

Full Length Research Paper

Effect of honey for treatment of some common oral lesions: Follow up of 50 cases

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Honey is the nectar that is collected from many plants and processed by honey bees (*Apis mellifera*). This study is a pilot study that observes and evaluates the clinical efficacy of topical application of honey bees in treatment of some common inflammatory, vesiculobullous and ulcerative oral lesions. A total number of 50 patients complaining of different oral lesions were enrolled in this study. Oral lesions were distributed as follows: 19 recurrent aphthous stomatitis (RAS), 5 recurrent herpes labialis (RHL), 2 recurrent intraoral herpes (RIOH), 18 atrophic/erosive oral lichen planus (OLP), 4 oral candidiasis and 2 oral psoriasis. Diagnosis of oral lesions was based either on clinical presentation and history in some oral lesions as in RHL or clinical and histopathological features. At the end of the study, the different oral lesions responded promptly to local application of honey. Clinical anecdotal evidence supporting the beneficial use of honey as a remedy for some common intraoral lesions was found.

Key words: Honey, oral lesions, aphthous stomatitis, lichen planus.

INTRODUCTION

Honey is nectar collected from many plants and processed by honey bees (*Apis mellifera*). It is used by human beings as food and as medicine for the treatment of various systemic diseases (such as respiratory diseases including asthma, urinary, gastrointestinal and skin diseases including ulcers, wounds, eczema, psoriasis, seborrheic dermatitis and dandruff) (Al-Waili, 2001; Zaghloul et al., 2001; Orhan et al., 2003).

Since some of these diseases are a consequence of oxidative damage, it seems that part of the therapeutical properties of honey is due to its antioxidant capacity that can inhibit or delay the oxidation of an oxidizable substrate in a chain reaction; therefore, honey appears to be very important in the prevention of many diseases (Al-Mamary et al., 2002; Aljadi and Kamaruddin, 2004; Beretta et al., 2005; Buratti et al., 2007). Moreover, it is a simple, inexpensive and effective method for skin grafts

storage and preservation (Subrahmanyam, 1993).

Management of most common oral inflammatory lesions, such as aphthous stomatitis and vesiculobullous lesions, such as herpes infections, remains unsatisfactory. However, topical corticosteroids may reduce the severity of the ulceration, but do not prevent their recurrence.

So, the objectives of this pilot study were to observe and evaluate the clinical efficacy of topical application of bee honey in the treatment of some common inflammatory, vesiculobullous and ulcerative oral lesions.

MATERIALS AND METHODS

A total number of 50 patients complaining of different oral lesions were enrolled in this study. Oral lesions were distributed as follows: 19 recurrent aphthous stomatitis (RAS), 5 recurrent herpes labialis (RHL), 2 recurrent intraoral herpes (RIOH), 18 atrophic/erosive oral

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lichen planus (OLP), 4 oral candidiasis and 2 oral psoriasis. Diagnosis of oral lesions was based either on clinical presentation and history in some oral lesions as in RHL or clinical and histopathological features. In cases of RAS, the diagnosis was based on history, clinical features and exclusion of other similarly appearing diseases.

Informed consent was obtained from all patients after thorough explanation of the efficacy of honey in the treatment of some dermal lesions, and they were instructed to spread a thin layer of pure, unboiled, commercial honey using sterile cotton applicator four times daily (after meals and at bedtime) as a sole remedy without using any other medication. No food, drinks, smoking or gum chewing was permitted for 30 min after application. They were asked to record their daily pain observation. A simple pain score was recorded as severe, moderate, mild or no pain. The patients continued with honey application until complete resolution of the lesion.

In lesions with erythema and/or ulceration, the size and character of the lesion, including extent and severity of the erythema and reticulation, were evaluated with a flexible transparent grid divided into calibrated 2 mm². By tracing the lesion using indelible ink marker, the lesion assessment was done by quantitative measurements through the squares of the tracing grid by a single examiner.

RESULTS

No systemic adverse reactions were noted in any case. In this study, the different oral lesions responded promptly to local application of honey. In all treated lesions (and for a long term follow up), a clinical resolution was observed with variable length of time elapsed for different lesions. An acceleration of healing was coupled with fewer days of pain or discomfort.

In cases of RAS, the patients were evaluated for both pain and ulcer size on days 1, 3, 4 and 8 of RAS episode.

At baseline, the subjective pain level of all 19 cases was severe. After 1 day of treatment with honey application, the pain level was reduced drastically as indicated by patients. 92% of patients reported no pain after one day of treatment. The mean ulcer size was 0.87 × 0.67 cm at base line. In most cases (92%), the ulcer size disappeared at the 3rd or 4th day after treatment except one case where the size was completely diminished by the 8th day. The mean healing period was 4 days.

Patients with RIOH reported immediate relief of pain after using honey at the first day and show complete lesion resolution by the 5th day of eruption of the lesion. Same results were observed in four cases of RHL, but the healing was completed by the 8th day.

The fifth case of RHL was diagnosed in the prodromal period of pain, tingling and itching with erythema at the angle of the mouth. The patient was a dental student and usually develops small vesicles surrounded by erythema at the same site every year with the stressful time of the final examination. At the present episode, she reported rapid relief of pain and tingling sensation after two days of treatment without eruption of the small vesicles.

All cases of OLP varied in severity and areas of

involvement. The diagnosis was based upon oral and skin clinical features and/or by histopathological study. One case (Figure 1a) was diagnosed by histopathological examination as bullous OLP at the left lateral border of the tongue. The patient was experiencing severe pain and persistent ulceration for 3 months. She was on prednisone 20 mg tablet used as mouth wash 4 times daily together with topical application of triamcinolone acetonide (kenalog in orabase) 3 times daily for 2 weeks. The patient experienced slight improvement in pain and size of lesion ulceration. After the histopathological report, the patient was treated by topical application of honey. She reported relief of pain within week after treatment. Resolution of the ulceration and erythema occurred in one month (Figure 2b). There was no recurrence of the lesion in 6 months follow up.

Another case with atrophic form of OLP was a combination of white papules with red atrophic areas in right and left buccal mucosa and upper and lower desquamative gingivitis (Figure 2a and 3a). She used topical corticosteroid therapy for 3 weeks with no improvement in lesion size, pain or character. She reported relief of pain 4 days after honey application. The lesion decreased from severe atrophic to a less severe to a mild reticulation and resolution of all atrophic areas. The gingival lesions became less atrophic with mild pain and gradually they were keratinized to normal looking gingival tissues in 6 weeks for gingival lesions (Figure 3b and c) and one month for buccal mucosal lesions (Figure 2b and c).

The other reticular OLP cases with atrophic erythematous patches showed transition to mild reticulation and resolution of atrophic erythematous patches in one to two months of honey application according to the severity and extent of the lesion in different areas of the oral cavity e.g. buccal mucosa, palate or dorsum surface of the tongue.

Three out of four cases of oral candidiasis were associated with fissured and/or hairy tongue and they were diagnosed using swab for candidal count and species. One month after topical application of honey, there was no candidal growth as proved by laboratory investigation.

The 4th case of oral candidiasis involved the right and left buccal mucosa and lower gingivae. It composed of pseudomembranous candidiasis following the antibiotic therapy. The patient, 22 years old, used daktarin oral gel for 3 weeks with no improvement. Three weeks after topical application of honey, the lesion disappeared with no candidal growth.

Intraoral psoriasis is rare and represents challenging problem regarding its management. The diagnosis was based on clinical (skin and oral) and histopathological features. The patients in the present study were 53, 48 years old and they had oral and skin psoriasis. The oral lesion appeared as well defined, flat, with erythematous patches that is surrounded by white raised margins in an annular and serpiginous pattern (Figure 4a). There was



Figure 1. Effect of honey in the treatment of bullous OLP. (a) Bullous OLP at the lateral border of the tongue. (b) One month after treatment.

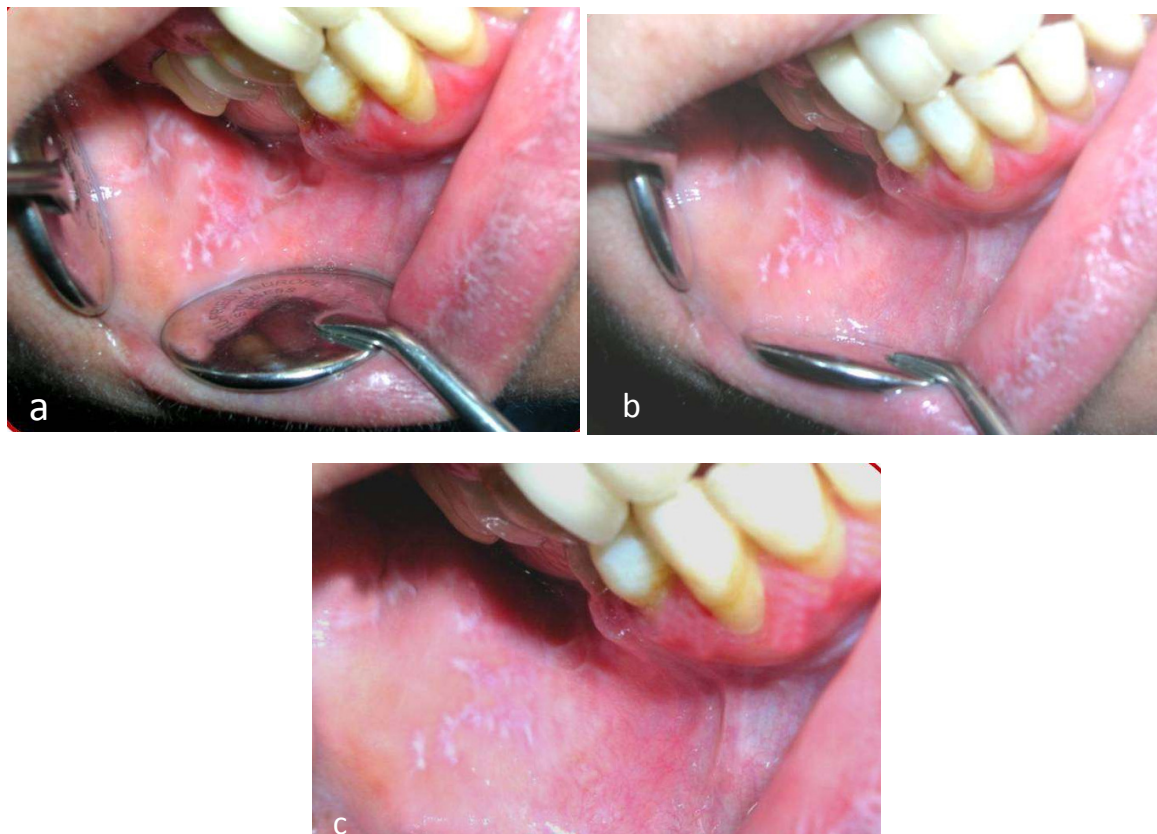


Figure 2. Healing of atrophic areas of OLP after honey application. (a) White papules with red atrophic areas of OLP at the right and left buccal mucosa, note the desquamative gingivitis at buccal surfaces of tooth No. 42 and 43. (b) Buccal mucosa after one month of treatment. (c) Dramatic resolution of atrophic areas after honey application, the buccal mucosa looking normal with keratotic papules.

complete resolution of erythematous area two months after topical application of honey without recurrence 8 months after resolution of the lesion (Figure 4b and c). One patient with psoriasis was treated with ultraviolet

radiation for her skin lesion (Figure 5a); on her own, applied honey on her skin lesion and she indicated decrease in the extent, itching, erythema and inflammation of the skin lesion (Figure 5b) and also decrease in the



Figure 3. Desquamative gingivitis of the upper anterior teeth. (a) Severe bright red diffused with white tissue tags representing desquamative epithelium of the gingiva. (b) One month after honey application. (c) Six weeks after honey application.

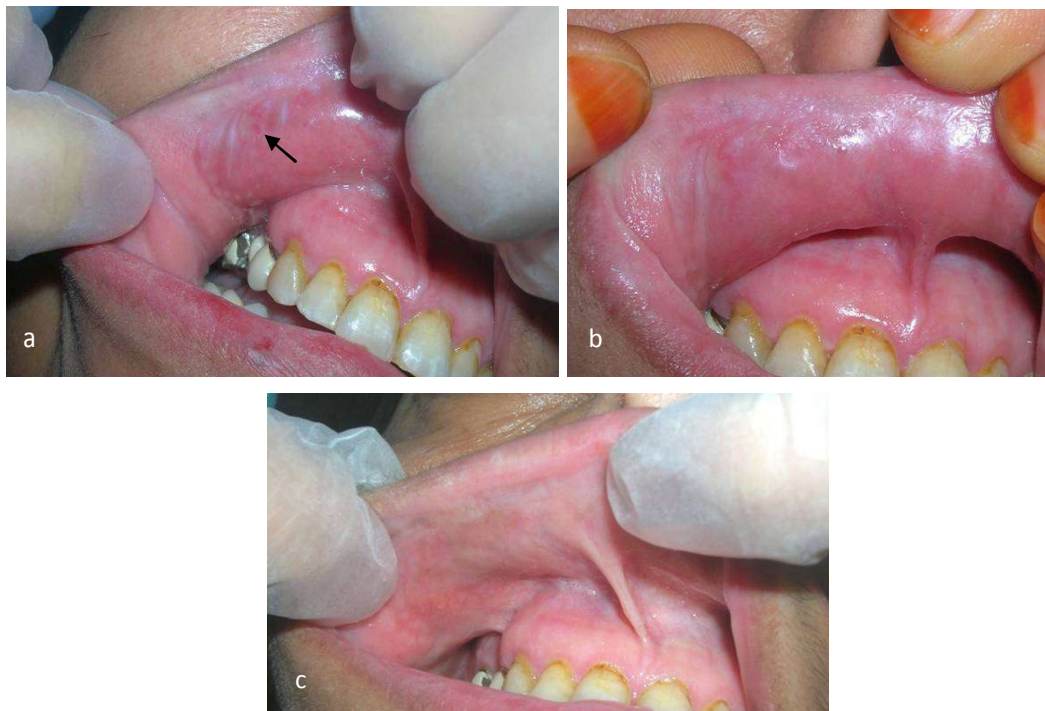


Figure 4. Oral psoriasis pre and post- treatment. (a) Before honey application. (b) After 2 months of treatment. (c) At the 8th month of follow up.

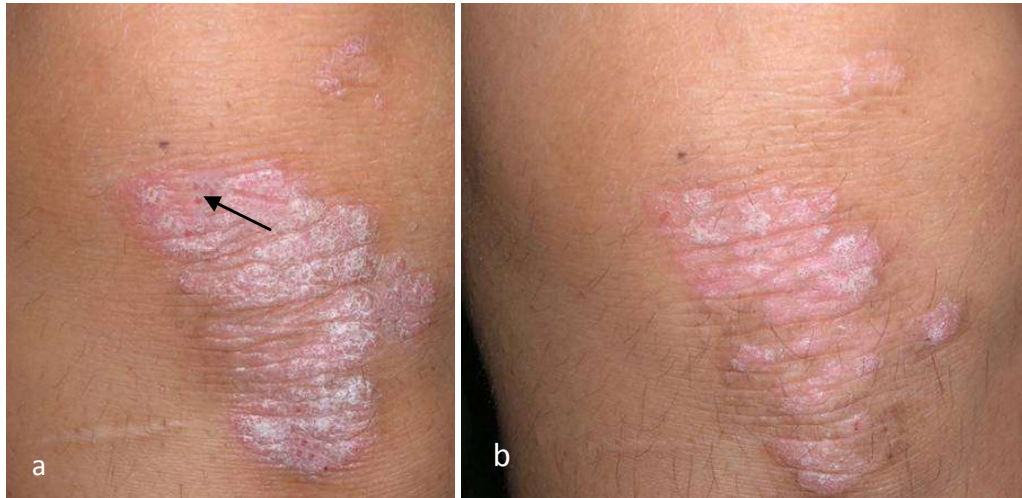


Figure 5. Skin psoriasis pre and after honey application. (a) Skin psoriasis pre- treatment. There are many inflammatory bleeding points, (b) after 1 month of honey application.

severity of hyperpigmented areas that followed the exposure of ultraviolet radiation.

DISCUSSION

The composition of honey is variable, depending primarily on the floral source; however, certain external factors also play a role, such as seasonal, environmental and processing factors. Honey has been reported to contain about 200 substances. Beside carbohydrates, which are their major component (70 to 80%), honey contains low amounts of various substances such as organic acids, proteins, amino acids, vitamins, enzymes, minerals, and various other molecules (pigments, flavonoids, antibacterial factors, among others) (White, 1975, 1979; Tan et al., 1989; Cherchi et al., 1994; Andrade et al., 1997; Anklam, 1998; Azeredo et al., 2003).

Although modern medicine has neglected honey as a therapeutic agent, because of the lack of systematic scientific study, a proliferation of publications is now being offered on the diversity of its therapeutic properties. Significant adverse effects have never been reported in the medical literature in association with local application of honey.

Nowadays, there is a rapidly increasing interest and research into natural health remedies and supplements including the therapeutic use of honey where its use as a dressing of infected wounds, burns and skin ulcers has been "rediscovered" (Orhan et al., 2003; Al-Mamary et al., 2002).

Topical application of honey has many advantages including antibacterial, antifungal and anti-inflammatory properties (Postmes et al., 1993; Molan et al., 1997; Bappsci et al., 2002). Unboiled, commercial honey reduces debrides, necrotic tissue and edema and promotes

angiogenesis, granulation tissue formation and epithelialization making skin grafts unnecessary and giving excellent cosmetic results (Bergman et al., 1983; Molan, 2001).

In this report, we present our clinical observation in 30 cases of various oral lesions treated with topical application of honey.

White et al. (1963) published a paper, which identified the major antibacterial substance in honey as hydrogen peroxide and also demonstrated that it is produced by the enzyme glucose oxidase of honey. The antibacterial properties of honey were reviewed in depth by Molan (1992, 1995), and again briefly by Armstrong and Otis (1995), where they reported that the antibacterial properties of honey is attributed to both physical factors (acidity; honey has an average pH of 3.9 and osmolarity, which is certainly inimical to bacterial growth) and chemical factors (hydrogen peroxide and volatiles). Effem (1988) reported that osmolarity is an important factor in the efficacy of honey when used as an antibacterial agent for skin wounds.

This antibacterial properties is effective when honey is applied *in vivo* (topically as in skin wounds and infection or internal for throat or stomach ailments) or *in vitro* using agar plate assays (Al-Waili, 2001).

It can be ascertained that honey is itself sterile and has a broad spectrum of antimicrobial actions inhibiting the growth of both Gram positive and Gram negative bacteria including *Staphylococcus aureus* and various strains of human pathogenic bacteria (Bergman et al., 1983).

It was used by ancient civilizations in the treatment of wounds, burns and skin ulcers, but it was superseded by modern dressings and antibiotic therapy. They have suggested that honey should be applied at regular intervals, from hourly to twice daily and that wounds can become sterile in 3 to 10 days (Zumla and Lulat, 1989).

However, the emergence of antibiotic-resistant strains of bacteria has confounded the current use of antibiotic therapy leading to the re-examination of former remedies. Subrahmanyam (1993) reported evidence that honey is hypertonic, sterile and bactericidal and therefore it is effective in skin grafts storage and preservation as reported in an experimental study that showed good histopathological preservation of skin grafts in honey and the uptake of grafts was 100% in the patients in whom honey-stored grafts.

Recently many researches used it successfully as topical application in treatment of skin diseases associated with bacterial infection and/or inflammatory mycosis without use of corticosteroid or antibiotic combinations. It causes faster eradication of bacterial infections, reduces antibiotic used and hospital stay, accelerates wound healing, and results in minimal scar formation (Tuck and Hayball, 2002).

This made us to speculate that, intraoral topical application of honey could prevent secondary infection associated with many vesiculobullous and ulcerative lesions such as RAS, RHL, and bullous LP. The mechanism of therapeutic effects of honey in skin lesions, as anti-inflammatory agent, might be attributed to reduction in the prostaglandin synthesis at site of application, elevation of nitric oxide in the lesions, inhibition of fungal or bacterial growth, inhibition of leukotriene B₄, and to its antioxidant and anti-inflammatory activities (Al-Waili, 2003).

Tonks et al. (2003) indicated that honey may initiate or accelerate the healing of chronic wounds and has, therefore, been claimed to have anti-inflammatory properties that may in part be related to the stimulation of inflammatory cytokines from monocytic cells when applied topically. Such cell types are known to play an important role in healing and tissue repair where it induced or stimulated the release of TNF- α , IL-1 β and IL-6 from MM6 cells, along with its antibacterial properties of hydrogen peroxide. Also, honey lowers plasma concentrations of prostaglandin E₂, prostaglandin F₂ alpha and thromboxane B₂ in healthy subjects (Tonks et al., 2003).

Besides, flavonoids, rich in honey, have potent antioxidant, cytoprotective and anti-inflammatory activities and inhibit histamine, IL 6 and IL 8 (Theoharides et al., 2001).

Recently, it was found that honey increased nitric oxide in saliva taken from normal individuals. Nitric oxide reduces incidence of skin infection in psoriasis (Giustizier et al., 2002). Moreover, honey reduces pain, oedema, exudates and scar formation. It seems to accelerate wound healing as documented histologically by measurement of the thickness of the granulation tissue, epithelialization from the periphery of the wound and reduction of the size of the open wound (Bergman et al., 1983).

This study reports that honey application reduced pain and inflammation, promoted healing process and stimulated tissue regeneration. This is inconsistent with previous

Studies that indicated these properties of honey. Honey apparently could inhibit growth of *Candida albicans* completely. Pure honey inhibited fungal growth and diluted honey appears capable of inhibiting toxin production (Wellford et al., 1994; Al-Waili, 2004). The present study showed successful treatment of candidal infections by using topical application of honey after three weeks.

RAS, OLP and psoriasis are usually treated with steroids either topically or systemically according to the severity of the lesion and the systemic condition of the patient. Steroids have many drawbacks, besides the side effects associated with long term use, they are not uniformly effective, can damage collagen, not licensed for use in the mouth and the candidiasis occasionally is a complication of their use (Scully, 2008).

RAS is characterized by recurrent episodes and OLP are characterized by periods of remission and exacerbation so the patients may be exposed to steroids therapy more than once. In the present study, honey application reduced inflammation, accelerated healing process and increased the pain free days in those lesions with resolution of the erythema or ulceration without need for steroid therapy. The mean healing period in RAS was 4 days which is lower than the previous reported studies.

RHL should be treated with topical application of acyclovir ointment within the first 24 h of the onset of the lesion; otherwise, it will be difficult for the lesion to respond to antiviral therapy (Scully, 2008). In this study, application of honey in the prodromal period, in one case, accelerated healing process with resolution of erythema and tingling sensation and prevented vesicular eruption. When it was applied after eruption of vesicles, in other cases, there was rapid resolution of the vesicles with no crust formation within 8 days.

LP is an inflammatory autoimmune disease that may affect both the skin and oral mucosa. OLP could represent as reticular, popular, or erosive ulcerative lesion of the oral mucosa. Oral lesions are often persistent. It is treated according to the severity of the condition, often by using topical or systemic corticosteroid drugs. Using topical honey for treatment of OLP and desquamative gingivitis dramatically reduced the inflamed areas.

Lastly, just to remember that, honey was mentioned in the Holy Quran more than 1400 years ago that wherein is healing for people. "And your LORD inspired the bee, saying "Take your habitations in the mountains and in the trees and in what they erect. Then, eat of all fruits, and follow the ways of your LORD made easy (for you)". There comes forth from their bellies, a drink of varying color wherein is healing for men. Verily, it is indeed a sign for people who think (Sura Al-Nahl, Aya 69)" (Khan and Al-Hilali, 1997).

Based on our clinical observation in different oral lesions included in this study, we can conclude that the honey significantly speeded resolution of the inflammatory and ulcerative oral lesions. It significantly lowered the pain sensation and reduced the duration of some

lesions and increased the number of pain free days. Honey is said to be very soothing and harmless. Topical application of bee-honey seems to be effective in treatment of some common oral lesions where they are routinely treated with cortisone therapy and so, it seems promising for some oral lesions.

Clinical anecdotal evidence supporting the beneficial use of honey as a remedy for some common intraoral lesions was found. Although, there were considerable limitations of the present study including small number of participants and simple method of scoring, the results obtained provide evidence to justify proceeding to a definitive randomized clinical trial. Further studies are needed to substantiate the results of this study in progress.

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