

Honey: an adjuvant therapy in acute infantile diarrhea

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Background Diarrheal disease is one of the major causes of mortality of infants and toddlers in developing countries. Bee honey is a functional food that has a unique composition, antimicrobial properties, and bifidogenic and anti-inflammatory effects.

Objective The present study was carried out to assess the effect of using pure honey as a form of adjuvant to oral rehydration solution (ORS) in the management of acute infantile diarrhea.

Patients and methods The effect of floral honey on 150 infants aged 6–24 months suffering from acute diarrhea with mild to moderate dehydration was assessed. They were randomized into three groups of 50 infants each. Group I received WHO ORS only. The other two groups received floral honey in various forms: group II: received 50 ml honey in 1 l of ORS; group III: received pure honey at a dose of 5 ml every 6 h/day, in addition to ORS. The studied groups were observed for rehydration time, vomiting, diarrhea, and recovery time. Stool culture was carried out at admission. Stool pH and serum sodium and potassium levels were estimated and followed up until recovery.

Results The recovery time was significantly shorter in group III, which was treated with pure honey and ORS (3.1 ± 0.6 days) as compared with group I and group II

($P < 0.05$). Moreover, pure honey and ORS shortened the recovery time significantly both in infants with bacterial and in those with nonbacterial diarrhea. A significant positive correlation was found between the degree of dehydration and frequency of diarrhea ($r = 0.340$, $P < 0.01$). The recovery time was significantly negatively correlated with the frequency of diarrhea and stool pH ($r = -0.340$, $P < 0.05$).

Conclusion Honey is a nonallergic, natural agent of high nutrient value. Pure honey administered as a form of adjuvant therapy in addition to ORS in cases of acute infantile diarrhea causes significant shortening of the recovery period, decreases the frequency of passing loose stools, and improves stool consistency. Further studies on pure honey as an adjuvant therapy in infantile diarrhea are recommended on a large scale. *Med Res J* 12:12–16 © 2013 Medical Research Journal.

Medical Research Journal 2013, 12:12–16

Keywords: adjuvant therapy, diarrhea, honey, infants

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Received 1 February 2013 accepted 26 March 2013

Introduction

Acute gastroenteritis is a very common disease. Worldwide, it affects three to five billion children every year and accounts for 1.5 to 2.5 million deaths annually (12% of all deaths) [1,2]. It is the reason for significantly high rates of mortality in developing countries and results in significant economic burden to developed countries [3].

Acute diarrhea of all etiologies can be safely treated with oral rehydration solution (ORS). The WHO, the American Academy of Pediatrics (AAP), and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) working group, and the Cochrane Library database recommend oral rehydration therapy and prompt realimentation for mild to moderate gastroenteritis [4,5]. Diarrhea control programs have proved to be highly effective [6]. The National Control of Diarrheal Diseases Project of Egypt reported a substantial increase in the awareness on and use of oral rehydration in the country between 1981 and 1990 and a fall in the infant diarrheal death rate from 35.7 to 9.3 per 1000 live births – a 74% reduction with no concomitant decrease in diarrheal incidence [7].

Honey has been used as a medicine since ancient times in many cultures and is still used in folk medicine. In fact, honey has been found to be effective against microorgan-

isms isolated from urinary tract infections [8] and in the treatment of infantile gastroenteritis [9]. Honey also possesses beneficial anti-inflammatory and antimicrobial properties owing to its high antioxidant content [10].

In the holy book of Muslims the 'Al Quran' and in the holy Hadith dating back to the eighth century AD, our gracious Prophet Mohammed recommended bee honey against diarrhea [11]. Moreover, the Roman physician Celsius (ca. 25 AD) also used honey as a cure for diarrhea [12]. The Islamic scientist Ibn Sina mentioned in detail about the nutrient, laxative, diuretic, and antitussive properties of honey [13].

This study was carried out to evaluate the clinical effectiveness of using bee honey as a form of adjuvant therapy to ORS in the management of acute infantile diarrhea.

Patients and methods

This study was a simple randomized prospective clinical trial carried out on 150 infants (6–24 months old) suffering from acute diarrhea with mild to moderate dehydration. Acute diarrhea is defined as passing three or more loose or watery stools or any number of loose stools containing blood during a 24 h period [14].

All patients were admitted to Al-Zahra University Hospital, Cairo, Egypt. The study was approved by the local ethical committee of the hospital, and informed consent from the infants' parents was obtained.

Patients were excluded if they presented with severe dehydration (unstable vital signs and poor perfusion), an altered level of consciousness, possible surgical abdomen, bloody or bilious vomiting, bloody diarrhea, abdominal distension and tense, absent bowel sounds, guarding or rigidity, right lower quadrant pain, or chronic health conditions (such as gastric or jejunal feeding tube dependence, known inflammatory bowel disease, known immunodeficiency syndrome, known metabolic disorders, insulin-dependent diabetes, heart or renal disorder, and neurosurgical history).

The patients were divided by simple randomization into one of the following three groups (50 patients each):

Group I

This group included patients who received WHO ORS only. The ORS was administered on the basis of the recommendations of the WHO [15].

Group II

This group included patients who received ORS with honey at a dose of 50 ml dissolved in 1 l of ORS, which resulted in a significant increase in the glucose content (109 mmol/l instead of 75 mmol/l) and osmolarity of ORS (310 mOsmol/l instead of 245 mOsmol/l), [16].

Group III

This group included patients who were rehydrated by WHO ORS. In addition, they were given pure honey at a dose of 5 ml every 6 h/day.

The honey used was pure unprocessed clover honey collected from Shabshir, Gharbia Governorate, Egypt. The honey was obtained directly from the beekeeper and was tested for the presence of *Clostridium botulinum* spores by centrifugation and filtration of the supernatant, followed by culture on cooked meat medium [17]. No spores were detected. The mixture of honey and ORS was prepared fresh and administered within a maximum of 2 h to avoid fungal growth [18].

Primary history of all patients was studied along with a thorough clinical examination, followed by a clinical evaluation every 24 h until full recovery, which included: (a) A dehydration score, according to the scoring system described by Duggan et al. [19], to determine the time required for initial rehydration and to maintain the patient in a rehydrated state. The rehydration solutions were administered using cups and spoons or through nasopharyngeal tubes, whenever indicated. Patients were considered fully rehydrated when all signs of dehydration disappeared, and the dehydration score became zero. (b) Number of motions per day. (c) Consistency of stools. (d) Number of episodes of vomiting (if present).

The recovery time was evaluated for all groups, which was defined as the time calculated from initiation of treatment to when normal soft stools were passed, with

the patient showing normal hydration and satisfactory weight gain [9].

Laboratory investigations included: (a) stool cultures for *Salmonella*, *Shigella*, *Escherichia coli*, *Staphylococcus aureus*, *Campylobacter*, and *Yersinia* by standard methods [20]; (b) daily monitoring of serum sodium and potassium levels [21,22]; and (c) daily monitoring of stool pH [23].

Statistical analysis

Statistical analysis was performed using SPSS program, version 20 (IBM SPSS Statistics 20, Fayetteville, Arkansas, USA). Data were statistically described in terms of mean and SD, and the three groups of patients were compared on the basis of the one-way analysis of variance test. A probability value was considered statistically significant when the *P* value was less than 0.05. The bivariate Pearson correlation was used and was considered significant at a *P* value less than 0.05 (two tailed).

Results

The descriptive data of the three studied cases groups is summarized in Table 1. In the present study, 81 infants were males (54%) and 69 infants were females (46%); their ages ranged from 6 to 24 months (mean 11.7 ± 5.0 months). Mild dehydration was observed in 69 infants (46% of the studied cases), and 81 infants (54%) were moderately dehydrated. Honey was well tolerated by both honey-treated groups.

The recovery time was significantly shorter in group III (treated with pure honey and ORS) (3.1 ± 0.6 days) as compared with group I and group II ($P < 0.05$). In addition, the recovery time for group II (honey 50 ml + 1 l ORS) and group I showed no significant difference ($P > 0.05$) (Table 1).

It was observed that pure honey shortened the recovery time significantly both in infants with bacterial and in those with nonbacterial diarrhea (Table 2).

A significant positive correlation was found between the degree of dehydration and frequency of diarrhea ($r = 0.340$, $P < 0.01$). The recovery time was significantly negatively correlated with the frequency of diarrhea and stool pH ($r = -0.340$, $P < 0.05$). However, a nonsignificant positive correlation was found between the recovery time and degree of dehydration (Table 3).

Discussion

The medicinal importance of honey has been documented since ancient times, and it has been known to possess antimicrobial and wound-healing properties. More than 1400 years ago, Allah and His messenger Mohammed advocated that honey can heal a variety of medical problems. Allah says, 'And the 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 colors wherein is healing for men. Verily in this is indeed a sign for people who think' [24].

Table 1 Characteristics of the studied patients

Parameters	Group I (N=50)	Group II (N=50)	Group III (N=50)
Age (months)	12.4 ± 5.1	11.5 ± 4.2	11.7 ± 5.0
Sex (male/female)	30/20	24/26	27/23
Weight (kg)	10.0 ± 2.1	10.6 ± 1.9	10.0 ± 2.0
Serum K	3.9 ± 0.3	3.9 ± 0.3	4.0 ± 0.3
Serum Na	137.0 ± 2.2	137.1 ± 3.3	136.4 ± 3.0
Stool pH	6.4 ± 0.5	6.5 ± 0.5	6.4 ± 0.5
Stool culture (+/-)	18/32	22/28	23/27
Dehydration (mild/moderate)	20/30	22/28	27/23
Frequency (/day)	4.5 ± 1.4	5.1 ± 1.4	4.1 ± 1.2
Recovery time (/day)	4.6 ± 0.7	5.0 ± 0.8	3.1 ± 0.6*

Data expressed as mean ± SD.

*P < 0.05 is significant compared with other groups by analysis of variance test.

Table 2 Recovery time among the different groups according to stool culture (one-way analysis of variance test)

	Positive stool culture	Negative stool culture	P
Group I	4.6 ± 0.5	4.5 ± 0.9	0.450
Group II	5.1 ± 0.7	4.8 ± 0.5	0.246
Group III	3.2 ± 0.3*	3.0 ± 0.4*	0.047

*P < 0.05 is significant compared with other groups by analysis of variance test.

Table 3 Correlations of the recovery time among the three studied groups

Recovery time	Frequency	Dehydration	Stool culture	Stool pH
Group I				
Pearson's correlation	-0.013	0.005	-0.191	-0.104
Significance (two tailed)	0.929	0.973	0.188	0.478
Group II				
Pearson's correlation	0.266	0.287	0.063	0.005
Significance (two tailed)	0.071	0.051	0.672	0.971
Group III				
Pearson's correlation	0.340 ^a	0.153	-0.147	-0.340*
Significance (two tailed)	0.017	0.292	0.312	0.017

*Correlation is significant at the 0.05 level (two tailed).

In Prophetic medicine, honey has been reported to have tremendous medicinal value. It is thought to wash away the harmful substances that might have accumulated in the intestines. Treatment with honey promotes rehydration of the body and is a quick cure to diarrhea and any vomiting and stomach upsets [25].

Honey is being accepted as a reputable and effective therapeutic agent by practitioners of conventional medicine and the general public because of its good clinical results [26]. Consuming honey in small quantities (1–2 tablespoons) generally has a positive effect on diarrhea due to food or mild infections. However, consuming honey in large quantities generally causes mild to severe constipation. Honey has been reported to be effective in the healing of infected postoperative wounds [27]. It has also been reported to inhibit the growth of several bacteria such as *Bacillus cereus*, *Staphylococcus aureus*, *Salmonella Dublin*, and *Shigella dysenteriae* [28,29]. It has also been reported to inhibit the growth of anaerobic bacteroides [30].

Moreover, Adebolu reported that, in the absence of antibiotics, natural honey can be used to treat bacterial

diarrhea. He found that natural honey was effective in inhibiting the growth of all the test organisms, with zones of inhibition ranging from 5.0 to 20.0 mm, except for *C. jejuni*. The inhibitory effect of honey on *E. coli* was comparable to that of amoxicillin (20.0 mm) and chloramphenicol (17.0 mm). Tetracycline had no inhibitory effect on any of the test organisms [31].

This is in favor of our present study. The recovery time of the studied diarrhea patients was significantly shorter in group III (the pure honey + ORS treated group) as compared with the other two patient groups. It was observed that the pure honey could shorten the recovery time significantly both in infants with bacterial and in those with nonbacterial diarrhea. A significant positive correlation was found between the degree of dehydration and frequency of diarrhea. The recovery time was significantly negatively correlated with the frequency of diarrhea and stool pH. However, a nonsignificant positive correlation was found between the recovery time and degree of dehydration.

Honey is a natural product with a very complex chemical composition. It is composed primarily of fructose and glucose but also contains 4–5% fructooligosaccharides, which serve as prebiotic agents [32]. It contains more than 180 substances, including amino acids, vitamins, minerals, and enzymes [33]. Honey has been reported to clear infection through a number of properties, including boosting the immune system, anti-inflammatory action, antioxidant activity, and stimulation of cell growth [34]. Moreover, the antimicrobial properties of hydrogen peroxide and nonperoxide components of honey were tested in several studies [35].

Molan [36] explained the effective role of honey in the treatment of diarrhea and dysentery by the fact that honey is a nutrient source for *Lactobacillus bifidus*, which by its *Lactobacillus bifidus* factor restores intestinal flora, changing the environment necessary for the growth of bacteria causing dysentery and leading to their eradication within few days. Wahdan [37] reported that honey increases the immune resistance of the whole body and thus helps control infections.

However, the results of the present study failed to find any significant difference between the results of group II (treated by 50 ml honey added to 11 ORS) and group I

(treated with ORS only). This is in contrast with the results of Abdulrhman *et al.* [16] who reported that addition of honey to ORS reduces the frequency of diarrhea in patients with gastroenteritis. Haffeejee and Moosa [9] studied the effects of a honey–electrolyte solution (containing 50 ml of honey per liter, i.e. 5%) in patients with infantile diarrhea. They found that the presence of honey in the solution could reduce the duration of bacterial infantile diarrhea when compared with controls.

The anti-inflammatory and antibacterial activity of bee honey can be explained by the osmotic effect. Honey is a supersaturated solution of sugars (84% mixture of fructose and glucose); the strong interaction of these sugar molecules with water molecules leaves few water molecules available for microorganisms [38]. This high sugar content of honey could be used to promote sodium and water absorption from the bowel.

Moreover, its acidic pH (between 3.2 and 4.5) inhibits many pathogens. The major antibacterial activity in honey has been found to be because of hydrogen peroxide, which is produced enzymatically glucose oxidase and phenolic compounds. The glucose oxidase enzyme is secreted from the hypopharyngeal gland of the bee into the nectar.

Conclusion

Honey is a nonallergic, natural agent of high nutrient value that has well-known antioxidant, anti-inflammatory, and antibacterial activities. Pure honey administered as a form of adjuvant therapy in addition to ORS in acute infantile diarrhea causes significant shortening in the recovery period, decreases the frequency of passing loose stools, and improves stool consistency. Further studies on pure honey as a form of adjuvant therapy in infantile diarrhea are recommended on a large scale.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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الملخص العربي

العسل: العلاج المساعد في الاسهال الحاد في الاطفال

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تعتبر أمراض الإسهال أحد الأسباب الرئيسية لوفيات الأطفال الرضع والأطفال الصغار في البلدان النامية. ويعتبر عسل النحل غذاء وظيفي يحتوي على تركيبة فريدة من نوعها، وله خصائص مضادة للميكروبات وتأثير مضاد للالتهابات. أجريت هذه الدراسة لتقييم تأثير استخدام العسل النقي باعتباره علاج مساعد للعلاج بمحلول معالجة الجفاف عن طريق الفم في علاج الإسهال الحاد في الأطفال. تم تقييم تأثير عسل الزهور على 150 مريضا تتراوح أعمارهم بين 6-24 شهرا، يعانون من الإسهال الحاد المصحوب بحالة خفيفة الى معتدلة من الجفاف. وتم تقسيمهم إلى مجموعة ضابطة، ومجموعتين تعالجا بعسل الأزهار في أشكال مختلفة. المجموعة الأولى: قدم لها 50 سم العسل في 1 لتر من محلول معالجة الجفاف عن طريق الفم. المجموعة الثانية: قدم لها العسل الصافي بجرعة من 5 سم كل 6 ساعات كل يوم، بالإضافة إلى محلول معالجة الجفاف عن طريق الفم. وقد تم ملاحظة فترة معالجة الجفاف وحدوث الإسهال والقيء والوقت اللازم للشفاء. وقد جرى تحليل البراز ودرجة حموضة البراز ونسبة الصوديوم والبوتاسيوم في الدم ومتابعة الحالات حتى الشفاء. وتبين من الدراسة ان الوقت اللازم للشفاء أقصر بكثير في المجموعة الثانية التي تعالج بالعسل النقي مقارنة مع مجموعة التحكم والمجموعة الأولى ($p < 0.05$). وعلاوة على ذلك، اثبت العلاج بالعسل الصافي بالإضافة الى محلول معالجة الجفاف تقصير وقت الشفاء بشكل إحصائي كبير سواء في حالات الإسهال البكتيري وكذلك الإسهال غير الجرثومي. وقد تم ايجاد علاقة إيجابية ذات دلالة إحصائية بين درجة الجفاف ومعدل الإسهال ($p < 0.01$, $r = 0.340$) وعلاقة سلبية بين الوقت اللازم للشفاء وعدد مرات الإسهال ودرجة الحموضة البراز ($p < 0.05$, $r = -0.340$). ونستخلص من هذا البحث ان عسل النحل غذاء طبيعي ذات قيمة غذائية عالية ولا يسبب الحساسية. وقد اثبت العلاج بالعسل الصافي بالإضافة الى محلول معالجة الجفاف الى تقصير فترة النفاة بشكل إحصائي كبير سواء في حالات الإسهال البكتيري وكذلك الإسهال غير الجرثومي في الاطفال كما ادى الى انخفاض عدد مرات البراز وتحسين قوام البراز. ونوصى بإجراء المزيد من الدراسات عن العسل النقي باعتباره العلاج المساعد للإسهال في الاطفال على نطاق واسع.