

Full Length Research Paper

Comparison between topical application of Honey, Bees wax and Olive Oil Propolis extract and Nystatin for treatment of Diaper Dermatitis in Infants

*Abeer El Sakka¹, Mamdouh Abdulrhman¹ and Iman H. Shehata²

¹Department of Pediatric, Faculty of Medicine, Ain Shams University.

²Department of Medical Microbiology and Immunology, Faculty of Medicine, Ain Shams University, 38 Abbassia, Cairo-Egypt 11566.

Accepted 07 November, 2013

Diaper dermatitis (DD) is the most common dermatological disorder in infants. It is frequently secondarily infected with *Candida albicans*. **Objective:** To assess the efficacy and clinical outcome of honey, bees wax and olive oil propolis extract mixture and Nystatin cream as treatment regimen in diaper dermatitis. **Methods:** A total of 76 infants with diaper dermatitis were randomly treated with either Honey mixture (n=37) or Nystatin cream (n=39). Symptom Score (SS) was assessed at base line before treatment, at 5 and 10 days after treatment. *Candida* culture was done before treatment and on the fifth day after treatment. **Results:** Symptom Score was significantly decreased more in Honey mixture than in Nystatin (P=0.04), (P=0.001) at 5 and 10 days respectively. At 10 days after treatment, Honey mixture showed statistically significant higher proportion of complete recovery (94.6%) compared with Nystatin (64.1%) (P<0.002). Microbiological cure rate was 100% with Nystatin, while 72.4% with Honey mixture (P=<0.001). **Conclusion:** Honey mixture was superior to Nystatin in recovery of symptoms at 10 days. Honey mixture might be used alone or as adjuvant therapy in treatment of Diaper Dermatitis in infants.

Key words: Diaper dermatitis, infants, honey, olive oil, nystatin.

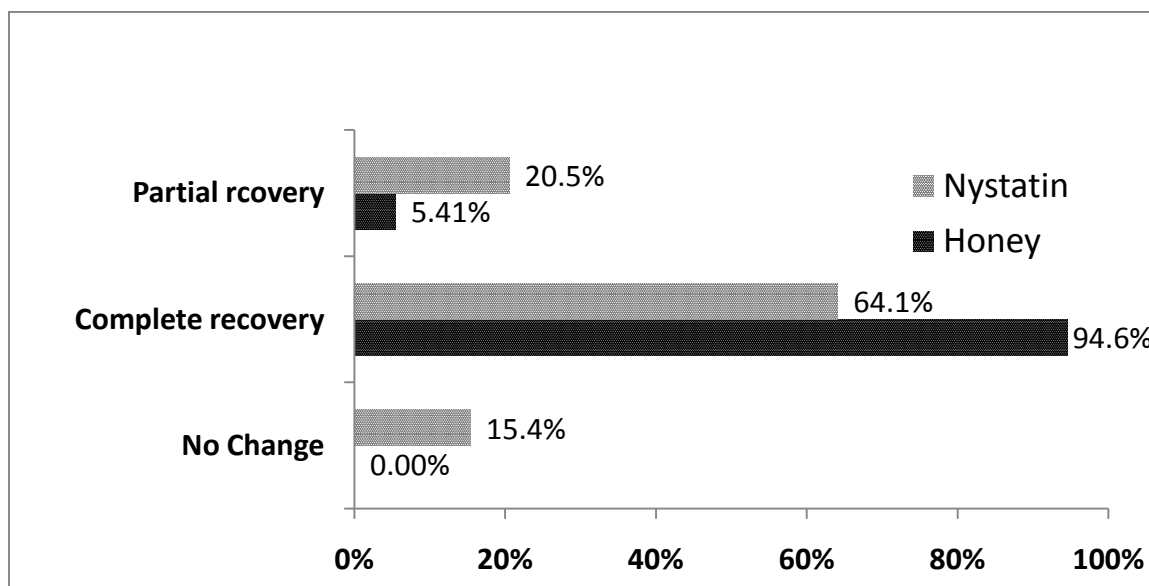
INTRODUCTION

Diaper dermatitis (DD) is one of the most common skin disorders of infants and toddlers (Ravanfar et al., 2012). The prevalence is estimated to be between 7 and 35%. The greatest frequency occurs between 9 and 12 months of age (Visscher and Chatterjee, 2000). Irritant diaper dermatitis (IDD) is characterized by confluent and brilliant erythematous lesions that vary in intensity with time (Hoeii et al., 2011). Four factors have been associated with the occurrence of diaper rash including; wetness of the skin, which reduces the ability to withstand frictional factors; elevated pH, which decreases normal skin micro flora and increases activity of fecal proteases; fecal enzymes (especially proteases and lipases) which along with moisture lead to maceration of the skin and increase permeability to bile salts that worsen the inflammation and;

micro-organisms. *Candida albicans* is the most important micro-organism found on the skin of infants with diaper rash. It can cause a primary infection or be a secondary invader (Kamat et al., 2010).

Among honey benefits are its anti-inflammatory (Al Waili and Boni, 2003), antioxidant (Frankel et al., 1998) and antimicrobial effects (Gheldo and Engeseth, 2002; Gross et al., 2004). The mechanism of antimicrobial actions of honey has not been fully defined, although acidity, osmolality and hydrogen peroxide production have been proposed as critical factors (Al Waili, 2004a). Honey is quite acidic, its pH being between 3.2 and 4.5, which is low enough to be inhibitory to many pathogens (Molan, 1992). The anti-inflammatory effect of honey may be due to its effect on lowering prostaglandin concentration (Steinberg et al., 1996). The honey antioxidant effect is due to honey polyphenols (Molan, 1997). Olive oil is a source of at least 30 phenolic compounds. The major phenolic compounds in olive oil are oleuropein, hydroxytyrosol and tyrosol. These showed

*Corresponding author. Email: drasakka@ymail.com

Figure 1. Recovery status 10 days after treatment.

strong antioxidant activity (Tuck and Hayball, 2002). Bees create propolis, a natural resin to build their hives. Studies indicate that propolis may show powerful local antibiotic (Oris et al., 2005), antifungal properties (Gregory et al., 2002) and immune-modulatory effect (Bratter et al., 1999).

The aim of this study was to evaluate the effectiveness of topical application of a mixture of honey, bees wax and olive oil propolis extract as natural products in diaper dermatitis in infants. The study also compared the efficacy of the mixture with Nystatin cream with regards symptom clearance at 5 and 10 days, the microbiological cure rates of the mixture versus Nystatin by comparing the results of fungal culture before and after treatment and the adverse effects of both treatment methods.

Subjects and Methods

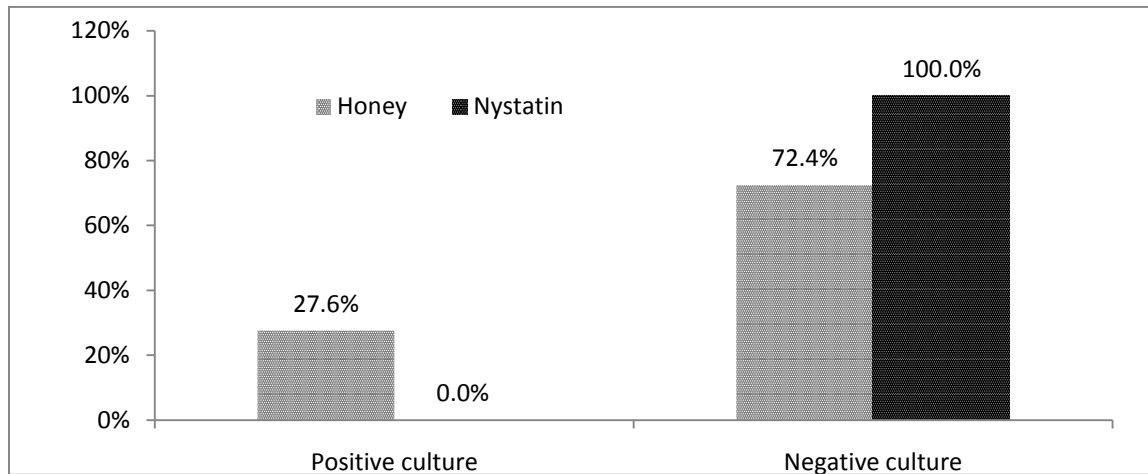
This study included 78 infants diagnosed with diaper dermatitis. We conducted a prospective randomized controlled study with either a mixture of honey, bees wax and olive oil propolis extract in proportion of (4:1:2) or Nystatin cream. Exclusion criteria were concomitant skin diseases as psoriasis, allergic contact dermatitis, anorectal warts and diagnoses of immunodeficiency diseases. Inclusion criteria were infants aged between one month and two years, hospitalized, presence of inflammation characterized by erythema and rash involving the diaper area, diaper dermatitis less than one week and no previous treatment had been started for diaper dermatitis.

The mixture was prepared for topical application using raw

poly floral honey. It was supplied directly from a beekeeper without heating or irradiation from El Mahala, Gharbia Governorate, Egypt. Virgin oil was provided from Marsa Matroh, Egypt. While the propolis was a raw green Brazilian propolis. Mothers were instructed to wash the diaper area with warm water at the time of diaper change. They were instructed to apply either Honey mixture paste or Nystatin cream to the affected diaper area according to the infant's assigned treatment group. Treatment was applied liberally (2mm thick) to the affected area after each diaper change or at least four times per day until clinical cure with a maximum of 10 days.

Mothers could not be blinded to the type of treatment because the Honey mixture paste was in small sealed containers. While the Nystatin cream was in the manufacturer's aluminum tubes. The nurse in charge supervised the application of the treatment. The dermatitis was given a 5-point scale at base line before treatment and on days 5 and 10. Zero score: no erythema. Scores 1-4 were given as follows 1-mild erythema, with minimal maceration and/or chafing; 2-moderate erythema with or without satellite papules with maceration and chafing, 3-Severe erythema with papulopustules and maceration, 4-Extreme erythema with erosions or ulceration.

BIO CULT AMIES+charcoal swabs (by liofilchem Bacteriology Products, Italy) were used for Candida culture before treatment has started and on the fifth day of treatment. Moistened swabs from diaper lesions were inoculated on the selective mycological medium "Sabourad glucose agar" and were incubated at 37C for two days. Any growth on plates was identified by colonial

Figure 2. Candida Culture 5 days after treatment.**Table 1.** Clinical Recovery at 5 and 10 days after treatment.

	Honey Mixture		Nystatin cream		X2	P-value
	N	%	N	%		
5 Days after treatment						
No Change	2	5.41%	9	23.08%		
Complete recovery	27	72.97%	21	53.85%		
Partial recovery	8	21.62%	9	23.08%	5.214	0.0740
10 days after treatment						
No Change	0	0.00%	6	15.38%	11.168	0.0020
Complete recovery	35	94.59%	25	64.10%		
Partial recovery	2	5.41%	8	20.51%		

morphology. Subsequent identification of *Candida albicans* was done by Gram stain showing gram positive oval budding yeast cells and pseudohyphae. Germ tube test was also performed to identify *Candida albicans*. Approval was obtained from the Ethics Committee of Ain Shams University Medical School. All parents signed a written informed consent prior to enrollment in the study. The authors have no conflicts of interest to declare. There were no external sources of funding for the study.

Statistical Analysis

Quantitative data were presented as mean and standard deviation. Independent t-test and repeated measurement ANOVA were used to test the hypothesis of equal means. Categorical data were presented as count and proportion. Chi-square and Fisher exact test were used to compare independent proportions and McNemar's test to compare

paired dichotomous observations. P value was considered significant if <0.05 .

RESULTS

The mean age of infants in the Honey mixture group (N=37) was 8.1 ± 4.4 months while that of the Nystatin group (N=39) was 8.6 ± 4.3 (P=0.670). In the Honey mixture group, 19 out of 37 (51.4%) were males compared to 19 out of 39 (48.7%) in the Nystatin group (P=0.818). Two cases of the Honey mixture group were withdrawn because the mothers considered its odor unpleasant.

At 5 days after treatment, no statistically significant difference between both groups regarding recovery of symptoms (P=0.074) Table 1. At 10 days after treatment, the Honey mixture group showed a statistically significant higher proportion of complete recovery (94.6%) compared to the Nystatin group (64.1%) (P=0.002) Figure 1.

Table 2. Symptom Score (SS) before, 5 days and 10 days after treatment.

	Groups				T test	P value
	Honey mixture		Nystatin cream			
	Mean	SD	Mean	SD		
SS Before	1.73	0.73	1.49	0.68	1.494	0.139
SS 5days	0.32	0.58	0.67	0.81	2.13	0.04
SS 10days	0.05	0.23	0.46	0.68	3.53	0.001

Although there was no statistically significant difference in symptom score between the two groups before the start of treatment, Honey mixture was superior to Nystatin cream in the drop of SS at 5 days ($P=0.04$) and 10 days ($P=0.001$) Table 2.

Comparing the effect of treatment on culture results, the cure rates were 72.4% for the Honey group ($P<0.001$) compared with 100% observed with Nystatin treatment group ($P<0.001$). However, comparing the rate of culture cure in both treatment groups, it appeared that the Nystatin group was superior ($P=0.005$) Figure 2.

DISCUSSION

Diaper dermatitis (DD) is one of the most common cutaneous diagnoses in infants. It can cause significant discomfort and predisposes infants to secondary infection (Ravanfar et al., 2012). Honey, olive oil and beeswax mixture have been tried before on 12 infants with satisfactory results and no adverse effects (Al Waili, 2004b). In that pilot study, symptom score significantly decreased at 3 and 5 days ($P<0.05$). Eradication of candida was observed in 2 out of 4 patients with positive culture. Our results support the observation of Wailli's study, 2004b. It also shows better complete recovery of symptoms at ten days when compared with Nystatin. The symptomatic improvement after use of Honey mixture could be explained by the anti-inflammatory effects of the mixture, based on the properties of the ingredients. Honey mixture could inhibit the growth of Staph aureus and Candida albicans in vitro (Al Waili, 2005). Natural honey showed antimicrobial activity when applied to infected surgical wounds in rats. It reduced redness, swelling, time to complete healing and time for eradication of bacterial infection due to Staph aureus or Klebsiella species. Its potency was comparable to that of local antibiotics (Al Waili, 2004c). The antioxidant activity of hydroxytyrosol and oleuropein in olive oil had been investigated in humans with favorable results (Saijia et al., 1998). They also showed antimicrobial activity in vitro against several bacterial strains (Bisignano et al., 1999).

Historically, propolis was used in Greece to treat abscesses while the Egyptians used it for mummification. Today, propolis is commonly found in chewing gum, cosmetics, lozenges and skin creams (Medline plus, 2013). A Brazilian commercial ethanol propolis extract was found to inhibit oral candidiasis (Santis et al., 2005).

Honey and similar honey mixture showed faster healing in chemotherapy induced oral mucositis (Abdulrhaman et al., 2012). Hoegar et al. (2010) compared the efficacy and safety of clotrimazole and Nystatin pastes in infants with diaper dermatitis. Microbiological cure was 100% for both agents. This is in concordance with our results as Nystatin showed 100% microbiological cure while only 64.1% clinical cure at 10 days after treatment. Adding this mixture of honey, beeswax and olive oil to the standard therapy of diaper dermatitis might be useful. Because all the constituents are natural, this treatment could be an alternative to pharmacological creams or corticosteroid use in DD. Safety of the mixture was noticed. The unpleasant odor might be improved upon if managed pharmaceutically.

REFERENCES

- Abdulrhaman M, El Barbary NS, Ahmed Amin D, Saeid Ebrahium R (2012). Honey and a mixture of honey, beeswax and olive oil–propolis extract in treatment of chemotherapy–induced oral mucositis: a randomized controlled pilot study. *Pediatr. Hematol. Oncol.* 4: 29 (3): 285-92.
- Al Waili NS, Boni NS (2003). Natural honey lowers plasma prostaglandin concentration in normal individuals. *J. Med. Food.* 6 (2): 129-133.
- Al Waili N (2004a). Topical application of honey olive oil and bees wax in patients with tineaversicolor, Tineacuris and tineacorporis. *Compl. Therapy Medical.* 12: 45-47.
- Al Waili NS (2004b). Clinical and mycological benefits of topical application of honey, olive oil and beeswax in diaper dermatitis. *Clin. Microbiol. Infect.* 11 (2): 160-163.
- Al Waili NS (2005). Mixture of Honey, Beeswax and Olive oil inhibits Growth of Staphylococcus aureus and Candida albicans. *Arch. Med. Res.* 36: 10-13.

- Al Waili NS (2004c). Investigating the antimicrobial Activity of Natural Honey and Its Effects on Bisignano G, Tomaino A, Lo Cascio R, Crisafi G, Uccella N, Saija A (1999). In vitro antimicrobial activity of oleuropein and hydroxytyrosol. *J. Pharm. Pharmacol.* 31: 971-974.
- Bratter C, Tregel M, Liebenthal C, Volk HD (1999). Prophylactic effectiveness of propolis for immunostimulation: a clinical pilot study. *ForschKomplementar Med.* 10: 6 (5): 255-60.
- Frankel S, Robinson GE, Berenbaum MR (1998). Antioxidant capacity and correlated characteristics of 14 unifloral honeys. *J. Apic Res.* 37 (1): 27-31.
- Gheldof N, Engeseth NJ (2002). Antioxidant capacity of honey from various floral sources based on the determination of oxygen radical absorbance capacity and inhibition of in vitro lipoprotein oxidation in human serum samples. *J. Agric. Food Chem.* 50 (10): 3050-3055.
- Gregory SR, Piccolo N, Piccolo MS, Heggors JP (2002). Comparison of propolis skin cream to silver sulfadiazine: a naturopathic alternative to antibiotics in treatment of minor burns. *J. Altern. Complem. Med.* 8 (10): 77-83.
- Gross H (2004). Effect of honey consumption on plasma antioxidant status in human subjects.com. Abstract presented at American Chemical Society. March 29. www.honey.com
- Hoeger PH, Stark S, Jost G (2010). Efficacy and safety of two different antifungal pastes in infants with diaper dermatitis: a randomized, controlled study. *J. Eur. Acad. Dermatol. Venereol.* 24: 1094-1098.
- Hoeii KA, Prossick TA, Levy ML, Dtutz JE, Corona R (2011). Over review of diaper dermatitis in infants and children. www.uptodate.com accessed on April 28, 2013.
- Kamat Adam HM, Cain KK, Campbell DE, Holston AM, Kelleher KJ, Leu MG, McInerney TK, Soghier LM, Wolraich ML, Wood BP (2010). Quick Reference Guide Pathogenic Bacterial Infections of Surgical Wounds and Conjunctiva. *J. Med. Food.* 7 (2): 210-222.
- to Pediatric Care. Elk Grove Village, Illinois. American Academy of Pediatrics Diaper Rash. 334-338.
- Medline Plus (2013). Drugs and Supplements. A service of the U.S. National Library of Medicine and the National Institutes of Health. www.nlm.nih.gov/medlineplus/druginfo/natural/patient-propolis. Accessed on May 5, 2013.
- Molan PC (1992). The antibacterial activity of honey. 1- The nature of the antibacterial activity. *Bee World* 1992: 73 (910): 5-28. Variation in the potency of the antibacterial activity. *Bee world* 1992: 73 (2): 59-76.
- Molan PC (1997). Honey as antimicrobial agent. In *Bee Products: Properties, Applications and Apitherapy.* 27-37.
- Oris RO, Sforcin JM, Rall VLM, Funari SRC (2005). Susceptibility profiles of Salmonella against the antibacterial activity of Propolis produced in two regions of Brazil. *J. Venom Anim. Toxins Trop. Dis.* 11 (2): 109-16.
- Ravanfar P, Wallace JS, Pace NC (2012). Diaper dermatitis: a review and update. *Curr. Opin. Pediatr.* 8 (24): 472-479.
- Saija A, Trombetta A, Tomaino A, Cascio R (1998). In vitro evaluation of the antioxidant activity and biomembrane interaction of the plant phenols oleuropein and hydroxyl-tyrosol. *Int. J. Pharmaceut.* 166: 123-133.
- Santis VR, Pimenta FJ, Aguiar SM (2005). Oral candidiasis treatment with Brazilian ethanol propolis extract. *Phytother Res.* 19 (7): 652-4.
- Steinberg D, Kaine G, Gedallia (1996). Antibacterial effect of propolis and honey on oral bacteria. *Am. J. Dent.* 9 (6): 236-239.
- Tuck KL, Hayball PJ (2002). Major phenolic compounds in olive oil: metabolism and health effects. *J. Nutri. Biochem.* 13: 636-644.
- Visscher MO, Chatterjee R (2000). Diaper dermatitis in the newborn. *Ped. Dermatol* 17: 52