Honey Versus Diphenhydramine for Post-Tonsillectomy Pain Relief in Pediatric Cases: A Randomized Clinical Trial

SOROUSH AMANI1, SOLEYMAN KHEIRI2, ALI AHMADI3

ABSTRACT

Introduction: Tonsillectomy is one of the most common surgeries done worldwide and often the first one a child sustains. Pain relief after tonsillectomy is helpful for oral feeding after surgery. Acetaminophen and diphenhydramine have been conventionally used for reducing pain. This study was conducted to compare the effect of honey and diphenhydramine on pain relief after tonsillectomy.

Materials and Methods: For this randomized clinical trial study, 120 patients of 5 to 12 years undergoing tonsillectomy were recruited. The patients were divided into four groups randomly. After tonsillectomy and beginning of eating, Group A took 5cc honey alone every hour, Group B was given 5 cc 50% honey (mixed with water) every hour, group C was treated with 1mg/kg diphenhydramine every 6 hours and group D was observed without any intervention. In all patients, severity of the pain was evaluated by ocher questionnaire at recovery, and 3, 6, 12 and 24 hours after surgery. The data were analyzed using ANOVA and the repeated measures ANOVA (SPSS version 17).

Results: The repeated ANOVA showed a significant decreasing trend of pain scores during the study for both pain scales (p < 0.05), but the rate of trend was similar between the four groups (p > 0.05). No statistically significant difference in pain was detected among the groups.

Conclusion: Although honey can help the pain decrease, more research is supported for confirmation of this effect.

Keywords: Curative agent, Pediatric cases, Treatment

INTRODUCTION

Considering that the main purpose of medical science is to reduce pain and keep people healthy, relieving pain specially after surgery seems essential [1]. Children who suffer from pain are more likely to become anxious and restless, perhaps leading to nightmare, eating and sleeping disorders. Although one of the riskiest and the commonest kinds of the pain occurs postoperatively, it has not been satisfactorily addressed.

Tonsillectomy is one of the most widespread surgeries done all around the world and it is often the first one which a child sustains [2]. Generally the indications for tonsillectomy could be primarily related to chronic upper airway obstruction [3]. As a result, post-tonsillectomy pain relief is expected to facilitate many children’s beginning of oral feeding and reduce dehydration, bleeding as well as infection [4, 5].

Although using opiate is the most useful way of pain reduction, therapists are afraid of using it. Although acetaminophen is usually prescribed as a pain reliever [8], it is not satisfactorily effective and may cause side effects. In some cases, local analgesia or intravenous steroids are used for relieving the pain after tonsillectomy [7]. The use of high-dose steroids, antibiotics, and local anesthesia, according to certain studies, have all yielded some benefits, but not all studies have shown a definite reduction of pain or a more rapid recovery [8].

Diphenhydramine also has long been used as a pain reducing agent after tonsillectomy because of its sedative effect, local anesthesia, and inflammation reduction [9]. Delayed hospitalizations may be due to non-hemorrhage reasons including fever, airway distress, and pneumonia, inadequate oral intake, vomiting, and pain [10].

Since healing effects of honey have been mentioned in Quranic and traditional medicine, it is used as a curative agent for many diseases [11, 12]. This natural food substance was used as a treatment of infectious injuries even 2000 years before the discovery of bacteria [13]. The recent studies have shown the restrictive effect of honey on 60 types of bacteria [14]. Honey could decrease prostaglandin E2, prostaglandin alpha 2, and thromboxane B2 in blood and hence contributes to pain relief [15]. High concentration of glucose and hydrogen peroxide in honey have an important role in fighting microbes in an infectious wound [16, 17].

In traditional medicine, honey is frequently recommended to relieve pain and heal wounds. Eating healthy foods is very important from Islam's points of view. According to Imam Ali (peace be upon him) “honey is the healing of all diseases and there is no disease in it. It reduces phlegm and refreshes the heart” [18]. Inspired by Holy Quran and Imams’ statements, regarding that honey is widely accepted in clinical trials, and finding no study of honey's effects on pain relief after tonsillectomy, we compare the effect of honey and diphenhydramine on pain relief after tonsillectomy in this study.

MATERIALS AND METHODS

Study type and patients

This study was a randomized, double-blind clinical trial conducted on 120 patients who referred Kashani Hospital, Shahrekord, Iran in 2009 to 2012 and underwent tonsillectomy. Initially, 126 patients were enrolled and 6 of them had not the inclusion criteria into the study. All patients were operated by one surgeon per the same method. The ability of recognizing numbers from 0 to 5, not suffering from allergy to eating honey and having swallowing reflex were inclusion criteria into the study. The patients were allocated into four equal groups of 30 each by computer-generated, randomly permuted codes (WHO/Geneva).

Ethical Clearence

The research followed the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients. This study was approved by Ethics Committee of Shahrekord University of Medical Science. This study was registered in Iranian Registry of Clinical Trials (IRCT) and achieved the code of IRCT201207086252N3.
**Intervention**

The main intervention in this study was honey and diphenhydramine. The honey used in the present study is produced in Kouhrang, Chaharmahal va Bakhtiari and is commercially available as Kouhrang pure honey in Iran. The diphenhydramine used was a diphenhydramine syrup (Alhavi, Iran) with registry number of 1228048234 in Iran’s pharmacology market.

The patients were randomly assigned to four groups (flow diagram is shown in [Table/Fig-1]). Group A took honey alone every hour with a 5cc dose from beginning of drinking liquids after surgery until midnight (12 pm) if they were conscious. Group B took honey with a 5cc dose from beginning of drinking liquids after surgery until midnight (12 pm) if they were conscious. Group C was taken diphenhydramine every 6 hours with a 5cc dose and Group D was monitored with no intervention. Meanwhile, all groups were given 10mg/kg acetaminophen every 6 hours and its dose and time of prescription were carefully controlled. In all of the patients, severity of the pain was evaluated by a freely usable scale, Oucher scale, at recovery and 3, 6, 12 and 24 hours after surgery. Oucher’s scale is a poster comprised of two scales: for older children, it uses a 0-10 or 0-100 scale, and for younger children, it uses a pictographic scale with six pictures on the right and the numbers 0-10 on the left. On the pictographic scale, the picture selected by the child must be translated to its numerical even value, ranging from 0-10: the lowest score. On the pictogram, the number uttered by the child designates his/her pain score. On the pictogram, the picture selected by the child must be translated to its numerical even value, ranging from 0-10: the lowest score. On the pictogram, the number uttered by the child designates his/her pain score. For younger children, it uses a pictographic scale with six pictures on the right and the numbers 0-10 on the left.**

**Statistical Analysis**

Descriptive statistics, including the mean and standard deviation were used for description of continuous variables. Chi-square test and the analysis of variance (ANOVA and ANCOVA) were employed to test whether the four groups are controlled in terms of respectively age and weight. In addition, comparison of the pain scores, heart rate, and respiratory rate was done by ANOVA in each stage of the study between the four groups. Finally, the repeated measures analysis of variance (ANOVA and ANCOVA) were employed to test whether the four groups are controlled in terms of respectively age and weight. In addition, comparison of the pain scores, heart rate, and respiratory rate was done by ANOVA in each stage of the study between the four groups. Finally, the repeated measures

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**Table/Fig-1**: Flow diagram of enrolment

<table>
<thead>
<tr>
<th>Pain Scale</th>
<th>Stage</th>
<th>Honey alone</th>
<th>Honey 50%</th>
<th>Diphenhydramine</th>
<th>Placebo</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual</td>
<td>Immediately after surgery</td>
<td>2.4 ± 2.2</td>
<td>2.9 ± 2.2</td>
<td>2.6 ± 2.3</td>
<td>2.6 ± 2.2</td>
<td>0.895</td>
</tr>
<tr>
<td>Numeric</td>
<td>Immediately after surgery</td>
<td>47 ± 44</td>
<td>58 ± 34</td>
<td>51 ± 46</td>
<td>62 ± 43</td>
<td>0.816</td>
</tr>
<tr>
<td>Visual</td>
<td>3 hours after surgery</td>
<td>2.3 ± 2</td>
<td>2.5 ± 2.1</td>
<td>2.2 ± 2.2</td>
<td>2.4 ± 1.9</td>
<td>0.973</td>
</tr>
<tr>
<td>Numeric</td>
<td>3 hours after surgery</td>
<td>45 ± 40</td>
<td>50 ± 42</td>
<td>45 ± 45</td>
<td>48 ± 37</td>
<td>0.953</td>
</tr>
<tr>
<td>Visual</td>
<td>6 hours after surgery</td>
<td>1.5 ± 1.7</td>
<td>2.2 ± 2</td>
<td>2.2 ± 2.2</td>
<td>2.8 ± 1.5</td>
<td>0.109</td>
</tr>
<tr>
<td>Numeric</td>
<td>6 hours after surgery</td>
<td>32 ± 32</td>
<td>45 ± 40</td>
<td>45 ± 41</td>
<td>56 ± 32</td>
<td>0.096</td>
</tr>
<tr>
<td>Visual</td>
<td>12 hours after surgery</td>
<td>1.2 ± 1.5</td>
<td>0.4 ± 1.2</td>
<td>0.8 ± 1.7</td>
<td>1.1 ± 1.3</td>
<td>0.157</td>
</tr>
<tr>
<td>Numeric</td>
<td>12 hours after surgery</td>
<td>26 ± 30</td>
<td>9 ± 26</td>
<td>16 ± 33</td>
<td>22 ± 25</td>
<td>0.112</td>
</tr>
<tr>
<td>Visual</td>
<td>24 hours after surgery</td>
<td>1.2 ± 1.4</td>
<td>1.2 ± 1.6</td>
<td>1.8 ± 1.9</td>
<td>1.7 ± 1.7</td>
<td>0.293</td>
</tr>
<tr>
<td>Numeric</td>
<td>24 hours after surgery</td>
<td>25 ± 29</td>
<td>24 ± 32</td>
<td>34 ± 36</td>
<td>37 ± 34</td>
<td>0.311</td>
</tr>
</tbody>
</table>

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**Table/Fig-2**: Pain scores based on numeric and visual scale during the study

**Table/Fig-3**: Respiratory and heart rate during the study, * beats/minute, ** breaths/minute

**Table/Fig-4**: Pain based on visual scale during the study.
ANOVA was used to compare the trend of pain during the study among the groups. The data were analyzed using SPSS (version 17) and p<0.05 was considered as statistically significant.

RESULTS
In this randomized clinical trial study, 120 children assigned to four groups were included. Their mean age was 7.2 ± 2.2 years, with a range of 5 to 12 years. No difference in age was shown between the four groups (p > 0.05). Totally, 53 patients (42.2 %) were female and the four groups were, in relation to gender, matched (p > 0.05). The average weight of patients was 21.6 ± 8.4 Kg (range, 10 - 50 Kg) and there was no significant difference in weight between the groups (p > 0.05).

The results of pain’s scores in the four groups, based on both numeric and visual scales, during the study have been shown in [Table/Fig-2]. [Table/Fig-3] also indicates the results of respiratory and heart rate during the study. Also, the mean of pain scores during the study has been illustrated in [Table/Fig-4,5].

Based on ANOVA, there was no significant difference in pain scores between the groups in terms of both numeric and visual scales. The repeated ANOVA showed a significant decreasing trend in pain scores during the study for both pain scales (p < 0.05), but the trend was similar among all groups (p > 0.05).

A (partially) significant difference in heart rate was shown between the four groups at the beginning, immediately after surgery, 3 hours, 12 hours, and 24 hours post-operatively, as well.

Also, a significant difference between the four groups was shown in terms of respiratory rate at the beginning, immediately after surgery and 24 hours after surgery. A partially significant difference was observed, in this regard, 12 hours post-operatively.

DISCUSSION
Although the intensity of pain in all groups decreased after surgery, honey alone and 50% honey groups experienced more pain relief compared to the other two groups. However, there was no statistically significant difference between honey alone, 50% honey, and diphenhydramine groups. While we found no similar study, to our knowledge, examining the effect of honey alone on post-tonsillectomy pain, some research indicated its relative efficacy in some conditions. Jull et al., for example, showed that honey could be more effective compared to customary dressing in superficial mild to moderate burns [20]. In Ozjuged et al., study on 60 post-tonsillectomy cases, divided into two groups, the first group was administered antibiotic, acetaminophen, and placebo, and the second group was administered antibiotic, acetaminophen, and honey. Their results showed that on the first two postoperative days, the difference between acetaminophen and acetaminophen plus honey groups was statistically significant regarding both visual analogue scale (VAS) and the amount of painkillers used (p < 0.001 for first two days). On the 3rd postoperative day and thereafter, the difference between groups regarding the amount of painkillers taken was significant until the 8th postoperative day (p < 0.001 for first 7 postoperative days, p = 0.003 for 8th day), although the difference regarding the VAS score was not significant (p = 0.05).

Together, that study, relatively consistent with ours, showed that oral honey administration after tonsillectomy in pediatric cases may reduce the need for analgesics via relieving postoperative pain [15]. In addition, Moore et al., suggested honey as an appropriate treatment for superficial wounds and mild burns [21].

In our study, honey alone group and 50% honey group had less pain than the other two groups but the difference was not statistically significant. The reason for this insignificant difference may relate to the evaluation of pain in children whose confliction with pain may not be comprehensible for us. Also, the pain in the present study was evaluated only within 24 hours after surgery.

Pain following tonsillectomy is caused by postoperative inflammation, nerve irritation, and pharyngeal spasm [22]. It is considered that the tonsillary fossa is healed in the form of an open wound after tonsillectomy; therefore, it could be expected that honey accelerates the recovery of wounds and decreases postoperative pain. However, it is not possible to keep honey in continuous contact with the tonsillary fossa as it is a wound dressing. As a result, honey application intervals were kept frequent. Some studies proposed that oral administration of honey in wound healing is much more effective than topical application [23,24]. In addition, 10 mg/kg acetaminophen was given to all four groups for ethical reasons.

CONCLUSION
A lot of studies have been conducted on anti-inflammatory and anti-bacterial effect of honey, but there are not so many about the effect of honey on pain. Our results indicated pain reduction in all four groups. However, more decrease in pain was observed in honey alone and 50% honey groups, but the difference was not statistically significant. Honey with anti-inflammatory effect can decrease the pain although the trend is slower compared to when the drugs that affect the central nervous system are administered. Together, more research is supported for confirmation of the effect of honey on pain relief.

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REFERENCES


Bose B. Honey or sugar in treatment of infected wounds? Lancet. 1982;320(8305):963-64.


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