

Honey Can Help Wound Healing After Cleft Lip Repair

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Abstract

One of the most common congenital anomalies is the cleft lip and when repaired properly by accelerated wound healing and by avoiding scar formation, it can create an acceptable esthetic appearance, restoring calm to the patient's family. Honey, as a natural material which is relatively inexpensive, can be used as a wound dressing in these patients.

Materials and Methods

Cleft lip patients, admitted for reconstructive surgery, were enrolled in this study. The parents were randomly given a tube of gel containing honey or placebo to apply on the suture line three times daily for 2 weeks. The patients were examined by a single examiner on days 1, 2, 7, 14, 21 and 30 postoperatively and variables related to their status and scarring were registered.

Results

Postoperative variables assessed on days 1 and 2 exhibited no changes. Significantly more changes were noted on days 14 and 21, especially on days 30, after surgery in the honey group compared to the placebo group. Two variables of swelling and color of the scar were significantly better in the honey group compared to the placebo group from the 7th to the 30th days. However, the variable of scar size was worse in the honey group on the 13th day compared to the placebo group, which might be attributed to measurement bias.

Conclusion

Honey can safely be used as a dressing material after surgery to accelerate healing and reduce scarring in patients with cleft lip.

Further studies are suggested to compare the efficacy of honey with that of other anti-scar ointments on the market.

Keywords: Cleft lip; wound healing; honey; scar formation

Introduction

Cleft lip and palate is the most common congenital defects in the maxillofacial region [1,2]. Cleft lip occurs in 1 in 1000 live births in the United States, whereas cleft palate deformity occurs in 1 in 2000 live births. Cleft lip deformities occur with the highest incidence among Native Americans (3.6 in 1000 births), Asians (2.1 in 1000), and whites (1 in 1000) and with the lowest incidence among blacks (0.41 in 1000) [3]. Management of cleft lip has varied along history. Patients born with a cleft lip/palate, undergo various surgical repairs of the cleft with different results and outcomes [4]. In cleft lip repair, attention to scar formation and wound appearance is very important to achieve more esthetic results.

Honey as a natural, safe and effective wound dressing has been recently accepted for wound dressing. Honey, the most ancient of wound treatments, is claiming its position in modern wound care; it is easy to apply, painless and comfortable, harmless to tissues, creates a moist healing environment, is antibacterial and stimulates healing and epithelialization [5].

Honey has been found to be useful in the treatment of burns by helping the rapid healing of wounds [6-8]. The high viscosity, acidic pH, inhibine factor, high osmolarity and nutrient content of honey contribute to the inhibition of bacterial growth, promoting wound healing [5,6]. In addition, many papers have reported successful use of honey in wound healing [7-10]. Honey with proven antibacterial activity has the potential to be an effective option for infected wounds or at risk of infection with various human pathogens [10-12]. As a dressing on wounds, honey provides a moist healing environment, rapidly clears infection, deodorizes and reduces inflammation, edema, and exudation. It increases the rate of healing by stimulation of angiogenesis, granulation and epithelialization [13]. As far as we searched, none of these studies have focused on dressing clean wounds, especially in cleft lip repair. Since in our region, Azerbaijan, Iran, natural honey is available and since Oryan et al reported that honey from Iran produces less edema, fewer polymorphonuclear and mononuclear cell infiltrations, less necrosis, better wound contraction, improved epithelialization, and lower glycosaminoglycan and proteoglycan concentrations [14], this prospective randomized study was designed in order to observe the effects of honey clinically on wound healing in cleft lip repair.

Materials and Methods

Patients with cleft lip, who underwent lip repair in the ENT Department of Tabriz Pediatric Hospital, were enrolled in this

randomized clinical trial. Since anomalies may alter wound healing, such as syndromic anomalies, they were considered exclusion criteria for this study. After surgery a tube of sterilized gel was given to parents to apply on the lip suture line. The content of the tube was randomly determined to be honey or placebo. The applied honey was pure honey from Azerbaijan region, which was prepared as a gel in the Faculty of Pharmaceutical Sciences by second author.

Subsequently, in order to sterilize and eliminate the potential botulism, the gel underwent gamma radiation in the Atomic Energy Organization in Tehran after determination of the dose. After making sure of the quality of the honey by the Faculty of Pharmaceutical Sciences, it was coded. The placebo, too, was prepared similar to honey in the form of a gel in the same faculty and underwent the same sterilization procedures in the Atomic Energy Organization. After coding the honey and placebo tubes in the Faculty of Pharmaceutical Sciences, the tubes were randomly given to the parents for application on the suture lines. In each group the sterilized honey or placebo was placed on the suture line in a thin layer for two weeks. All the subjects in both groups received oral antibiotics for one week after the surgical operation and the present study did not deprive them of their routine treatment procedure.

The children were examined at 1-, 2-, 7-, 14-, 21- and 30-day postoperative intervals by a single examiner. Table 1 presents the recorded data, including the wound and the scar produced at the location of the scar line. The criteria used for evaluation of wound healing and scar formation were those previously described by Vijaya et al in a study on honey [15]. SPSS 22 was used for analysis of data after the nature of the tube (honey or placebo) was determined. Independent t-test was used for statistical analysis at $P < 0.05$.

Table 1. wound and scar specifications with 0 to 3 scales.

Wound specification	Scale 0	Scale 1	Scale 2	Scale 3
Color	Normal pigmentation	Slightly red	Reddish black	Pale yellow/black or blue
Margin on the surface	Adherence to margin	Smooth, even and regular	Rough, regular and inflamed	Rough, irregular
Swelling	No swelling	Slightly red, tender and hot with painful movement	Red with painful movement and local temperature	Hot, resists touching
Size of scar	<5 mm	5 mm < x < 10 mm	10 mm < x < 20 mm	>20 mm
Scar color	No skin color	More pigmentation than the surrounding skin	Darker pigmentation	Hyperpigmentation

Scar surface	Normal, smooth and regular	Smooth and irregular	Regular and rough	Irregular and rough
Scar consistency	Normal	Soft	Firm	Hard
Scar condition	Normal and even	Depressed	Elevated	Ugly abnormal look

Of 45 patients who completed the follow-up visits, 23 patients used honey gel and 22 patients used placebo gel. The results of follow-ups are shown in Tables 2 and 3.

The majority of variables exhibited no particular changes at 1- and 7-day intervals. In particular, no tangible changes were observed on days 1 and 2, which might be attributed to the lack of the rapid effect of gel on the healing process. On the 7th day, swelling and scar color significantly decreased in the honey group compared to the placebo group, indicating the positive effect of honey. At 14-, 21- and 30-day postoperative intervals the effect became more evident; in this context, on the 30-day interval all the variables were better in the honey group compared to the placebo group, except for the scar condition. Some variables such as scar condition were different between the two groups but the differences were not significant.

As mentioned above, the two variables of swelling and scar color exhibited the greatest differences between the honey and placebo groups at 7- and 30-day intervals and were the best variables to show changes in this respect (Graphs 1 and 2). Scar sizes were the same between the two groups during the

Results

Fifty patients with cleft lip admitted into the ENT Department, Tabriz CPediatric Hospital from February 2013 to October 2013 were enrolled in this study. After lip repair all the parents were given a tube of gel to apply on the suture line three times a day for two weeks. Five patients were excluded from this study because of the inadequate care provided by the parents and irregular use of gel; therefore, forty-five patients completed the one-month follow-up course. Eighteen patients were female (40%) whereas 27 were male (60%); 28 patients (62.2%) had unilateral cleft lip and 17 (37.8%) had bilateral cleft lip. A total of 26 patients (57.8%) had complete cleft lip.

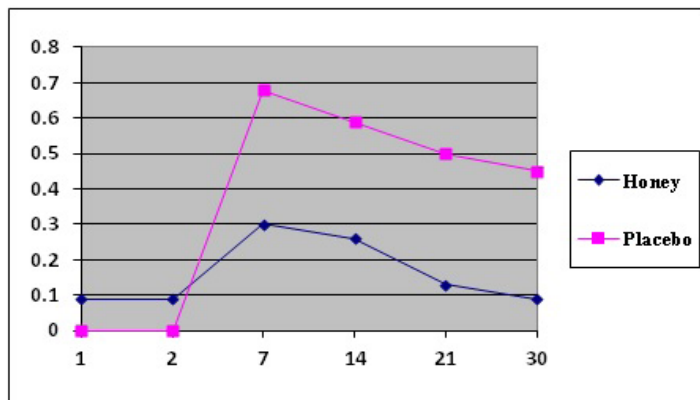
Table 2. The results of assessment of both groups (honey and placebo) 1, 2 and 7 days after surger.

Wound specification	Day 1			Day 2			Day 7		
	Honey (mean)	Placebo (mean)	p-value	Honey (mean)	Placebo (mean)	p-value	Honey (mean)	Placebo (mean)	p-value
Color	.04	.00	.334	.04	.00	.334	.39	.45	.676
Margin on the surface	.00	.00	-	.04	.00	.334	.13	.32	.136
Swelling	.09	.00	.164	.09	.00	.164	.30	.68	.011
Size of scar	.00	.00	-	.00	.00	-	.00	.00	-
Scar color	.00	.00	-	.00	.00	-	.22	.64	.004
Scar surface	.00	.00	-	.00	.00	-	.04	.23	.073
Scar consistency	.00	.00	-	.00	.00	-	.04	.09	.535
Scar condition	.00	.00	-	.00	.00	-	.04	.00	.334

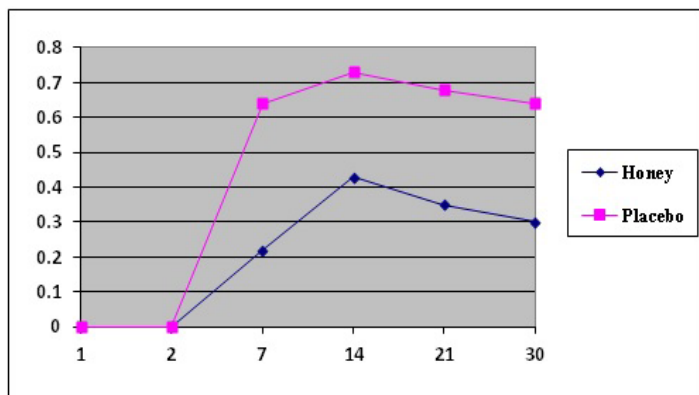
Table 3. The results of assessment of both groups (honey and placebo) 14, 21 and 30 days after surgery.

Wound specification	Day 14			Day 21			Day 30		
	Honey (mean)	Placebo (mean)	p-value	Honey (mean)	Placebo (mean)	p-value	Honey (mean)	Placebo (mean)	p-value
Color	.35	.68	.025	.35	.64	.055	.30	.64	.026
Margin on the surface	.22	.68	.003	.30	.73	.008	.26	.73	.003
Swelling	.26	.59	.025	.13	.50	.007	.09	.45	.005
Size of scar	.00	.00	-	.26	.00	.083	.35	.00	.041
Scar color	.43	.73	.048	.35	.68	.025	.30	.64	.026
Scar surface	.09	.59	.000	.17	.73	.000	.22	.73	.001
Scar consistency	.30	.68	.011	.39	.73	.023	.48	.77	.086
Scar condition	.13	.27	.302	.35	.73	.053	.43	.77	.100

initial days but on the final days were disproportionately lower in the honey group compared to the placebo group and the difference was statistically significant on the 30th day, too. It is surprising that honey had resulted in an increase in scar size despite improving other relevant variables of the wound. Considering the small sizes of scars in the subjects in the present study, the large scale of the measurements made (sizes less than 5 mm as the scale of zero) might be considered a reason for measurement bias.



Graph 1. The graphs of wound swelling in the honey and placebo groups.



Graph 2. The graphs of scar color in the honey and placebo groups.

Evaluation of other variables at 14-, 21- and 30-day intervals revealed the superiority of honey over placebo in creating a proper appearance for the wound and scar, although scar condition was not significantly different between the placebo and honey groups.

Discussion

As pointed out previously a large number of studies have been carried out on the effect of honey on healing of infections wounds, the majority of which have reported the favorable antibacterial and antiinflammatory effects of honey (5–7). A study in Cochrane database has evaluated several studies on the subject in recent years. On the whole, 19 clinical trials were

evaluated, which were reported to be of low quality. Authors believed that the evidence on the effect of honey on wounds and burns was inadequate and they recommended more comprehensive studies to evaluate the effect of honey [16].

In addition, Ingle et al compared the effect of honey with that of dressing the wounds and cuts with Intracite Gel and did not report any particular differences between the two groups; however, due to the lower cost of honey, they recommended use of honey in such cases [17]. A systematic review by Moore et al in relation to the comparison of honey with different dressing materials, including silver sulfa, amniotic membrane etc, showed that honey resulted in shortening of the healing period, although this review, too, showed the inadequacy of evidence [6].

A study by Molan et al on the use of honey for dressing wounds showed that honey results in moistening of the healing environment, rapid debridement of the wound and a decrease in inflammation, edema and exudation. In addition, it gives rise to better esthetic results by promoting angiogenesis, granulation and epithelialization, making skin grafts unnecessary [13].

Molan carried out another systematic review in 2006 and analyzed 17 clinical trials with 1965 subjects, which had reported positive findings about the effect of honey on wound healing [18]. The results of the present study, too, showed the positive effect of honey on wound healing.

In addition to studies on the acceleration of wound healing with the use of honey, some researchers have emphasized the effect of honey on decreasing scar formation with the use of honey. Different drugs, such as celecoxib, have been introduced to decrease scar formation after surgical wounds [19] and the effect of honey has not been neglected [20,21]. The majority of studies on the effect of honey on wound healing have focused on chronic wounds and burns; however, in some studies the effect of honey has been evaluated on acute wounds, especially after surgeries [22,23]. In a study by Vijaya et al, similar to the present study, the visible characteristics of wounds and scars were used to evaluate the effect of honey. Although in the results reported no mention was made of the values and scores, it was reported that in 80% of patients use of honey resulted in a smooth wound surface and color without any irregularities. In addition, in that study the duration of wound healing in the honey group was better than that in the control group but the difference was not significant [15].

Variables used in the present study to evaluate wounds consisted of the following: color, the margins of surfaces and swelling; the variables used to evaluate scars consisted of the following: the size, color, surface, consistency and the position of the scar. Evaluation of these variables showed no differences between the honey and placebo groups between days 1 and 2, indicating that honey had not exerted any effects on wound

healing yet. Of course, the wound healing process has different stages which usually begin after 24 hours. Therefore, in the early stages no specific changes are expected, which is different from the results of a study by Yilmaz et al, who reported significant differences on the 7th day but no significant differences were observed between the two groups on the 14th day [24]. It appears the significant difference on the 7th day is, to some extent, consistent with significant differences in swelling and scar color on the 7th day in the present study, indicating the effect of honey in decreasing inflammation; however, a lack of difference on the 14th day in that study is not consistent with the results of the present study. On the 14-, 21- and 30-day postoperative intervals the tissue changes were more prominent and the differences between the two groups were significant. Of all the different variables evaluated, tissue swelling was less in the honey group, consistent with the results of other studies which have emphasized the antiinflammatory effect of honey [13,18]. The properties of scar, including color, surface texture, consistency and condition, were better in the honey group compared to those in the placebo group; however, the difference in relation to scar condition was not significant. These findings were consistent with those of a study by Vijaya et al, although, as pointed out above, they have not reported the results in detail and have made no mention of examinations on different days or intervals [15]. The scar size variable on the 30-day postoperative interval in the honey group was worse than that in the placebo group, which is not consistent with other findings. In order to explain this discrepancy, it is necessary to take a look at tables. In the placebo group, the scale size has always been zero; therefore, a minimum difference can be considered significant, which in itself can lead to measurement bias. As a result, the scale selected for scar size lacks the necessary accuracy for its correct measurement and requires to be corrected. However, one of the effects of honey on the wound was formation of granulation tissue and epithelialization, consistent with the results of previous studies [13,18]. In some studies, an increase in granulation or an increase in the thickness of granulation tissue has been reported [25,26]. In a study by Bergman, in addition to the higher rate of tissue repair with the use of honey, the thickness of granulation tissue and the distance of epithelialization from the wound margin were greater [27]. It is probable that an increase in scar size with the use of honey is a temporary and physiologic phenomenon to accelerate the wound healing process. In order to confirm or rule out this hypothesis it seems rational to carry out another controlled trial with a longer evaluation period so that a correct judgment can be made in relation to the increase or decrease in scar size.

Conclusion

The results of the present study showed that honey can improve the appearance of wounds and scars, confirming the results of previous studies in relation to the effect of honey

on wound healing. Therefore, it can be used with confidence after cleft lip surgeries. Further studies are necessary for evaluation and documentation of the effect of honey on wounds and acceleration of wound healing. With the continuous use of honey during the first two weeks, significant changes in acceleration of wound healing, along with improvements in scar appearance during the following 2-week period are expected. In the present study the effect of honey on wound healing was compared with that of placebo. Considering the availability of various anti-scar ointments on the market, it is recommended that another study be carried out to compare the effect of honey with that of anti-scar ointments in accelerating wound healing process and improving the esthetic appearance.

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