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Comparison of Propolis Skin Cream to Silver Sulfadiazine: A Naturopathic Alternative to Antibiotics in Treatment of Minor Burns

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ABSTRACT

Background: Propolis, a naturopathic substance derived from bees wax extract, has recently been praised for its antimicrobial, anti-inflammatory, and cicatrization-enhancing properties.

Objective: In our study, we compare these properties in a high-grade Brazilian propolis skin cream directly with silver sulfadiazene (SSD) in the treatment of minor burns (superficial second degree) in the ambulatory care setting (less than 20% total body surface area burned).

Settings/location: The study was conducted at the burn clinic in Pronto Socorro para Queimaduras, Gioania, Brazil.

Subject: Patients were admitted to the study only if their initial presentation for burn care was within 48 hours postinjury and if bilateral wounds of similar depth and quality were present.

Interventions: Patients had propolis skin cream applied to one wound and SSD applied to the other selected wound on initial presentation and underwent debridement and dressings change the following morning. Patients subsequently returned to the clinic every 3 days to have the wounds checked and dressings changed. At these check-ups, wounds were cultured for microbial growth and photographed to document inflammation and cicatrization. Patients were instructed not to disturb their wounds or change their dressings at home, thus propolis skin cream and SSD were applied to the wounds only at the specified 3-day intervals.

Results: Our preliminary results do not show any significant difference in microbial colonization between wounds treated with SSD and propolis skin cream, however, wounds treated with propolis skin cream consistently showed less inflammation and more rapid cicatrization then those treated with SSD.

Conclusion: Propolis skin cream appears to have a beneficial effects on the healing of partial thickness burn wounds. If dressings had been changed more frequent the antimicrobial and wound healing effects would have been enhanced.

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INTRODUCTION

PROPOLIS (Gr. *pro* = before + *polis* = city) is a natural resin produced by honey bees from a mixture of pollen, tree bark, and other plant components and is used in construction of their hives as well as a sealant for repair and embalmer for insect carcasses. Humankind has also found a number of uses for this substance as an antimicrobial, an anti-inflammatory, even an antacid as evidenced by folk traditions still strongly preserved by many modern South Americans. Likewise, science and the medical community have begun a level of inquiry of the resin well beyond that of mere curiosity such that today there is no dearth of laboratory data validating claims of antimicrobial (Mizovea and Calder, 1996) and anti-inflammatory action (Mizovea et al., 1997). Additional studies have shown propolis to be tumorical, antifungal, antiamoebic, and antipyretic (Grunberger et al., 1980; Parks et al., 1998). However, what is lacking presently are clinical studies confirming these results in humans that would bridge the gap between folk tradition and laboratory data.

In considering a logical point of introduction for such clinical studies one can easily arrive at the decision to involve patients with minor burns for several reasons. Minor burns are those that are generally classified as superficial second-degree, thus involving only the epidermis and superficial dermis but sparing deep dermal skin appendages such as sweat glands and hair follicles. Barring any significant clinical complications, care of such wounds consists solely of supportive wound dressing changes until the wound reepithelializes and spontaneously closes within approximately 2 weeks. Despite the simplicity of such wounds, which make them ideal for initial study of Propolis, the hidden intricacy of burn wound pathophysiology underlying such injuries makes them all the more intriguing.

When human skin undergoes a thermal insult resulting in a second-degree (or greater) burn, a chemical cascade of intracellular and intercellular messengers is initiated to allow the injured tissue to form a temporary barrier between itself and the environment, to initiate the process of reconstruction of damaged tissue, and to motivate the organism as a whole to afford the greatest amount of protection to the damaged area. One such chemical mediator of interest in the burn wound is thromboxane A_2 (TxA_2), which has been shown to antagonize the inflammatory response such that localized tissue ischemia is heightened well after the initial insult as well as contribute to increase sensitivity of the wound in the initial healing (Heggers et al., 1980, 1985). Pascal and coworkers (1994) demonstrated that propolis was also a savenger of oxygen-free radicals. Previously mentioned studies on the chemical nature and anti-inflammatory properties of propolis have led investigators to believe that some of its clinically observed benefits may be because of TxA_2 inhibition and elimination of oxygen-free radicals in the burn wound.

Yet another benefit to the selection of superficial burn wounds for clinical study of propolis is related to the pathophysiologic phenomenon observed in burn wounds that creates a three-tier layering effect on wound hemodynamics. After injury, the tissue forms a layer of coagulation on the surface, a layer of stasis below this coagulation, and a final layer of hyperemia below the first two (Jackson, 1953). Of critical interest to investigators in this study is the zone of stasis that, by serving as a barrier and buffer of the noninjured tissue to the wound overlying it, allows us to consider the effects of topically applied agents such as propolis skin cream or silver sulfadiazene locally without concern of effects of distribution of the agent systemically or to other (nonlocal) wound sites.

Given these ideal parameters for clinical investigation of propolis, an equally ideal population was desired and thus an exceptionally busy burn hospital treating mostly ambulatory burn patients in the country of origin of our Propolis skin cream being studied was chosen to conduct our comparison of the gold standard, silver sulfadiazine, (SSD; Boots Pharmaceuticals Inc., Lincolnshire, IL) versus Propolis Skin Cream.

MATERIALS AND METHODS

Patients for the study were selected from patients presenting for the initial treatment to the Emergency Hospital for Burns in Goiania,

Brazil whose injuries met the following criteria:

1. Partial thickness (superficial second degree) heat or scald injuries (chemical and electrical injuries excluded);
2. Less than 20% (total body surface area [TBSA] burns; any patients with complications requiring hospital admission were excluded regardless of TBSA);
3. No significant collateral trauma (broken bones, lacerations, subdermal hematomas, etc.);
4. Patients' initial presentation to the clinic must be within 48 hours postinjury;
5. Patients must not be pregnant;
6. Patients must not be allergic to sulfa drugs;
7. Patients must present with a minimum of two burns in well-separated areas of the body (each wound geographically isolated from the other) which are clinically comparable in terms of size, burn severity (depth), and exposure/protectability. Institutional review was given by UTMB's Institutional Review Board for permission to analyze data from this study. (UTMB IRB # 99-269)

Once the patient has been selected for the study and agreed to participate, baseline swab cultures are taken from the two chosen sites and the wounds were then cleansed superficially with sterile washcloths and saline solution. One site is chosen for the application of propolis skin cream, the other received SSD, thus each patient served as their own control. The selection of sites for each topical agent for each patient were performed as randomly as possible although it was not possible to apply the creams blindly because they inherently look and smell different. All patient dressings (including initial presentation, debridement, and subsequent dressing changes) were performed in the following manner: swab culture, cleansing with washcloth/saline, direct application of cream to wound, with a gauze covered with an ace-bandage wrap. No other topical agents and/or dressings were permitted and use of any such devices was cause for removal from the study.

On initial presentation, patients were given instructions to return the following morning for surgical debridement. Surgical debridement at this hospital consisted of general anesthesia induced by thiopental and/or halothane (without intubation) and generally lasted 10–15 minutes. No local anaesthetics (e.g., lidocaine) were administered to patients in the study. Wounds were debrided with sterile cloths and/or scraping devices (for more resilient scabs), thus fully removing any necrotic skin, blisters, or any scab material formed prior to treatment. Subsequently, patients returned every 3 days to the outpatient clinic for wound culturing, inspection/clinical assessment (documented by photography when appropriate), and dressing changes.

Patient culture series were taken from both test sites on each patient and were held for 72 hours. Qualitative and quantitative observations were made on colony forming units (CFUs) at 24, 48, and 72 hours after sample collection. Culturing was performed by "rolling" the tip of a sterile cotton swab over the surface of the open wound for one full turn in one direction and then once again back in the opposite direction. The tip of the swab was then rolled across the surface of the blood agar plate using the same technique. This provided a 1:1 wound surface to plate surface area culture (approximate size of about 1 cm by 3 cm). The number of CFUs seen on each plate was recorded as were any unusual visual aspects of such colonies. No attempt was made to identify cultured organisms as Gram's staining and light microscopy materials were not readily available.

Patients were considered to be finished with the study once their wounds appeared to be closed (dry, free from infection, and largely, if not completely, reepithelialized). This point was determined by the clinical assessment of the attending physician responsible for the patient. Frequently, one wound healed before another in these patients. In this case, the date of closure for the healed wound was noted and no further treatment as per the study protocol was given to that wound area, however, unrelated treatment as per hospital protocols continued after this point apart from the study. The unhealed wound in this case continued with its treatment as per study protocol until it had closed, at which point the patient would no longer be observed for the study and hospital protocols would determine further treatment was needed for both wounds.

RESULTS AND DISCUSSION

Elementary analysis of wound colonization (Figs. 1 and 2) did not reveal clinically significant differences between wounds treated with propolis skin cream and those treated with SSD. In both the first and second post-treatment cultures, the total number of patients in the lowest grade category of colonization (0–10 CFUs) was higher for SSD (11 in the first culture series and 7 in the second) than for propolis skin cream (8 and 5, respectively). The highest grade category of colonization (too-numerous-to-count or TNTC CFUs) was lower for SSD (6 in the first culture series and 7 in the second) then for propolis skin cream (9 and 10, respectively). Intermediary categories (10–20 and 20–50 CFUs) did not show any remarkable differences or notable trends in the data collected.

It should be noted that the data (Figs. 1 and 2) clearly supports the assumption that SSD would maintain an overall lower number of colonization (i.e., a closer approximation to a sterile wound), however, this observation seems to be moot in the treatment of such minor wounds as such differences in total colonization were far to small to make a clinical impact on the healing process of the wound (Figs. 1 and 2). One must recall that all skin carries a normal flora and that a true sterile wound is actually impossible in the treatment of such patients.

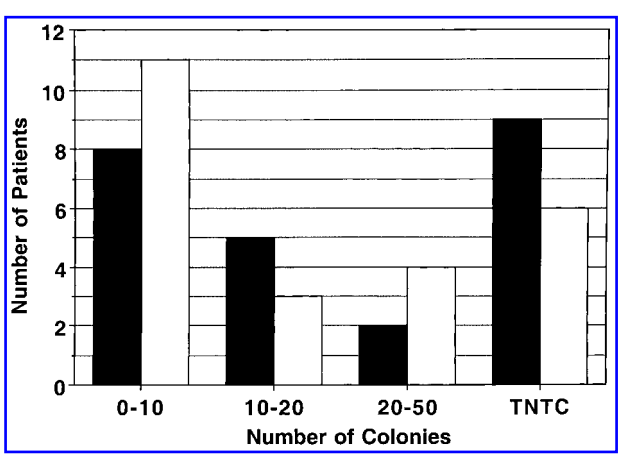

FIG. 1. First post-treatment cultures (collected approximately 5 days postinjury; results at 72 hours postculture); ■ propolis skin cream; □ silver sulfadiazene (SSD). TNTC, too numerous to count.

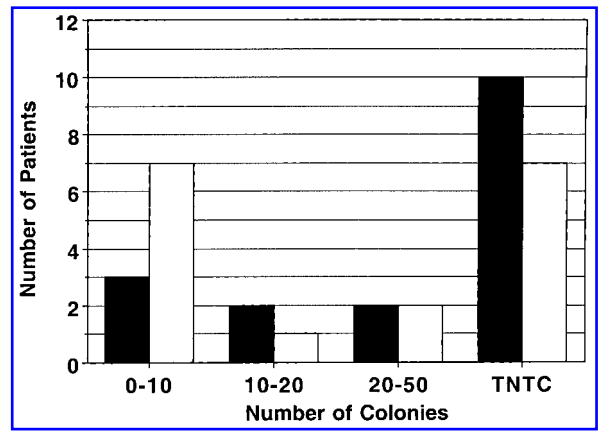

FIG. 2. Second post-treatment cultures (collected approximately 8 days postinjury; results at 72 hours postculture); ■, propolis skin cream; □ silver sulfadiazene (SSD). TNTC, too numerous to count.

It is furthermore noted that although no definitive identification of organisms was attempted, none was clinically indicated as all of the CFUs observed on the blood-agar cultures (for both propolis skin cream- and SSD-treated wounds) appeared consistent with characteristics of normal flora organisms. With few exceptions, all CFUs appeared as small, round, grayish-white colonizations that appeared within 48 hours after culturing and did not appear to increase in number (only in size) after 72 hours after culturing. Occasionally, β-hemolytic colonies were observed and, in two cases, small yellow colonies were observed. Cultures on McConkeys Selective Agar were performed at least once on every variant of the organisms observed but isolated, however, each inoculated plate revealed no growth after 72 hours. It is deduced from these data that the majority of organisms producing CFUs on the blood agar plates were gram-positive organisms (most likely *Staphylococcus* and/or *Streptococcus* species) are consistent with normal skin flora.

Clinical observation complimented by patient complaints indicated a consistently lesser degree of inflammation in patients treated with propolis skin cream. On clinical observation, wounds treated with SSD appeared to display a greater degree of inflammation as notable by the four clinical signs of the inflammatory process: heat, redness, swelling, and pain. Of

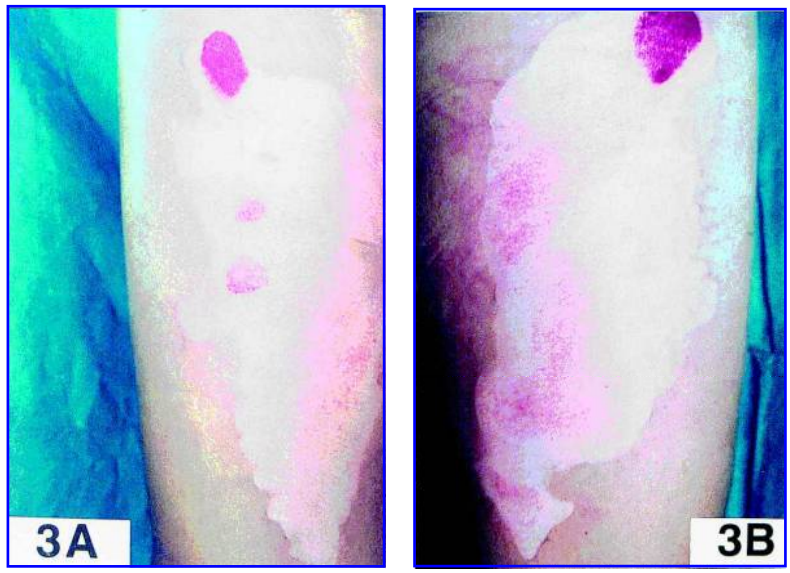

FIG. 3. **A:** Initial patient presentation after debridement: left leg, silver sulfadiazene (SSD); **B:** right leg, propolis skin cream.

these, heat, redness, and swelling appeared to be lessened in wounds treated with propolis skin cream as determined by clinical observations of varying attending physicians. The latter of these manifestations was inferred by direct questioning of the patients at dressing changes. Patients were not prompted to answer in favor or disfavor of one wound's condition over another but were merely asked if the wounds significantly irritated them. Because formal evaluation of pain was not one of the study's original goals and no scientific scale for inquiring or assessing patient, pain may only be offered as anecdotal evidence that the gross majority of patients who volunteered specific responses regarding their pain indicated that their wounds treated with SSD were more painful than those treated with propolis skin cream. Similarly, no quantitative analysis of heat, redness, or swelling was available to investigators but the clinical effects noted by the clinicians was borne out empirically by the overall healing times for the wounds.

Clinical observation revealed consistently lower time to wound closure for wounds treated with propolis skin cream (Figs. 3 and 4). The average time to allow for closure (as defined in the methods section) of wounds treated with propolis skin cream was approximately 2 days less than for those treated with SSD (9.09 versus 10.96 days, respectively). As noted in the methods section, it was not possible to blind clinicians completely in their observations of the two wounds sites being compared, however, wounds were cleaned (by nursing staff) and presented to clinicians for assessment without the aid of the patient's chart or other hints whenever possible.

Before drawing conclusions for this study, some additional factors such as patient demographics, education, and intricacies of protocol

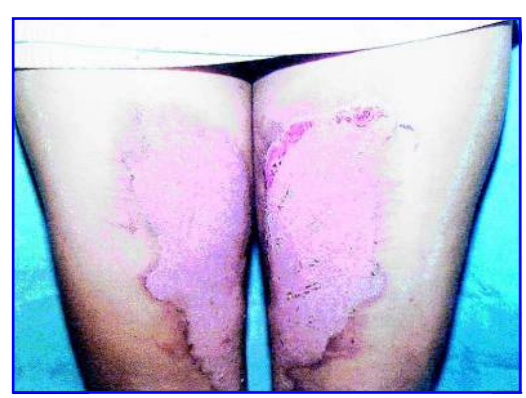

FIG. 4. Eleven days postinjury: silver sulfadiazene (SSD)-treated side (**left**) still not completely closed; propolis skin cream treated wound is completely reepithelialized.

administration in a foreign institution should be addressed. It should be noted that 33 patients were originally selected for the study based on the prestated requirements, however, only 23 patients completed the entire course of the study. Of the 10 patients who did not complete the study, 5 were dropped within 48 hours of their selection on the basis that the strict parameters for the protocol had been broken. This can be largely attributed to an "accommodation period" of the investigator to his colleagues at the hospital in which communication and/or comprehension of study protocols was occasionally less than 100%.

The remaining 5 patients who did not complete the study may be grossly attributed to assumed differences in patient lifestyles and/or level of education because these patients did not return to the ambulatory clinic as instructed to complete their treatment. With final regard to patient demographics, it is noted that patients presented to the hospital anywhere from 30 minutes to 48 hours postinjury and their ages ranged from 1 to 60 years of age with an average of 24 years of age and a mean of 18 years of age.

CONCLUSIONS

The data and observations collected in this study have lent considerable support to the hypothesis that the use of propolis skin cream in the treatment of minor burn patients may be a viable and desirable alternative to the use of SSD. It has been noted by many in the field of burn care that minor wounds of this nature will heal spontaneously nearly in nearly 100% of cases regardless of the topical agent given, however, it is proposed here that propolis skin cream offers several advantages in treatment compared with the most popular topical agent currently in use. The major benefits of this alternative include:

1. Reduced healing time of wound;
2. Reduced discomfort for patient (both duration and intensity of pain in wound healing);
3. Reduced cost of treatment;
4. Reduced risk of allergic incompatibility with treatment (regarding highly common sulfa allergies).

There is major explanation as to why the propolis skin cream could not effectively reduce bacterial colonization. The therapeutic approach of treatment every third day while practical in this setting, is definitely limiting. Had the treatment regime been three times daily the colonization rate could have been reduced significantly for both treatment modalities. It could have also influenced the anti-inflammatory and cicatrization rate.

It is noted that further clinical investigation in minor burn patients is needed to confirm these conclusions. In further investigation, it should be desirable to enforce even stricter selection criteria such that only wounds that are nearly perfectly symmetrical (two wounds of equal size and depth in precisely analogous positions, i.e., the palms of both hands) dimensions are admitted.

Furthermore, it would be advantageous to ascertain colonization levels, the depth of contamination of the wound, and the histologic progress of the wound's repair by serial wound biopsies with proper pathologic, histologic, and microbiologic laboratory analysis of specimens. It would also be desirable to establish more concrete parameters for the use of propolis in the broad spectrum of all burn patients. This study claims to establish propolis skin cream as a clinically equivalent agent to SSD for prophylaxis against wound infection and clinically superior for inflammation reduction and cicatrization in burns patients presenting with less than 20% total body surface area burned and within 48 hours of injury. The authors reemphasize that if the treatment sequence was increased to once per day or three times per day, the results might be more dramatic in respect to the antimicrobial effect and the healing response. However, the authors are unable to conclude what limits exist in regards to propolis skin cream's efficacy in patients whose burn area and time of initial clinical presentation exceed these parameters.

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Plus, a propolis derivative processed by Corigem™ Propolis Products pursuant to its private formula prior to delivery for use in this study. It was supplied by Corigem™ Propolis Products, Melville, New York 11747, (516)465-2182. The results reached herein were achieved with Corigem™ Propolis Skin Cream Plus. No conclusions can be reached as to how propolis, or any other propolis derivative, would have performed in the situations described herein. The authors wish to thank Messrs. Douglas Lord and Allan Lord for making the authors aware of the Corigem™ Propolis Skin Cream Plus product tested in this study.

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