HF. It should be noted that the method of calcium gluconate gel applications in this study was adapted because of practical considerations, and differs from that recommended for actual medical treatment of HF dermal burns. Recommended treatment involves the liberal application of calcium gluconate gel and the massaging of the burned area for several hours. If used as definitive treatment, the gel should be used 4 to 6 times daily for 3 to 4 days.

Iced Aqueous Zephiran Soaks. Chilled Zephiran solution, maintained in a water bath containing ice cubes at a temperature of 1.3 to 2.5°C, was applied to compresses (consisting of three layers of 2 × 2-inch sterile gauze pads) covering the HF-exposed dermal sites. The compresses remained in place for 3 hours, and fresh chilled Zephiran solution was administered to them every 3 minutes with a large-volume syringe.

Iced Calcium Acetate Soaks. Chilled calcium acetate solution, maintained in a water bath containing ice cubes at a temperature of 1.6 to 2.1°C, was applied to compresses covering the HF-exposed dermal sites every 3 minutes for 3 hours, as described for the Zephiran soaks.

Iced Phillips'® Milk of Magnesia. Compresses (three layers of 2 × 2-inch sterile gauze pads) were soaked in chilled Phillips' Milk of Magnesia, which was maintained in a water bath containing ice cubes at a temperature of 0.8 to 2.1°C, and then applied to the HF-exposed dermal sites. Compresses soaked in fresh Phillips' Milk of Magnesia were replaced every 3 minutes over a 3-hour treatment period.

Gross Examination and Photography

Untreated control and treated dermal lesions were observed, described, and photographed 30 minutes, 4 hours, and 1, 4, 7, 10, 14, and 21 days after initiation of treatments. A 35-mm Nikon 2000 camera with a Medical-Nikkor 120 mm f/4 IF lens (Nikon Inc., Garden City, NY) was used to take photographs. Kodak Ektachrome 100 HC film (EC 135–36; Eastman Kodak, Rochester, NY) was used to make color slides.

Subjective Assessment of Lesions Using Photographs

Using 35-mm slides projected at the same size scale, the gross appearance (size and severity) of each untreated dermal lesion produced by 38% HF for each specific exposure period (either 7 or 12 minutes) was subjectively and simultaneously compared with each treated dermal lesion on the contralateral side of the same pig by a panel of five investigators who were not cognizant (blinded) of the treatment being evaluated. A consensus score for each lesion, indicative of treatment effectiveness, was assigned by the panel to each comparison at intervals of 1, 4, 7, 14, and 21 days after initiation of the treatments. Positive scores were assigned when the treated lesion appeared either slightly (+1), moderately (+2), or substantially (+3) smaller and/or less severe than the untreated control lesion. Negative scores were assigned when the treated lesion appeared either slightly (−1), moderately (−2), or substantially (−3) larger and/or more severe than the untreated control lesion. A score of zero (0) was assigned when the treated site was comparable in appearance to the untreated control site.

Microscopic Pathology

Immediately after the animals were killed on day 21, full-thickness skin (including epidermis, dermis, and subdermis) was excised from each treated and each untreated control site, placed in a labeled cassette, and preserved in 10% neutral buffered formalin. Standard paraffin-embedded, hematoxylin and eosin-

TABLE 1
Weighted Significance Values Assigned to Histopathological Findings and Depth of Injury Weight Factors Assigned to the Layers of Skin

Layer of Skin	Histopathological Finding*	Weighted Significance Value†	Depth of Injury Weight Factor‡
Epidermis	Hyperkeratosis	1.0	
	Hyperplasia	2.0	1
	Inflammation, suppurative	3.0	
	Ulceration	4.0	
Dermis	Edema, outer corium	0.8	
	Acute hemorrhage	1.0	
	Inflammation, nonsuppurative	1.2	2
	Inflammation, suppurative	1.8	
	Necrosis, connective tissue	2.2	
	Ulceration	3.0	
Subdermis	Acute hemorrhage	1.0	
	Mineralization	2.0	
	Chronic inflammation	2.0	3
	Fibroplasia	2.0	
	Necrosis, adipose tissue	3.0	

* A severity grade was assigned to each histopathological finding by a veterinary pathologist (1, minimal; 2, mild; 3, moderate; 4, severe).

† Weighted significance values were assigned to the histopathological findings so that the total value for each layer of skin equaled 10.

‡ Depth of injury weight factors were used to emphasize the significance of deeper tissue damage when calculating each total relative efficacy score (RES_{tot}).

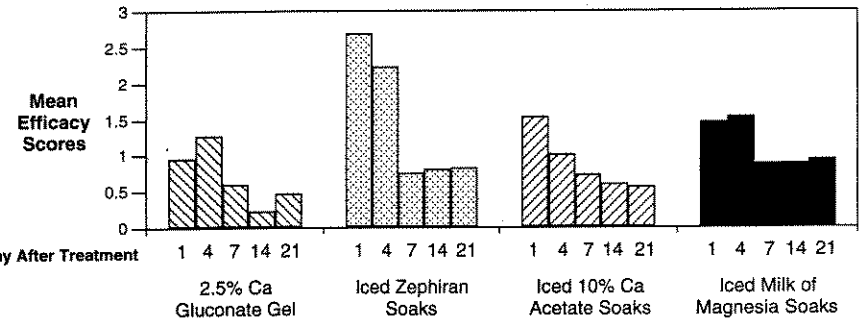

Fig. 1. Mean efficacy scores for superficial burns (skin exposed to HF for 7 minutes). For superficial burns, a mean efficacy score ($n = 40$) is presented for each of the four experimental treatments. Dermal lesions are evaluated and scored subjectively by comparing the visual appearance (size and severity) of untreated HF-exposed control sites with those of treated HF-exposed sites, using 35-mm slides projected at the same-size scale. Positive scores (+1, +2, or +3) indicate that the treated lesion appears either slightly, moderately, or substantially smaller and/or less severe than the untreated control lesion. Higher scores denote greater efficacy.

stained sections were examined microscopically by a veterinary pathologist. For each lesion, a severity grade of 1, 2, 3, or 4 (representing a minimal, mild, moderate, or severe degree of microscopic injury) was assigned to each histopathological finding by the pathologist. As shown in Table 1, each histopathological finding was also assigned a weighted significance value because some findings were thought to represent a greater degree of injury than others.

Using mathematical methods published previously,[1] the effectiveness of each treatment of 7-minute and 12-minute HF-exposed skin sites was evaluated by calculating a relative efficacy score (RES), representing the percentage improvement of a treated vs an untreated skin lesion for each skin layer (epidermis, dermis, and subdermis) separately, and a total relative efficacy score (RES_{tot}), representing the percentage improvement of an entire treated skin lesion (all three skin layers combined) vs an entire untreated skin lesion.[1] For calculation of the RES_{tot}, a depth of injury weight factor of either 1, 2, or 3 was assigned to the epidermis, dermis, or subdermis, respectively, for the purpose of giving deeper tissue damage more significance than superficial damage (Table 1).

Statistical Analysis

Data were analyzed parametrically using analysis of variance and Duncan's Multiple Range Test.

Results

Gross Pathology

Results of the subjective photographic assessment of lesions caused by 7- and 12-minute HF exposures are graphically represented in Figs. 1 and 2, respectively. Table 2 presents the results of statistical analysis of the photographic data, mean efficacy scores, and ranking of treatments.

Superficial Burns (skin exposed to HF for 7 minutes). Based on the mean efficacy scores 1 day after treatment was administered, iced Zephiran soaks showed statistically significantly greater efficacy than the other treatments. The iced 10% calcium acetate soaks and the iced Phillips' Milk of Magnesia soaks were less effective, whereas the 2.5% calcium gluconate gel was least effective at this time. On day 4, iced Zephiran soaks were again ranked as the most effective treatment, both iced Phillips' Milk of Magnesia soaks and 2.5% calcium gluconate gel applications were ranked less effective, and 10% calcium acetate soaks were ranked least effective. On days 7, 14, and 21 after initiation of treatment, all four therapies were ranked comparably for effectiveness, with the exception of 2.5% calcium gluconate gel, which was ranked less effective on day 14.

Deep Burns (skin exposed to HF for 12 minutes). One day after treatment was started, iced 10% calcium acetate soaks were ranked as the most effective treatment, whereas

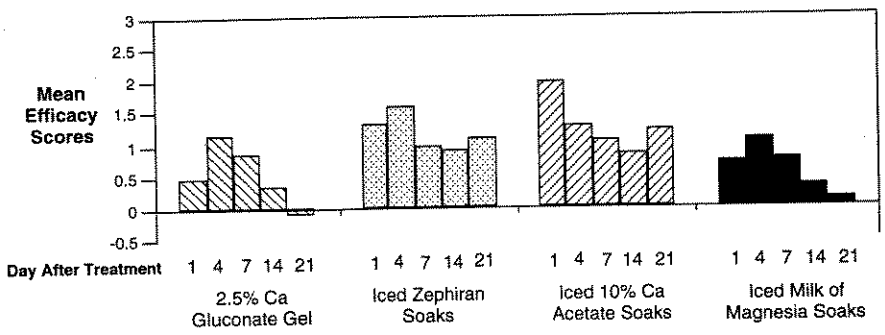

Fig. 2. Mean efficacy scores for deep burns (skin exposed to HF for 12 minutes). For deep burns, a mean efficacy score ($n = 40$) is presented for each of the four experimental treatments. Dermal lesions are evaluated and scored subjectively by the same procedures described in Fig. 1.

iced Zephiran soaks were the next best treatment, and both iced Phillips' Milk of Magnesia and 2.5% calcium gluconate gel applications were least effective. At 4 and 7 days after treatment, the four treatments were ranked comparably. On days 14 and 21, both iced 10% calcium acetate soaks and iced Zephiran soaks showed statistically significantly greater efficacy than iced Phillips' Milk of Magnesia soaks and 2.5% calcium gluconate gel applications.

Microscopic Pathology

Superficial Burns (skin exposed to HF for 7 minutes). Based on the ranking of the RESs for the four experimental treatments presented in Fig. 3, iced Zephiran soaks reduced tissue damage most effectively in the epidermal layer. Iced Phillips' Milk of Magnesia soaks (although statistically comparable with all treatments) appeared to be less effective than the iced Zephiran soaks. Both the iced 10% calcium acetate soaks and 2.5% calcium gluconate gel applications were least effective in the epidermal layer. In the dermal layer, the iced Zephiran soaks were, by far, the most effective treatment for reducing tissue damage. After iced Zephiran soaks, the iced Phillips' Milk of Magnesia soaks, the 2.5% calcium gluconate gel applications, and the iced 10% calcium acetate soaks were ranked less effective in the dermal layer. In the subdermal layer, no residual histopathological lesions were present at day 21 at either the treated or control skin sites, with the exception of a minor finding at a single site in an animal treated with iced 10% calcium acetate soaks. Because the subdermal layer was not substantially affected by the 7-minute exposure to HF without treatment, an RES could not be calculated.

Deep Burns (skin exposed to HF for 12 minutes). Based on the ranking of RESs for the four experimental treatments presented in Fig. 4, three treatments (iced Zephiran soaks, iced 10% calcium acetate soaks, and 2.5% calcium gluconate gel) were shown to be about equal in reducing tissue damage in both the epidermal layer and the dermal layer. The iced Phillips' Milk of Magnesia soaks were found to be ineffective in both the epidermis and dermis. In the subdermal layer, all four treatments were ranked comparably and appeared very effective.

Figure 5 depicts the ranking of treatments for both superficial and deep burns based on ability to reduce damage to the skin as a whole (RES_{tot}). In this evaluation, the importance of the three skin layers (epidermis, dermis, and subdermis) was assessed by assigning greater weight to deeper injury. For superficial burns, the iced Zephiran soaks were most effective, with the greatest improvement being shown in the dermis. Although statistically significantly comparable to the Zephiran soaks, the iced Phillips' Milk of Magnesia soaks appeared less effective, but showed good improvement in both the epidermal and dermal layers. The 2.5% calcium gluconate gel applications and iced 10% calcium acetate soaks were least effective, with each demonstrating greater effectiveness in the dermis than in the epidermis. For deep burns, iced 10% calcium acetate soaks, iced Zephiran soaks, and 2.5% calcium gluconate gel applications were ranked comparably as the better treatments, with the dermis and subdermis showing greater improvement than the epidermis in all cases. Iced Phillips' Milk of Magnesia soaks were ranked least effective for deep burns, appearing ineffective in the epidermal and dermal layers, yet showing effectiveness in the subdermal layer.

Discussion

In this study, the efficacy of four experimental treatments for HF dermal burns was assessed by statistically analyzing (1) the mean efficacy scores derived from a subjective comparison of the visual (gross) appearance (size and severity) of treated HF-exposed sites with those of untreated HF-exposed sites over a period of 21 days, and (2) the RESs derived from a comparison of the histopathological findings of treated HF-exposed skin sites with those of untreated HF-exposed skin sites at the termination of the study on day 21. The histopathological findings were used to assess treatment efficacy for the three layers of skin (epidermis, dermis, and subdermis). Lesions produced in this study by 7-minute exposures to HF were considered superficial and representative of mild HF burns in humans, whereas lesions produced by 12-minute HF exposures were considered deep and representative of severe burns in humans.

Superficial HF Dermal Burns

Based on the gross appearance of lesions 1 and 4 days after initiation

TABLE 2
Mean Efficacy Scores* and Ranking† of Treatments Based on Analysis of Photographic Data

Burn Type	Treatment	Days After Treatment				
		1	4	7	14	21
Superficial Burn (7-min HF Exposure)	Iced Zephiran Soaks	2.68 A	2.23 A	0.75 A	0.80 A	0.83 A
	Iced Milk of Magnesia Soaks	1.45 B	1.53 B	0.88 A	0.88 A	0.93 A
	Iced 10% Ca Acetate Soaks	1.53 B	1.00 C	0.73 A	0.60 A,B	0.55 A
	2.5% Ca Gluconate Gel	0.95 C	1.27 B,C	0.60 A	0.23 B	0.48 A
Deep Burn (12-min HF Exposure)	Iced 10% Ca Acetate Soaks	1.95 A	1.25 A	1.05 A	0.85 A	1.23 A
	Iced Zephiran Soaks	1.30 B	1.58 A	0.98 A	0.90 A	1.10 A
	Iced Milk of Magnesia Soaks	0.73 C	1.08 A	0.75 A	0.33 B	0.13 B
	2.5% Ca Gluconate Gel	0.48 C	1.18 A	0.88 A	0.35 B	−0.13 B

* Mean Efficacy Scores for each day after treatment represent 10 independent scores of four animals (n = 40).
† Treatment groups A, B, and C are statistically different (α = .05).

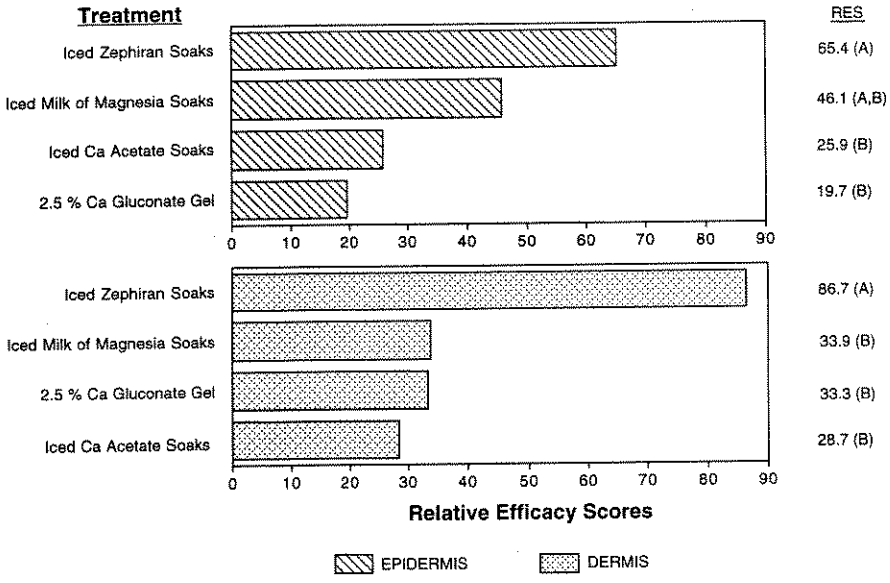

Fig. 3. Relative efficacy scores for superficial burns. For superficial burns, a relative efficacy score (RES) is depicted for each of the four experimental treatments at the epidermal and dermal layers. Relative efficacy scores at the subdermal layer are not shown because no residual histopathological lesions were present at day 21 at either the treated or the untreated control sites, with the exception of a single site in one animal. The greater the RES, the more efficacious the treatment is considered. The control value is taken as zero. Means with the same letter are not significantly different (α = 0.1).

of treatment, iced Zephiran soaks appeared to reduce superficial damage more rapidly than the other three treatments. For the most part, all four treatments were considered equally efficacious when evaluated 7 to 21 days after initiation of treatment.

Histopathological evaluation of lesions excised on day 21 indicated that iced Zephiran soaks were more efficacious for superficially burned skin than the other treatments, particularly for the dermis. Iced Phillips' Milk of Magnesia soaks, iced 10% calcium acetate soaks, and 2.5% calcium gluconate gel applications were effective, but to a lesser degree.

Deep HF Dermal Burns

When lesions were evaluated grossly 1 day after therapy initiation, iced 10% calcium acetate soaks were most effective, iced Zephiran soaks were the next most effective, and both iced Phillips' Milk of Magnesia and topical application of 2.5% calcium gluconate gel were least effective. No statistically significant differences in effectiveness between therapies were apparent on days 4 and 7 after initiation of treatment. On days 14 and 21 after treatment, evaluation of the gross appearance of the lesions ranked both iced 10% calcium acetate soaks and iced Zephiran soaks as better therapies for deep burns than either iced Phillips' Milk of Magnesia soaks or 2.5% calcium gluconate gel applications. Based on histopathological assessment of the three dermal layers of deep burns, iced Zephiran soaks, iced 10% calcium acetate soaks, and 2.5% calcium gluconate gel applications were equally effective in reducing damage at each skin layer. The microscopic findings showed that Iced Phillips' Milk of Magnesia soaks were ineffective in the epidermal and dermal layers of deep burns but were comparably effective to the other three treatments in the subdermal layer.

When skin lesions were evaluated as a whole, including all three skin layers, iced Zephiran soaks were ranked as the better treatment for superficial HF dermal burns, with a major effect on the dermal layer. Though no statistically significant difference was shown, the iced Phillips' Milk of Magnesia soaks appeared slightly less effective than the iced Zephiran soaks for superficial burns, showing benefit to both the epidermis and dermis. Both the 2.5% calcium gluconate gel applications

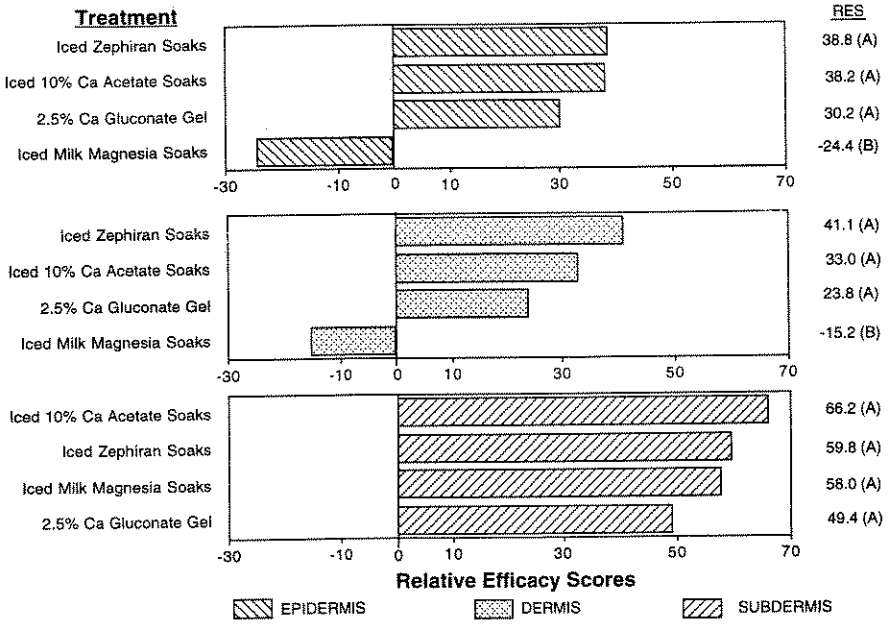

Fig. 4. Relative efficacy scores for deep burns. For deep burns, a relative efficacy score (RES) is depicted for each of the four treatments at the epidermal, dermal, and subdermal layers. The greater the RES, the more efficacious the treatment is considered. The control value is taken as zero. Means with the same letter are not significantly different ($\alpha = 0.1$).

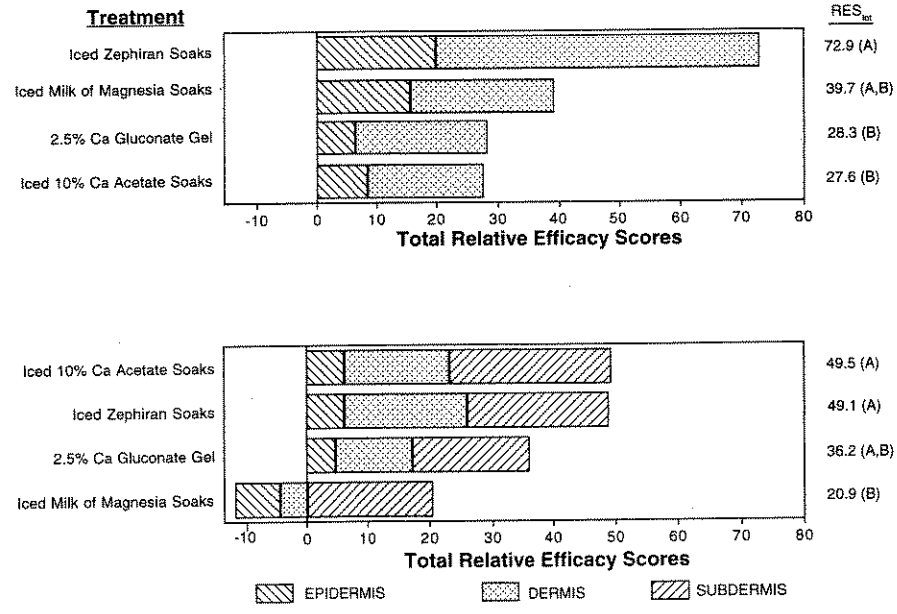

Fig. 5. Total relative efficacy scores for superficial burns (top) and deep burns (bottom). For superficial and deep burns, a total relative efficacy score (RES_{tot}) is depicted for each of the four treatments. The RES_{tot} for superficial burns includes the efficacy scores of two layers of skin combined and the RES_{tot} for deep burns included the efficacy scores of all three layers of skin combined. The bars representing the RES_{tot} are subdivided to reflect the contribution of each layer of skin. The greater the RES_{tot}, the more efficacious the treatment is considered. Means with the same letter are not significantly different ($\alpha = 0.1$).

and iced 10% calcium acetate soaks were ranked less effective than the two former treatments, with more effectiveness being demonstrated in the dermal layer than in the epidermal layer in both cases. For deep HF dermal burns, iced 10% calcium acetate soaks, iced Zephiran soaks, and 2.5% calcium gluconate gel applications were equally ranked for efficacy. For each of these treatments, both the dermis and subdermis displayed greater improvement than the outer epidermal layer. Iced Phillips' Milk of Magnesia soaks appeared to be ineffective in the epidermal and dermal layers for the more severe burns produced by the 12-minute exposure to HF. In contrast, the effectiveness of the Milk of Magnesia soaks in the subdermal layer was beneficial and comparable with the other treatments, which may reflect blocking of further penetration of F^- by binding with Mg^+ in the superficial skin layers.

This experimental study substantiated the value of both topical iced Zephiran soaks and, to a lesser degree, topical applications of gel containing 2.5% calcium gluconate. Results emphasized that iced Zephiran soaks were more efficacious for superficial HF dermal burns than the other therapies. The study also confirmed the results of our previous investigation,[1] which showed that 10% calcium acetate soaks were effective for the treatment of deep HF dermal burns and corroborated the work of other investigators[3,4] that demonstrated the beneficial effects of magnesium-containing antacids for topical treatment of HF-exposed skin.

The therapy chosen for treatment of HF dermal exposures is an extremely important consideration, particularly when appropriate first aid must be administered as quickly as possible. This includes copious flushing with water, followed by more definitive treatment. This study did confirm the advantage of the two clinically established treatments, iced Zephiran soaks and 2.5% calcium gluconate gel applications. An additional advantage is that these treatments can be initiated immediately by nonmedical personnel after flushing with water. If these treatments are not immediately available,

consideration should be given to the alternative treatments evaluated in this study. Although antacids, such as Phillips' Milk of Magnesia, are readily available, they should be used only as a first-aid measure, and only until a more proven treatment is available. Calcium acetate is a commodity chemical and is accessible, but again, there is limited documented clinical experience for its use.

With severe burns, topical treatments may not be adequate and one must always consider the possibility of using subcutaneous or intradermal injections of 5% calcium gluconate solution.[5] In certain situations, eg, burns of the fingers, intraarterial and intravenous calcium gluconate have been used successfully.[6,7] For HF exposures other than those involving the skin, including systemic effects, more detailed information concerning therapy should be consulted.[8–11]

References

1. Dunn BJ, MacKinnon MA, Knowlden NF, et al. Hydrofluoric acid dermal burns: an assessment of treatment efficacy using an experimental pig model. *J Occup Med.* 1992;34:902–909.
2. Mofenson HC, Caraccio, TR. Fluorine and fluoride. In: Haddad LM, Winchester JF, eds. *Clinical Management of Poisoning and Drug Overdose.* 2nd ed. Philadelphia: W.B. Saunders; 1990:1049–1055.
3. Brent J. Hydrofluoric acid exposures: the role of poison centers. Presentation at the HF Industry Safety Seminar, Hilton Head, South Carolina, August 28, 1990.
4. Burkhart KK, Brent J, Kirk MA, Baker DC, Kulig KW. Comparison of topical magnesium and calcium treatment for dermal hydrofluoric acid burns. *Ann Emerg Med.* 1994;24:9–13.
5. Trevino MA, Herrmann GH, Sprout, WL. Treatment of severe hydrofluoric acid exposures. *J Occup Med.* 1983;25:861–863.
6. Henry J, Hla K. Intravenous regional calcium gluconate perfusion for hydrofluoric acid burns. *Clin Toxicol.* 1992; 30:203–207.
7. Vance MV, Curry SC, Kunkel DB, Ryan PJ, Ruggeri SB. Digital hydrofluoric acid burns: treatment with intraarterial calcium infusion. *Ann Emerg Med.* 1986;15: 890–896.
8. MacKinnon MA. Hydrofluoric acid burns. *Dermatol Clin.* 1988;6:67–74.
9. Upfal M, Doyle C. Medical management of hydrofluoric acid exposure. *J Occup Med.* 1990;32:726–731.
10. Bentur Y, Tannenbaum S, Yaffe Y, Halpert M. The role of calcium gluconate in the treatment of hydrofluoric acid eye burn. *Ann Emerg Med.* 1993;22:1488–1490.
11. Caravati EM. Acute hydrofluoric acid exposure. *Am J Emerg Med.* 1988;6:143–150.