

## THE EFFECT OF HONEY SUPPLEMENTATION ON APHTHOUS ULCERS IN EGYPTIAN CHILDREN

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### ABSTRACT:

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**Background:** Aphthous ulcers are the most common oral lesions among children. These lesions are usually recurrent, painful, and interfere with eating and drinking ability. Honey, as a natural product of honey bees, is a well-known wound/ulcer healer.

**Aim of work:** To test the effect of honey supplementation on the recovery time of aphthous oral ulcers in a group of Egyptian children.

**Patients and Methods:** This was a randomized case control clinical study, conducted on 50 children recruited from the outpatient clinic of pediatric hospital of Ain Shams University. All patients were subjected to history taking especially as regards the onset and duration of oral lesions; physical examination especially the number of oral lesions. The pain severity was assessed by the pain score (VAS-10), the number of daily doses of acetaminophen and the eating and drinking ability. All patients were tested for blood HSV1 IgM. Patients were divided into 2 groups; each consisted of 25 patients; Group (A), in which the patients received honey; both orally and topically, in addition to acetaminophen as a pain killer, and Group (B), who received only acetaminophen. Follow up of patients was done every other day until complete healing.

**Results:** Aphthous stomatitis was more common among males, and HSV1 IgM was positive in only 6% of the patients. The recovery time, defined as the time interval, in days, between the start of treatment and complete healing, with no pain, no fever, no drooling and no eating or drinking difficulty, was significantly shorter in the honey treated group (A) [mean  $\pm$  SD = 8.72  $\pm$  0.61 days], as compared to the no-honey (control) group (B) [mean  $\pm$  SD = 12.84  $\pm$  1.62 days] ( $P=0.000$ ). None of the patients in the honey group reported any adverse effect to honey supplementation.

**Conclusion:** Honey was found to be an effective and safe therapeutic agent in the treatment of aphthous stomatitis in a group of children suffering from aphthous oral ulcers.

**Keywords:** honey, aphthous, ulcers, stomatitis, children

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### INTRODUCTION:

One of the most common oral cavity painful lesions is Aphthae (cancer sores) which were first mentioned by Hippocrates (460–370 BC), who used the term “aphthai”<sup>(1)</sup>. Aphtha is defined as a round

abrasion or ulceration of oral or (genital) mucosa of a 2-to 5-mm diameter. Lesions are usually covered by a fibrinous pseudo-membrane, may be single or multiple, and usually resolve in 10-15 days, but generally recur. Lesions are painful and are often exacerbated by food intake<sup>(2)</sup>.

Aphthous ulcers affects as many as 25% of the population worldwide<sup>(3)</sup>. However, the incidence varies from 5% to 50% depending on the ethnic and socioeconomic groups studied. The onset of recurrent aphthous stomatitis (RAS) usually peaks between the ages of 10 and 19 years in children of high socioeconomic status and decreases in frequency with advancing age, geographic location or sex. RAS prevalence was found to be higher in females, among professional school students than in the same subjects 12 years later when they had become practicing professionals<sup>(4)</sup>.

The specific etiology of RAS is unknown. Many factors combined together may lead to its development in each patient. Regardless, the etiology of RAS is multi-factorial and may be related to trauma, nutritional deficiency, allergy, altered immune response, infection, stress<sup>(5)</sup> or imbalanced composition of the oral microbiota<sup>(6)</sup>. The lack of clear understanding of the etiology of RAS hinders the efficient treatment of this disease<sup>(7)</sup>.

Several topical medications with distinct mechanisms are used in managing RAS lesions<sup>(8)</sup>. Local anesthetics (lidocaine, benzocaine, polidocanol) have a benefit in pain relieve. It is particularly important in children when painful lesions may lead to eating difficulties and dehydration. Possible application forms are solutions, gels, and adhesive pastes<sup>(9)</sup>. Also, based on the immunologic nature of RAS, topical steroids may often control RAS. Steroids act on the lymphocytes and alter the response of effector cells to precipitants of immunopathogenesis<sup>(10)</sup>. Systemic treatment, including immunomodulatory drugs such as corticosteroids, dapsone, colchicine, tetracycline, thalidomide or biologic agents (such as TNF- $\alpha$  inhibitors) is indicated for severe and recurring ulcerations when topical management is not sufficient.<sup>(11)</sup>

Recently, researchers attention is drawn to honey to be used as a natural alternative medicine produced by honey bees.<sup>(12)</sup> Research denotes it as a novel antioxidant agent,

exhibits a broad-spectrum therapeutic properties such as anti-inflammatory, antibacterial, antimutagenic, expedite wound healings, antidiabetic, antiviral, antifungal, and anti-tumoral effects<sup>(13)</sup>. Honey is an excellent accelerator of ulcer healing and has therapeutic effect in the treatment of mucosal ulcers<sup>(14)</sup>. Honey decreases herpetic pain and the use of analgesics and improves the ability to eat and drink<sup>(15)</sup>.

The healing effect of honey on recurrent aphthous stomatitis is ascribed to its anti-microbial<sup>(16,17)</sup>, wound healing<sup>(18)</sup>, anti-inflammatory<sup>(19,20)</sup>, anti-oxidant<sup>(21)</sup>, immunomodulatory<sup>(22,23)</sup> and pre- and probiotic effects<sup>(24)</sup>. The anti-microbial effects of honey are due to its acidity (pH being 3.2 – 4.5), osmolarity, peroxidal and non-peroxidal factors. Also, honey contains kynurenic acid<sup>(25)</sup>, which has anti-nociceptive action. Application of honey was effective in reducing ulcer size, pain, in encouraging healing and reducing the recurrence of aphthous ulcerations<sup>(26)</sup>. Also, revascularization, where new blood vessels returned to the damaged tissue, when treated with honey was unexpectedly faster<sup>(27)</sup>. It results from honey's high osmotic pressure, which dehydrates tissue edema and holds the wound edges together, and by the existence of hydrogen peroxide, which stimulates the growth of epithelial cells<sup>(28)</sup>. Honey gel was more effective in causing healing as it is absorbed systemically.<sup>(27)</sup>

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## **AIM OF THE WORK:**

This study aimed to assess the effect of honey supplementation (oral intake and topical application) on the recovery time of aphthous ulcers in a group of Egyptian children.

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## **PATIENTS AND METHODS:**

This was a randomized case control clinical study, conducted in the outpatient clinic of pediatric hospital of Ain Shams University

during the period from January 2020 and January 2021. The study included 50 previously healthy children, aged 5 to 12 years and presented with aphthous mouth ulcers. Children suffering from diabetes mellitus were excluded.

### **Study tools:**

All patients were subjected to the following during the first visit (day 0):

#### **1-History taking:**

- a) **Complete medical history, including** age; sex; history of diseases that may cause oral ulcers. Drug history, with special emphasis on drugs that may cause oral ulcers, and family history of recurrent aphthous ulcers were also taken.
- b) **All the details of the oral ulcers including**, onset, number, size, duration, recurrence rate, associated pain or discomfort and the effect on oral intake.

#### **2- Clinical Examination:**

- a) Clinical examination, including vital signs (pulse, respiratory rate, blood pressure and temperature).
- b) Anthropometric measures, including body weight, height and body mass index (BMI)
- c) Oral ulcers and the degree of oral lesions severity:

The severity of oral lesions was classified into:

A- Mild (up to 10 lesions on the tongue or oral mucous membrane)

B- Moderate (11 to 20 lesions with swelling of the gums)

C- Severe (> 20 on the tongue or oral lesions and gum lesions)<sup>(29)</sup>.

#### **d) Pain was assessed through**

##### **1) Wong-Baker FACES pain scale:**

Facial Expressions Grading Scale was developed by Donna Wong and Connie Morain Baker in 1981 and was revised in

1983. There are six facial expressions on the scale. The lowest score is 0 while the highest one is 5. While applying the scale; the state of having no pain is expressed with a happy face while those who feel a bit pain or quite painful express themselves with a sad face: face 0 means so happy and have no pain, 1 means Got a bit pain, 2 means got a bit more pain, 3 means the pain is denser, 4 means got quite a lot pain, 5 means got the highest pain you could imagine. Then the child is told to pick the face that expresses his/her pain<sup>(30)</sup>. It combines pictures and numbers to enable the user to rate pain. It can be used for children over the age of 3.<sup>(31)</sup>

##### **2) Visual analogue scale VAS**

Using a visual analogue scale (VAS) [Figure 1] is easy to use and reliable. It can be used in all age groups from 5 years old, who know numbers<sup>(32)</sup>. The subjects were instructed how to point to the position on the line between faces to indicate how much pain they might feel. In this system the total scores range on the line between faces to indicate how much pain they might feel. In this system the total scores range from 0 to 100 based on measuring the distance in millimeters from the left end bar to mark made by the child on the 10 cm line anchored by happy to sad faces, with a higher score indicating more severe pain<sup>(33)</sup>.

e) **Ability to eat and drink** was classified as normal or subnormal with difficult eating and drinking.

f) **The number of acetaminophen doses** taken daily to reduce pain.

g) **Duration of fever** after starting of treatment.

**3-Laboratory tests: All done at baseline before the onset of the study.** Tests included: Herpes Simplex type 1 (HSV-1) IgM in the blood, Complete blood picture with differential, CRP and Erythrocyte Sedimentation Rate (ESR).

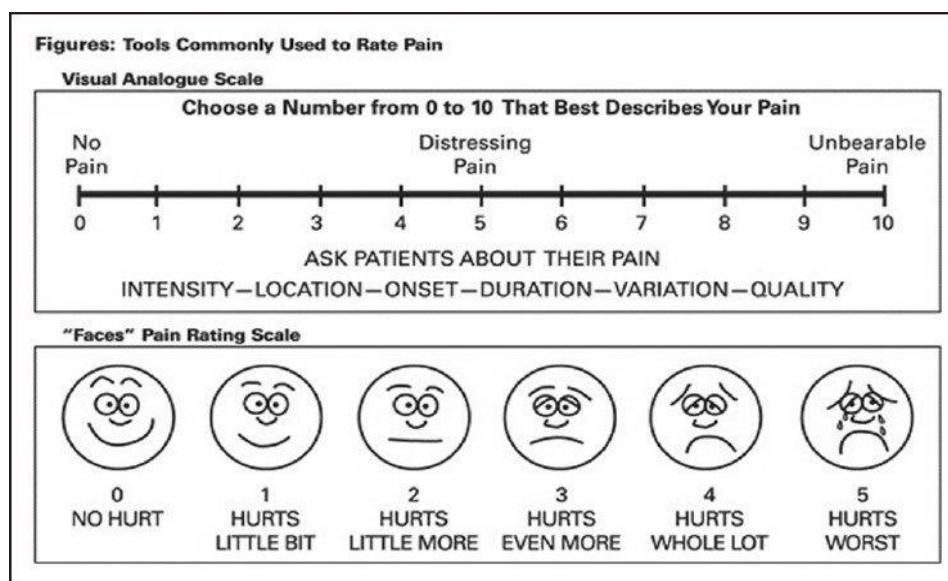


Figure (1): Visual analogue scale (VAS) for assessment of children’s pain perception<sup>(33)</sup>.

**Honey used in the study:**

The honey used in this study was a raw, unprocessed Clover honey supplied by a beekeeper from El Gharbia Governorate, Egypt. The honey was kept in well-sealed containers away from light until the time of use. This honey was subjected to physicochemical analysis in the laboratories of the Ministry of Health and Population, Egypt. The honey had a pH of 1.5; moisture content of 19%, a sucrose content of 4.5g/100g. Negative detection of dextrin, commercial glucose, industrial invert sugar, added sucrose and starch. The Hydroxy methyl furfuraldehyde (HMF) content was 23.02 mg/kg. Values of HMF less than 40 mg/kg indicate fresh honey not exposed to heat. Microscopic examination of samples from honey confirmed the presence of pollen grains, which were mainly of Clover (*Trifolium alexandrinum*).

Patients were divided into two groups through a computer randomization system called research randomizer on web, and divided into two equal groups; each group consisted of 25 patients.

- **Group A (25 children):** children of this group (honey group) received 10 ml undi-

luted honey three times daily, with an interval of 2 hours. The first 3 ml of the 10 ml honey were topically applied over the ulcers, then after 2 minutes the remaining 7 ml were swallowed by the patient.

- **Group B (25 children):** children of this group (control group) didn’t receive honey.

Parents of all patients of both groups were asked to give acetaminophen to their children in a dose of 15 mg/kg/dose every 6 hours as needed according to patient's need and degree of pain.

**All patients were assessed every other day until recovery:**

In every visit the following was reassessed as before:

- 1) Oral ulcers and the degree of oral lesions severity.
- 2) Pain thorough Wong-Baker FACES pain scale and Visual analogue scale (VAS-10).
- 3) Eating and drinking ability.
- 4) The numbers of acetaminophen doses.
- 5) Duration of fever.

**Estimation of recovery time:**

Recovery time is defined as the time interval, in days, between the start of treatment and complete healing, with no pain, no fever, no drooling and no eating or drinking difficulty.

**Ethical Considerations:**

An informed verbal consent was obtained from the parents before enrollment in the study according to the Faculty of Medicine, Ain Shams University Research Ethical Committee. The participants had the right to withdraw from the study at any time.

**Statistics Analysis:**

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean ±standard deviations and ranges when their distribution was parametric, and median, inter-quartile range (IQR) when data were non-parametric. Also, qualitative variables were presented as numbers and percentages.

The comparison between groups with qualitative data was done by using the *Chi-*

*square test* and *Fisher exact test* instead of the Chi-square only when the expected count in any cell found less than 5.

The comparison between two groups with quantitative data and parametric distribution was done by using an *independent t-test* while non-parametric distribution was done by using *the Mann-Whitney test*.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:

P > 0.05: Non significant

P < 0.05: Significant

P < 0.01: Highly significant

**RESULTS:**

The flowchart (**Fig 2**) shows that 55 patients were enrolled in the study. Five were excluded because they didn't meet inclusion criteria. Each group included 25 patients; group A (honey) and group B (control). No one lost to follow up or discontinued the intervention.

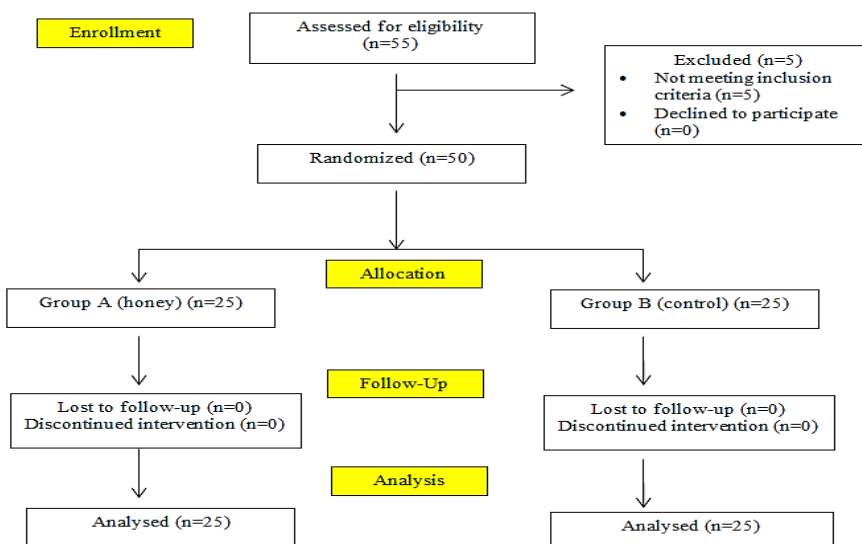


Figure 2: Flow chart

Baseline characteristics of study groups regarding the age, sex and anthropometric measures did not show significant difference between the honey and control groups ( $P>0.05$ ). Age ranged between 4 to 11 years with a mean  $\pm$ SD (7.08 $\pm$ 2.43) in the honey group; and ranged between 4 to 12 years with a mean  $\pm$ SD (7.64 $\pm$ 2.74) in control group. Regarding the baseline laboratory results, all patients of both groups had normal platelet count although there was a statistically significant difference between groups. All other laboratory results did not show significant difference between the honey and control

groups ( $P>0.05$ ). The prevalence of HSV 1 in both groups (50 patients) was 6%, with no statistically significant difference between groups.

Table 1 and 2 shows that on day 0 (at presentation) and on day 3 the characteristics of mouth ulcers, including the ulcer duration, pain score, number of acetaminophen doses, severity of oral ulcerative lesions and eating and drinking ability did not differ significantly between the honey and control groups ( $P> 0.05$ ).

Table 1: Descriptive characteristics of mouth ulcerative lesions at presentation (day 0)

Measure	Honey group (no. = 25)	Control group (no. = 25)	Test value	P
Ulcer duration (days) Median (IQR) Range	2 (2 – 3) 0 – 4	2 (1 – 3) 0 – 4	-0.449 <sup>#</sup>	0.654
Pain score (VAS-10) Median (IQR) Range	7 (6 – 7) 5 – 8	6 (6 – 7) 5 – 8	-0.863 <sup>#</sup>	0.388
Number of pain killer doses/day Median (IQR) Range	3 (3 – 4) 3 – 4	3 (3 – 4) 3 – 4	-0.865 <sup>#</sup>	0.387
Lesion severity [no (%)] Mild Moderate Severe	2 (8%) 14 (56%) 9 (36%)	3 (12%) 12 (48%) 10 (40%)	0.406 <sup>*</sup>	0.816
Eating and Drinking Normal Difficult	0 (0.0%) 25 (100.0%)	0 (0.0%) 25 (100.0%)	–	–

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Table 2: Descriptive characteristics of mouth ulcerative lesions on day 3

Measure	Honey group (no. = 25)	Control group (no. = 25)	Test value	P
Pain score (VAS-10) Median (IQR) Range	5 (5 – 6) 3 – 7	6 (5 – 6) 3 – 7	-1.886 <sup>#</sup>	0.059
Number of acetaminophen doses/day Median (IQR) Range	3 (3 – 3) 2 – 4	3 (3 – 3) 2 – 4	--1.363 <sup>#</sup>	0.173
Lesion severity [no (%)] Mild Moderate Severe	4 (16%) 16 (64%) 5 (20%)	3 (12%) 13(52%) 9 (36%)	1.596*	0.450
Eating and Drinking Normal Difficult	4 (16.0%) 21 (84.0%)	3 (12.0%) 22 (88.0%)	0.166*	0.684

Table 3 shows statistically significant difference between the honey and control groups as regards the pain score (VAS-10), number of acetaminophen doses, lesion severity and eating and drinking ability in day (5). There was a significant more decrease in

pain score (VAS-10), number of acetaminophen doses ,lesion severity and eating and drinking difficulties with P-values of 0.006, 0.019,0.001 and 0.004, respectively in the honey group than the control group.

Table 3: Descriptive characteristics of mouth ulcerative lesions on day 5

Measure	Honey group (no. = 25)	Control group (no. = 25)	Test value	P
Pain score (VAS-10) Median (IQR) Range	3 (2 – 3) 1 – 5	4 (2 – 5) 1 – 5	--2.746 <sup>#</sup>	0.006
Number of acetaminophen doses/day Median (IQR) Range	2 (1 – 2) 1 – 3	2 (1 – 3) 1 – 4	-2.343 <sup>#</sup>	0.019
Lesion severity [no (%)] Mild Moderate Severe	16 (64%) 8 (32%) 1 (4%)	6 (24%) 6 (24%) 13 (52%)	15.117*	0.001
Eating and Drinking Normal Difficult	19 (76.0%) 6 (24.0%)	9 (36.0%) 16 (64.0%)	8.117*	0.004

Table 4 also shows a highly statistically significant difference between the honey and control groups regarding all the descriptive

characteristics of mouth ulcerative lesions on day 7, being less in the honey group (P<0.01).

Table 4: Descriptive characteristics of mouth ulcerative lesions on day 7

Measure	Honey group (no. = 25)	Control group (no. = 25)	Test value	P
Pain score (VAS-10) Median (IQR) Range	1 (0 – 1) 0 – 3	2 (1 – 3) 0 – 4	-2.710 <sup>#</sup>	0.007
Number of acetaminophen doses/day Median (IQR) Range	1 (0 – 1) 0 – 2	1 (1 – 2) 0 – 2	-2.956 <sup>#</sup>	0.003
Lesion severity [no (%)] Mild Moderate Severe	21 (84%) 4 (16%) 0 (0%)	10 (40%) 10 (40%) 5 (20%)	11.475*	0.003
Eating and Drinking Normal Difficult	24 (96.0%) 1 (4.0%)	12 (48.0%) 13 (52.0%)	14.286*	0.000

Table 5 shows a comparison between the honey and control groups as regards the time to recovery of different symptoms. Although the median duration of fever in both groups was 2 days, with no statistically significant

difference between groups (P = 0.07), the ulcers, the pain, the drooling and the eating and drinking difficulty disappeared more faster in the honey group (P <0.01).

Table (5): Comparison between the honey and control groups as regards the time to recovery of different symptoms.

Time to recovery		Honey group	Control group	Test value	P-value	Sig.
		No. = 25	No. = 25			
Fever (days)	Median (IQR)	2 (1 – 2)	2 (2 – 3)	-1.809 <sup>#</sup>	0.070	NS
	Range	1 – 3	1 – 4			
Oral ulcers (days)	Median (IQR)	3 (3 – 4)	7 (4 – 8)	-3.116 <sup>#</sup>	0.002	HS
	Range	1 – 8	1 – 12			
	Range	1 – 6	1 – 11			
Drooling (days)	Median (IQR)	3 (2 – 3)	5 (3 – 7)	-2.951 <sup>#</sup>	0.003	HS
	Range	1 – 5	1 – 10			
Eating & Drinking difficulty (days)	Median (IQR)	3 (3 – 4)	7 (4 – 8)	-3.116 <sup>#</sup>	0.002	HS
	Range	1 – 8	1 – 12			



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As for the recovery time, which is defined as the time interval in days, between the start of treatment and complete healing, with no pain, no fever, no drooling and no eating

or drinking difficulty, there was a highly statistically significant difference between the honey and control groups, being much less in the honey group ( $P < 0.0001$ ) as shown in Table 6.

Table 6: Recovery time (days) in the honey and control groups.

	Honey group (no. = 25)	Control group (no. = 25)	Test value	P
Recovery time (days)				
Mean $\pm$ SD	8.72 $\pm$ 0.61	12.84 $\pm$ 1.62		
Range	8 – 10	11 – 16	-11.861 <sup>#</sup>	0.000

Figure 3 showed the pain score, as assessed by VAS-10, started to show significant decrease from day 5 in the honey group, as compared to control group ( $P = 0.006$  and

0.007 in days 5 and 7, respectively). In day 3 there was no significant difference between the honey and control groups regarding the pain score.

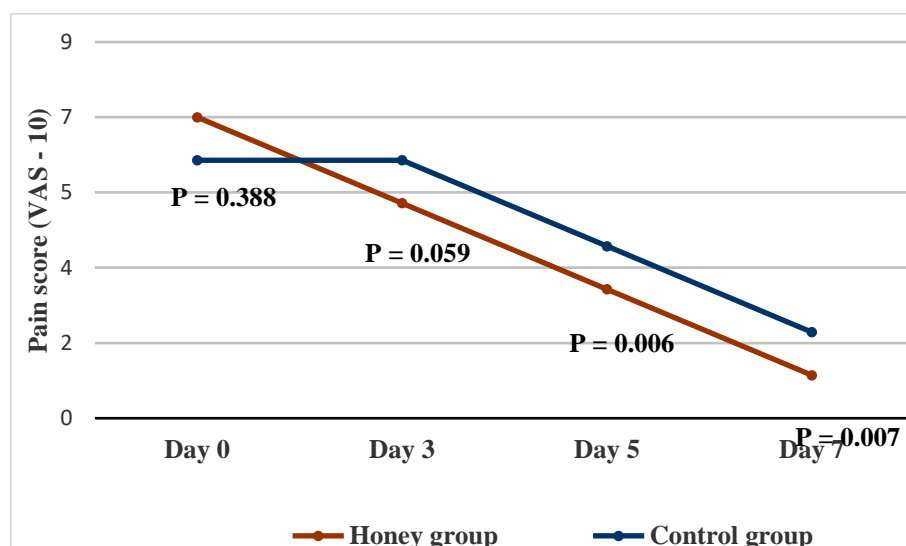


Figure 3: Pain score in the honey and the control groups throughout the period of the study

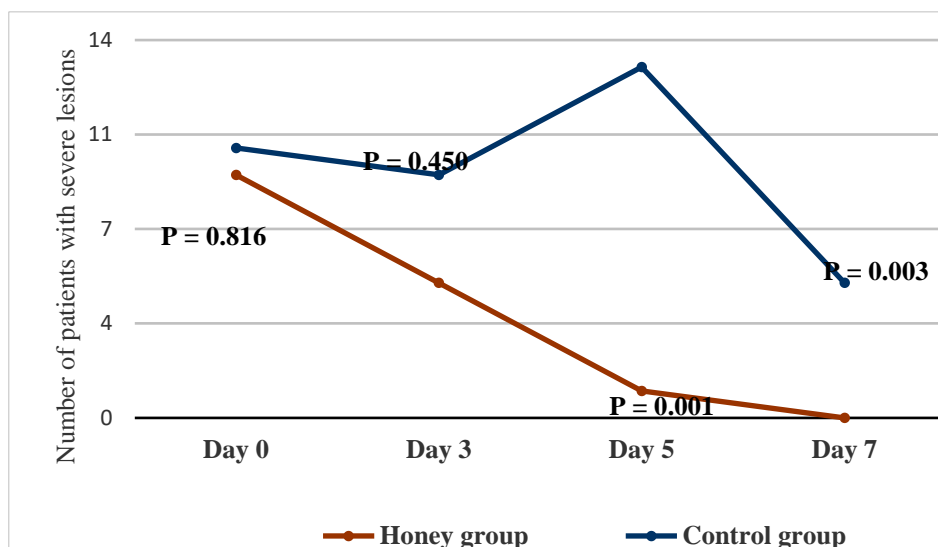


Figure 4: Number of patients with severe oral lesions throughout the period of the study

Figure 4 showed that the number of patients with severe oral lesions started to show significant decrease also from day 5 in the honey group, as compared to control group (P = 0.001 and 0.003 in days 5 and 7, respectively). In day 3 there was no significant difference between the honey and control groups as regards the number of patients with severe lesions.

It should be also mentioned that none of the patients of the honey group reported any adverse reaction related to the use of honey e.g., allergy.

## DISCUSSION:

In the current study we found that aphthous stomatitis was more in males, being 56%. Nearly similar results were obtained in the study of **Cigek et al (2004)** and **Kaur et al (2022)**<sup>(34,35)</sup>, who found the prevalence of aphthous stomatitis was more in males; being 50.2% and 67%, respectively. On the other hand, **Hegde et al (2017)** reported that out of the 72 patients with recurrent aphthous stomatitis, 54.7% were females<sup>(36)</sup>. Also, in **Abdullah et al (2013)** study, out of 282 RAS was ++ more common among females 176 (62.4%) and males 106 (37.58%) with

(p<0.004)<sup>(37)</sup>. **Lo et al (2021)** study also revealed higher percentage among females (55.4%)<sup>(38)</sup>.

In the present study, HSV-1 IgM was positive in only 3(6%) cases. Similarly, **Bharadwaj et al (2022)** found that the prevalence of herpetic ulcers of all recurrent aphthous stomatitis cases was only 5 to 10%.<sup>(39)</sup> Based on these results, the majority of cases of aphthous oral ulcers are not due to herpes simplex virus. Therefore, the empirical use of acyclovir in patients suffering from aphthous stomatitis is not indicated. Acyclovir has a lot of side effects, some of which are considered serious as neuropsychiatric complications like anxiety, hallucination, involuntary movements and depression<sup>(40)</sup>. These side effects should be taken into account before prescribing this drug. Further, the mean recovery time of herpes labialis in the honey group in the study of **Al Waili (2004)** done on 16 patients, was 2.5 days, which was significantly shorter, as compared to patients receiving acyclovir as a treatment; being 5.8 days<sup>(41)</sup>. On the other hand, **Semprini et al (2019)** compared topical New Zealand medical grade kanuka honey (90% honey/10% glycerine) with topical 5% acyclovir for the treatment of herpes simplex labialis, both applied 5 times daily in 952 patients aged 29 to 54

years and suffering from herpes labialis (diagnosed on clinical grounds), and they found no evidence of a difference in efficacy between topical honey and acyclovir<sup>(42)</sup>

The pain due to oral lesions, as assessed by the pain score (VAS-10), number of acetaminophen doses and the drinking and eating ability, significantly improved in the honey group, as compared with the no-honey (control) group. In the current study, the pain score decreased from 7 in day 0 (day of presentation) to 5, 3, 1 in the 3rd, 5th and 7th day of the study, respectively. In the control group, on the other hand, the pain score started to show improvement on the 5th day of the study, and it decreased from 6 in day 0 to 2 in day 7. In the study of **Mir et al (2022)**, in which patients aged between 20 and 30 years, who also used honey as a therapeutic agent in aphthous stomatitis, found a decrease in the pain score, as also assessed by VAS-10, from 6 in the 1st day visit to 1.5 in the 3rd day visit<sup>(43)</sup>. Further, **Pandharipande et al, (2019)** studied the effect of honey on a group of patients aged 18 – 65 years, and suffering from aphthous stomatitis, and they found a significant improvement in pain score (VAS-10) in the honey group; with a reduction of the mean pain score from 6 in the 1st day visit before honey treatment to 3 in the 7th day of treatment<sup>(44)</sup>.

In the present study, the median number of acetaminophen doses/day decreased from 3 in day 0 (before starting honey therapy) to only one dose/day in the 7th day of the study. Similarly, the study of **Awad and Hamad (2018)**, conducted on children aged from 2 to 8 years showed a significant reduction of acetaminophen doses in the patients, who received honey as a treatment<sup>(15)</sup>. Also, **Hbib et al (2020)** study showed a significant reduction in the number of acetaminophen doses in the honey group<sup>(45)</sup>.

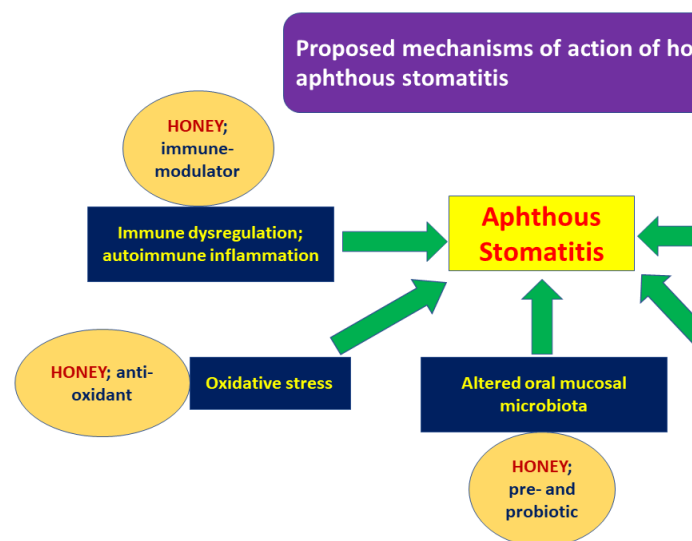
Regarding the eating and drinking ability, the present study showed a significant improvement in the honey group, starting from the 5th day of honey therapy. In the study of

**Awad and Hamad (2018)**, a significant improvement of eating and drinking ability started to be observed from the 3rd day of honey treatment<sup>(15)</sup>. On the other hand, in the **Hbib et al (2020)** study, the eating and drinking ability started to show significant improvement after 7 days of honey treatment<sup>(45)</sup>.

Regarding the oral lesion severity; it started to decrease significantly from the 5th day of our study. In the study of **Awad and Hamad (2018)**, the oral lesion severity started to show significant improvement from the 3rd day<sup>(15)</sup>. Also, the study of **El-Haddad et al (2014)** showed a significant reduction in the lesion severity in the honey group, compared to the other groups; being 2.7 days, 5.9 days and 7.1 days in the honey, triamcinolone, and orabase groups, respectively ( $P < 0.05$ )<sup>(26)</sup>.

In general, in the present study, the recovery time of aphthous ulcers, defined as the time interval, in days, between the start of treatment and complete healing, with no pain, no fever, no drooling and no eating or drinking difficulty was significantly shortened in the honey group, being 8.7 days, compared to 12.8 days in the children who did not receive honey ( $P = 0.000$ ). These positive effects of honey on aphthous ulcers were also observed in the studies of **Samet et al (2007)**, **Mohamed and Al-Douri (2008)**, **Gupta et al (2018)**, **Pandharipande et al (2019)**, **Gamal- Abdelnaser et al (2021)** and **Mir et al (2022)**<sup>(46,14,47,44,48,43)</sup>. On the other hand, in the treatment of minor recurrent aphthous stomatitis of 20 patients, **Halim et al (2013)** found in their study no significant difference between the honey and salicylate gel groups, with regard to pain score improvement<sup>(49)</sup>.

The etiology of RAS is multifactorial. It may be related to infection, stress, inflammation, immune dysregulation or altered oral microbiome. Because honey has anti-microbial, anti-oxidant, anti-inflammatory, immune-modulator and pre-and probiotic effects, it may act as a multi-targeted therapeutic agent in aphthous stomatitis (figure 5).



**Figure 5: Proposed mechanisms of action of honey in aphthous stomatitis.**

**Conclusion:**

In conclusion, honey was found to be an effective and safe therapeutic agent in the treatment of aphthous stomatitis in a group of children suffering from aphthous oral ulcers. Significant improvement of symptoms, including pain, eating and drinking ability and severity of oral lesions was observed in the patients treated with honey, as compared with the patients who did not receive honey.

**Conflicts of interest:**

There was no conflict of interest.

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### تأثير عسل النحل على الأطفال المصريين الذين يعانون من التهاب الفم القلاعي المتكرر

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**الخلفية:** القرحة القلاعية هي الآفات الفموية الأكثر شيوعاً بين الأطفال. الآفات مؤلمة و تؤثر على القدرة على الأكل والشرب و هي متكررة . العسل منتج طبيعي يشير الباحثون إلى أنه يسرع من الشفاء من القرحة.

**الهدف من البحث:** لاختبار تأثير مكملات العسل على وقت الشفاء من القرحة القلاعية عند الأطفال المصريين.

**المرضى و الطرق:** كانت هذه دراسة سريرية عشوائية أجريت على 50 طفلاً من العيادات الخارجية بمستشفى الأطفال بجامعة عين شمس، تم إخضاع جميع المرضى للتاريخ التفصيلي . تاريخ مفصل لقرحة الفم بما في ذلك وقت ظهورها ومدتها وعددها و الفحص السريري وفحص القرحة والاختبارات المعملية بما في ذلك فيروس الهربس البسيط امينوجلوبين م. تم تقسيم المرضى إلى مجموعتين (25 مريضاً في كل مجموعة) ، المجموعة (أ) تناول العسل والمسكنات والمجموعة (ب) تناول المسكنات فقط. تم متابعة جميع الأعراض كل يومين حتى تم الشفاء التام من القرحة وتم تقدير وقت الشفاء.

**النتائج:** كان التهاب الفم القلاعي المتكرر أكثر شيوعاً بين الذكور وفيروس الهربس البسيط 1 امينوجلوبين م كان إيجابياً فقط في 6 ٪ من المرضى. أظهرت المجموعة المعالجة بالعسل تحسناً ملحوظاً بشكل أسرع في الأعراض بما في ذلك شدة القرحة ودرجة الألم وصعوبة الأكل والشرب وكذلك انخفاض عدد جرعات مسكنات الألم بشكل ملحوظ. كما أن شفاء القرحة والألم وسيلان اللعاب وصعوبة الأكل والشرب كان أسرع في مجموعة العسل .بينما لم يكن هناك فرق في تحسن الحمى. كان وقت الشفاء حتى الشفاء التام مع عدم وجود أعراض أقصر بشكل ملحوظ في مجموعة العسل .

**الاستنتاج:** إعطاء العسل للأطفال المصابين بالتهاب الفم القلاعي المتكرر ، يسرع وقت الشفاء.