



The Effect of Gargling Cold Normal Saline in Comparison to Normal Saline Mixed with Honey on Postoperative Pain Relief in Tonsillectomy or Adenotonsillectomy: A Randomized Clinical Trial

Hosnieh Raoufian ¹, Ebrahim Nasiri ^{2,*}, Reza Ghafari³ and Hoshang Akbari⁴

¹Student Research Committee, Faculty of Allied Medical Sciences, Mazandaran University of Medical Sciences, Sari, Iran

²Department of Anesthesiology and Operating Room, Traditional and Complementary Medicine Research Center, Addiction Institute, Faculty of Allied Medical Sciences, Mazandaran University of Medical Sciences, Sari, Iran

³Otolaryngology and ENT Surgery Department, School of Medicine, North Khorasan University of Medical Sciences, Bojnourd, Iran

⁴Department of Anesthesiology, Faculty of Allied Medical Sciences, Mazandaran University of Medical Sciences, Sari, Iran

*Corresponding author: Department of Anesthesiology and Operating Room, Traditional and Complementary Medicine Research Center, Addiction Institute, Faculty of Allied Medical Sciences, Mazandaran University of Medical Sciences, Sari, Iran. Email: rezanf2002@yahoo.com

Received 2019 June 05; Revised 2019 November 06; Accepted 2019 December 10.

Abstract

Objectives: The present study was conducted to compare the effect of gargling normal saline mixed with honey and cold normal saline on postoperative pain relief in children undergoing tonsillectomy or adenotonsillectomy during 2018.

Methods: This clinical trial was performed on 105 children aged 5 - 14 years. The participants were randomly allocated to three 35-member groups, viz. normal saline mixed with honey, cold normal saline, and the control. The patients underwent general anesthesia and then were operated by a single surgeon. Gargle was administered in the first and second groups every six hours up to 48 hours following the surgery. There was no intervention in the control group. The pain was recorded by the Wong-Baker FACES Pain Rating Scale (WBS) at the recovery time and 6, 12, 18, 24, 36, 48 hours and 7 days after the surgery. Data were analyzed using repeated measures ANOVA.

Results: Among the participants, 47 subjects (44.8%) were males and the rest were females, with a mean age of 8.6 ± 2.5 years. The three groups were similar in terms of sex, weight, duration of surgery, and bleeding during surgery. The pain at the site of surgery during both resting and swallowing was different at 6, 12, 18, 24, 36, 48 hours, and 7 days following the surgery ($P < 0.001$).

Conclusions: Gargling cold normal saline and normal saline mixed with honey led to reduced pain after tonsillectomy or adenotonsillectomy; however, the latter had a higher effect on the postoperative pain relief.

Keywords: Tonsillectomy, Pain, Honey, Complementary Therapies

1. Background

Tonsillectomy and adenotonsillectomy are two common surgeries in the ENT (ear, nose, and throat) (1), in which postoperative pain as the major complication occurs during swallowing due to the stimulation of nerve endings in the tonsil bed, throat muscle spasm, and post-ingestion inflammation (2). These surgeries are mostly performed on pediatric age group who are more susceptible to postoperative pain and complications of typical methods of pain management than adults (3).

Despite the emphasis on postoperative pain management, approximately 50% of children still experience severe pain after surgery (4). The usual method of pain control is the use of opioids and non-steroidal anti-inflammatory drugs (NSAIDs) that also have various side effects (5, 6) including weakening of the respiratory sys-

tem, itching, nausea, and vomiting after surgery (7, 8). In other studies, drugs such as dexamethasone, morphine, lidocaine, tramadol, ketamine, and bupivacaine have been used to control postoperative pain, each of which has its own specific side effects (7-9). Accordingly, postoperative pain control in children requires methods with minimum complications and maximum efficiency (10).

One of the non-drug methods is the use of honey for pain control, for which abundant applications have been reported in some studies and in Iranian medicine references (5, 11). Honey is a saturated mixture of fructose, glucose, maltose, sucrose, and other carbohydrates with low water content, which is required for the growth of pathogenic microorganisms. Additionally, honey has antimicrobial properties attributed to its acidic pH and stimulates the growth of cells replacing damaged tissues (12).

Antioxidant, anti-inflammatory, and antibacterial properties, as well as accelerated skin recovery and pain relief are the benefits reported for honey as a natural therapeutic method (5, 13). One of the most effective ways recommended for managing pain is exposure to the cold that contributes to the contraction of superficial blood vessels, organ senselessness, and pain relief by reducing both cell metabolism and need for oxygen in tissues (14, 15).

2. Objectives

The present study sought to compare the effect of gargling normal saline mixed with honey and cold normal saline on the postoperative pain in children undergoing tonsillectomy or adenotonsillectomy during 2018.

3. Methods

The present study is a randomized clinical trial on children aged 5 - 14 years conducted at Imam Hasan (as) Hospital in Bojnourd (Iran) during 2018 - 19. Based on a similar study (16), a sample size of 32 individuals per group was determined using the formula for sample size calculation to compare mean values of the two groups at a confidence level of 95%, a test power of 80%, and a standard deviation of 0.4. The effect of intervention on the pain score was assumed to be at least 0.5 (out of 0 - 5) compared to the control group. Considering a 10% probable drop, a total of 105 patients was randomly assigned to three 35-member groups. Inclusion criteria were elective tonsillectomy/adenotonsillectomy, ASA (American Society of Anesthesiologists) classes I & II, an age range of 5 - 14 years, and written parental consent. Exclusion criteria were bleeding, the need for re-intubation, need for re-operation, first-attempt failure at intubation, hemorrhagic and coagulation disorders, and systemic diseases (e.g., diabetes). Eligible patients were recruited through sequential sampling method. Initially, patients were assigned to normal saline with honey, normal saline cold, and control groups by block randomization method in six items (AABBCC) of each block of the control group (C), normal saline (B), and honey (A). Eighteen blocks were selected randomly. The study group name and patient number were specified from one to 105. Patients' entry numbers (1 - 105) were written outside and group name or intervention type inside and rear an envelope, and when patients referred gradually, the envelope was opened to determine the intervention type. General anesthesia was the same for all the subjects. All surgeries were similar and performed by a single surgeon. Adenoidectomy and tonsillectomy were performed with adenoid curette and cold dissection, respectively. Tonsils were taken by an Allis forceps and then removed from the

bed with Metzenbaum scissors. In the presence of bleeding from tonsils during operation, the suture-ligature technique was applied for the closure of the fistula. The groups consisted of normal saline mixed with honey (honey), cold normal saline (cold), and a control (routine). Honey was obtained from Kouhdasht Co. (Iran) and normal saline 0.9% from the Injection and Pharmaceutical Products Co., Iran. In the honey group, 0.9% normal saline solution (100 ml) was mixed with honey (10 ml). The cold group received 0.9% normal saline solution of 4°C. The above solutions (100 ml) were gargled by patients every 6 hours. There was no intervention in the control group. Patients received no food and liquids at least half an hour before pain assessment.

To control the pain, the three groups received 5 cc of diphenhydramine syrup as usual, and acetaminophen syrup was administered after the surgery every 8 and 6 hours, respectively. The diet of all patients was clear and cold fluids for the first 24 hours, then a soft diet for the next four days, followed by a regular diet. Data were collected using a questionnaire, the validity of which was confirmed by ten faculty members, and its reliability was determined by a Cronbach's alpha of 0.85. The questionnaire included demographic and specific surgical related variables such as sex, age, weight, duration of surgery, intra-operative bleeding, type of surgery (tonsillectomy or adenotonsillectomy), sleep status, parents' satisfaction with intervention, the amount of opioid drug received on the first and second days, and the severity of pain at the recovery period and 6, 12, 18, 24, 36, 48 hours, and 7 days after surgery during rest and swallow. The pain was assessed using Wong-Baker FACES Pain Rating Scale (WBS) with confirmed validity in previous Iranian and international studies, and a reliability of 0.93 measured with Cronbach's alpha (16-18). The WBS consists of two numerical and facial elements ranging from zero for children with a smiling "no-pain" face to 5 for those with a crying face, reflecting "no hurt" and "worst hurt," respectively. According to the scores, the severity of pain was classified into four groups, viz. zero, low (1 & 2), moderate (3 & 4), and high (5) pain. In the first 18 hours and the 7th day after the operation, the pain assessor was a single trained expert who was blind to the type of groups. To avoid patients' awareness of the intervention type, their rooms were separated, and the pain was reported within 24, 36, and 48 h after surgery by the mothers (mothers attended three face-to-face and practical training sessions on pain assessment).

3.1. Statistical Analysis

Sample size was estimated based on a similar study (17). Samples were divided into three groups using block randomization and six blocks were assigned to three groups

of 35 individuals. Since most of the variables were quantitative in this study, data were analyzed using descriptive statistics, including mean, standard deviation, and frequency. Repeated measure statistical test was used to compare quantitative variables in repeated and previous measurements in each group. One-way ANOVA was used to compare continuous numerical variables. Chi-square and Fisher's exact tests were used for categorical variables. Sample size was based on a similar study (19) determined by a calculation formula to compare mean values in independent societies at 95% confidence level with alpha and beta errors of 5% and 20%, respectively, and an expected difference of at least 0.5 for mean pain difference score and sample size. Finally, 32 patients were assigned to each group. The effects of normal saline combined with cold and normal saline on the subjects were examined by repeated measure statistical tests. The effects of normal saline with honey and cold normal saline on postoperative pain, and control treatment were compared between the three groups using the analysis of variance (ANOVA). Scheffe and Dunnett T3 post hoc tests were used to find mean differences between the two groups. A confidence level of 95 was considered in all statistical tests at a significance level of $P < 0.05$. Moreover, SPSS 21 software was used for data analysis. Graphs were drawn with Excel 2010. One-way ANOVA test and Scheffe and Dunnett T3 post hoc test were used according to the central limit theorem, a sample size of 35 subjects (above 30 samples) in each group, and assuming the equality of variance between groups with normal distribution. Interquartile range (IQR) pain in the operative region was calculated. The ITT method was used for analysis.

4. Results

A total of 105 eligible patients was randomly assigned to three 35-member groups (Figure 1), of which 47 (44.8%) subjects were males. The risk factor for all patients was ASA I. The mean age and mean weight of the subjects were 8.6 ± 2.5 years and 26.1 ± 7.5 kg, respectively. The duration of surgery was 41.8 ± 5.5 minutes. The findings revealed no insignificant differences between the three groups in terms of weight, sex, age, and duration of surgery ($P > 0.05$). Generally, 28 (26.7%) and 77 (73.3%) subjects merely underwent tonsillectomy and adenotonsillectomy, respectively, and their frequency was the same in the three groups ($P > 0.078$). The amount of intraoperative bleeding was not significantly different in the three groups ($P > 0.492$). Also, the amount of opioid received on the first day was not different in the three groups. On the second day, none of the patients received opioids (Table 1).

There was no significant difference in the severity of pain during resting at the recovery time; however, there

were significant differences among the three groups at 6, 12, 18, 24, 36, 48 h, and 7 days after surgery ($P < 0.001$). Scheffe's and Dunnett T3 post Hoc test showed significant differences in the pain score between the honey and control groups and between the cold and control groups. Repeated measures ANOVA revealed a higher reduction in the postoperative pain at different stages in the honey and cold groups than the control group ($P < 0.05$) (Figure 2). Median and IQR pain at rest at recovery room and 6, 12, 18, 24, 48 hours, and 7 days after the surgery were 4 (4,5), 4 (4,5), 4 (3,4), 3 (3,3), 3 (2,3), 2 (2,3), and 1 (1,2) respectively.

There were no significant differences in the severity of pain in the three groups during swallowing at the recovery time and 6 hours after surgery, but this difference was significant at 12, 18, 24, 36, 48 h, and 7 days following the surgery ($P < 0.05$). Scheffe's and Dunnett T3 post hoc test confirmed that there were no significant differences in the pain scores between the honey and cold groups at 6, 12, 18, 24, and 36 h after surgery, but the respective difference was significant only 48 h and 7 days after the surgery ($P < 0.021$). Repeated measures ANOVA showed that decreased postoperative pain at different stages was higher in the honey and cold groups than the control group ($P < 0.05$) (Figure 3). Median and IQR pain at swallowing in the recovery room and at 6, 12, 18, 24, 48 hours, and 7 days after surgery were 5 (4,5), 4 (4,5), 4 (3,4), 3 (3,4), 3 (2,3), 2 (2,3), and 1 (1, 3) respectively.

The difference in the intensity of pain at different times showed significant reductions in the pain during resting and swallowing in the honey and cold groups in comparison to the control group (Table 2).

The combination of honey with normal saline was effective and controlled pain better than the other methods. The severity of the frequency percentage of the throat pain during resting and swallowing at 6 and 12 h after surgery was not different among the three groups ($P > 0.080$) while it was different at 18, 24, 36 h, and 7 days after the surgery ($P < 0.001$) (Table 3).

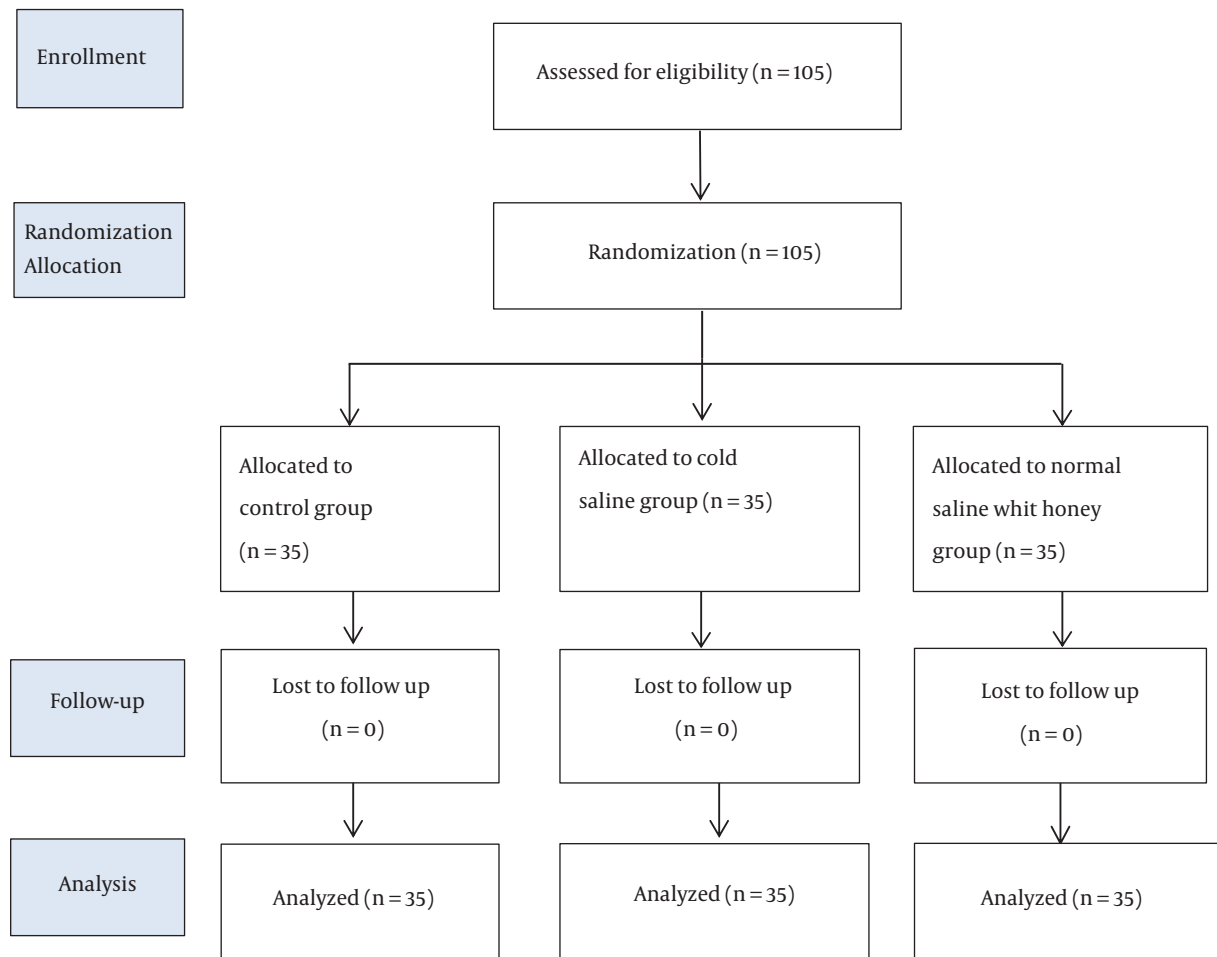
Honey and normal saline groups had no pain 7 days after the surgery, but 80% of the control group had moderate pain (Table 3).

The average satisfaction levels of the parents with the condition of children's recovery and relaxation at 48 h after surgery were 71 ± 11.7 , 69.8 ± 13.6 , and 51 ± 8.2 in the honey, cold, and control groups, respectively, showing a significant difference between the three groups ($P < 0.001$). The satisfaction rate in the honey group was higher than those of the other two groups. Totally, 15 (42.9%), 11 (31.4%), and 9 (25.7%) children in the honey, cold, and control groups, respectively, had good postoperative sleep, indicating a significant difference among the three groups ($P < 0.04$). The throat itching in the three groups was not different in terms of severity (i.e., severe, moderate, and mi-

Table 1. Mean Distribution of Age, Weight, Sex, Duration of Surgery, Frequency, and Frequency of Surgery Type

Groups	Weight ^a	Gender, No.		Age ^a	Duration of Surgery ^a	Surgery Type, %	
		M	F			T	A & T
Honey	42.4 ± 7.6	18	17	8.8 ± 2.7	42.4 ± 4.6	31.4	68.6
Cold	26.8 ± 8.2	17	18	8.6 ± 2.4	42 ± 5.5	25.7	74.3
Control	25.7 ± 6.8	12	23	8.4 ± 3.2	40.9 ± 6.2	22.9	77.1
P value	0.797	0.070		0.745	0.472	0.078	

Abbreviations: T, tonsillectomy; A & T, adenotonsillectomy.

^aValues are expressed as mean ± SD.**Figure 1.** Flowchart of the trial process

nor) ($P > 0.922$). Similarly, the respiratory state of the patients was not different among the three groups ($P > 0.05$). Also, 50 patients (47.6%) had nausea and vomiting at the first 24 h after the operation while the rest did not have such a problem, which was not significantly different between the three groups ($P > 0.233$).

5. Discussion

The results of our study showed that average pain levels in the honey group at the recovery time and 24 h, 48 h, and 7 days after surgery were 4.4 ± 0.5 , 2.3 ± 0.5 , 1.5 ± 0.5 , and 0.43 ± 0.5 , respectively, during resting, and $4.71 \pm$

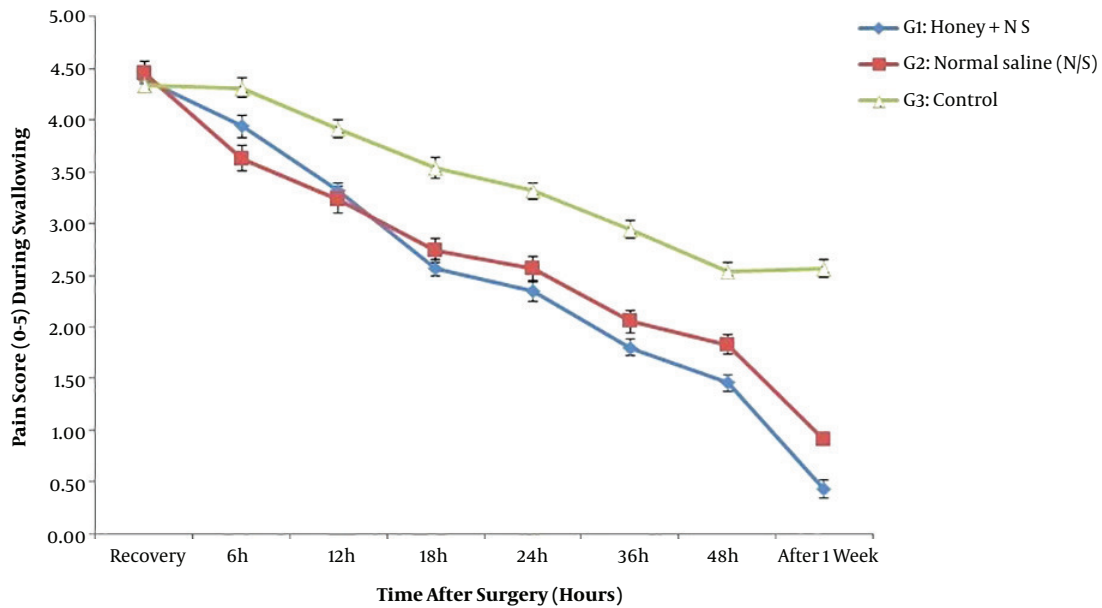


Figure 2. Comparison of mean throat pain during recovery and at 6, 12, 18, 24, 36, 48 h, and 7 days after surgery, divided into three groups at rest

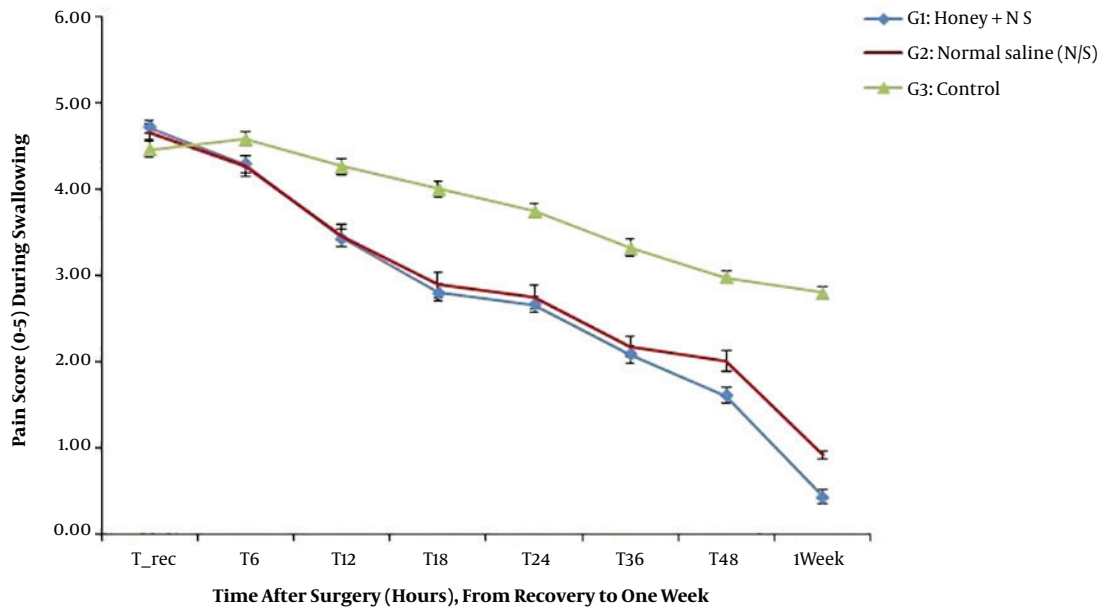


Figure 3. Comparison of mean throat pain at recovery, and at 6, 12, 18, 24, 36, 48 h, and 7 days after the surgery, divided into three groups during the swallowing study

0.5, 2.66 ± 0.5 , 1.6 ± 0.6 , and 0.43 ± 0.5 , respectively, during swallowing. A similar study by Amini et al. also examined the effect of honey on the relief of pain in children at 24 h after tonsillectomy. They reported a higher reduction of postoperative pain in the honey group compared with other study groups, which is consistent with our observa-

tions. A point of difference is that, in addition to considering pain during resting and swallowing in the present study, the follow-up period was one week in which 85% of patients in the honey group had no pain or considerably slight pain on the seventh day postoperatively (17). Likewise, Mohebi et al. compared the impact of honey on re-

Table 2. The Rate of Pain Score Reduction at Different Stages of Measurement During Resting and Swallowing Compared with The Pain at the Recovery Time in the Three Trial Groups

Groups	Time After Surgery ^a						
	6 h	12 h	18 h	24 h	36 h	48 h	7 days
Honey	0.43/(0.5)	1.1/(1.3)	1.8/(1.9)	2.1/(2.1)	2.6/(2.6)	2.9/(3.1)	3.97/(4.2)
Cold	0.8/(0.5)	1.2/(1.2)	1.7/(1.7)	1.8/(1.9)	2.3/(2.5)	2.6/(2.7)	3.49/(3.9)
Control	0.1/(0.1)	0.5/(0.2)	0.9/(0.4)	1.1/(0.7)	1.5/(1.1)	1.9/(1.4)	1.6/(1.6)

^aValues are expressed as resting/(swallowing).

Table 3. Frequency Percentage of Throat Pain Severity at Low, Moderate, and Severe Levels at 6, 24 Hours and 7 Days Postoperatively During Rest and Swallowing

Groups	Frequency of Pain Severity (Low/Moderate/Sever), After Surgery								
	6 Hours (%)			24 Hours (%)			7 Days (%)		
	Low	Moderate	Sever	Low	Moderate	Sever	No pain	Low	Moderate
Resting									
Honey	-	82.9	17.1	62.9	37.1	-	57.2	42.8	-
Cold N/S	2.9	85.7	11.4	42.9	57.1	-	8.6	91.4	-
Control	-	62.9	37.1	-	100	-	-	20	80
Swallowing									
Honey	-	62.9	37.1	37.1	62.9	-	57.1	45.9	-
Cold N/S	-	60	40	40	60	-	8.6	91.4	-
Control	-	52.9	57.1	-	97.1	2.9	0	20	80

duced pain in children after tonsillectomy in honey and control groups and showed that honey was effective in reducing postoperative pain, which is in line with this study; in the former, however, patients received oral honey while in the latter, normal saline mixed with honey was gargled for further contact of honey with the throat mucus (20).

Also, Abdullah et al., who studied the effect of honey on mitigating pain after tonsillectomy, pointed out that pain reduction in the honey group was higher than that in the control group. The main difference between this and the present study is that in the former, the participants received honey orally three times a day while honey was gargled by our subjects every six hours (13). Samdariya et al. investigated the role of honey in lessening pain after radiation-induced mucositis in head and neck cancer patients and concluded that honey significantly decreased the severity of mucositis-associated pain and overall radiotherapy treatment duration. Their results are in agreement with those of the present study, indicating that the use of honey diminishes the pain in damaged biological tissues (21). In a case report, Kalrozi indicated that honey dressing improved head injury resulting from trauma and accident and reduced pain in patients, which is consistent with our results (19). Contrarily, Lavaf et al. reported that honey and phenytoin creams had no effects on the episiotomy wound healing and intensity of pain in nulli-

parous women. This inefficacy was attributed to the depth of episiotomy ulcers in patients, the method of making creams, and their usage (22). Traditionally, honey has a substantial therapeutic and nutritional value, which is the key property of honey due to carbohydrates such as monosaccharide, fructose, and glucose. Honey accelerates and facilitates wound healing, and its antimicrobial and anti-inflammatory properties reduce the ulcer pain, including throat ulcer caused by tonsillectomy/adenotonsillectomy (13).

The present results revealed that average pain levels in the cold group at the recovery time and 24 h, 48 h, and 7 days after surgery were 4.4 ± 0.6 , 2.6 ± 0.7 , 1.8 ± 0.6 , and 0.91 ± 0.3 , respectively, during resting, and 4.69 ± 0.5 , 2.74 ± 0.8 , 2 ± 0.7 , and 0.91 ± 0.3 , respectively, during swallowing. These results agree with those presented by Shin et al. on 40 patients with the aim of determining the impact of cold-water cooling of tonsillar fossa and pharyngeal mucosa on post-tonsillectomy pain. Both studies are similar in terms of the duration of throat pain follow-up, but the pain reduction was different, such that the pain diminished by 3.5 points compared with the first day in the present study while it declined by 3.5 points in their study, indicating that the rate and the amount of decline in pain were more significant probably due to the sample size in the former (15). Moghimi et al. investigated the effectiveness of cryother-

apy on the severity of labor pain in nulliparous women and confirmed the efficacy of cryotherapy on reducing the labor pain in nulliparous women (23). These results are consistent with our study; however, the age range of participants and the type of surgery are different. Gharebagh et al. also studied the effect of cold therapy on knee surgery postoperative-pain. They reported that average pain in the cryotherapy group was significantly different from that in the control group, which is consistent with our findings regarding the effect of local cold on the reduction of pain in the tissues damaged as the result of surgery (24). The efficacy of cryotherapy as an efficient and affordable method for pain management after tonsillectomy and adenotonsillectomy is attributed to the inhibition of awareness of pain by stimulating peripheral nerve receptors and slowing down the rate of pain transmission to the central nervous system, ultimately leading to pain relief. Regarding the results obtained from the present study, the cold and honey groups had considerable postoperative-pain relief at different follow-up times compared with the control group. Moreover, the process of pain reduction was faster in the honey and cold groups. Honey group had better pain management than the cold group with scores of 3.97 and 3.49, respectively, suggesting that the parents in the honey group were more satisfied with the general condition, relaxation, and recovery of their children. Previous studies rarely provided a report on the satisfaction of parents with the interventions. In this regard, only Cheraghi et al. denoted the importance of parents' role and cooperation in assessing and controlling post-tonsillectomy pain (2).

The incidences of complications such as nausea, vomiting, throat itching, and respiratory problems were not different among the examined groups, but the children in the honey group had a better sleep than the cold and control groups. Previous studies only reported results of throat pain and did not present any report on possible complications studied in our trial. Axiomatically, this study also has some limitations, including mothers' non-equal learning in terms of pain assessment. However, it was attempted to minimize this problem by providing mothers with the image of Wong-Baker FACES Pain Rating Scale and face-to-face training on scoring at their children's bedside. One of the strengths of our study was the use of honey gargling and its integration with normal saline containing balanced salt to further control the pain.

5.1. Conclusions

According to our findings, gargling normal saline mixed with honey and cold normal saline led to reduced pain following tonsillectomy and/or adenotonsillectomy; however, the former outperformed the latter in terms of the amount and speed of pain relief at different measurement times after the surgery. The methods used in the

honey and cold groups are more cost-effective, simpler, safer, and more accessible than the control group; furthermore, the respective solutions can be easily used orally. It is, therefore, recommended to use normal saline mixed with honey and cold normal saline after both tonsillectomy and adenotonsillectomy.

Acknowledgments

The kind assistance of the respective deputy, colleagues, and patients who helped us with this study is highly appreciated. This paper was extracted from a M.Sc. thesis by Hosnieh Raoufian, a master student of the operating room and supported by the Deputy of Research and Technology of Mazandaran University of Medical Sciences.

Footnotes

Authors' Contribution: Study concept and design: Ebrahim Nasiri; data acquisition: Hosnieh Raoufian and Reza Ghafari; analysis and interpretation of data: Ebrahim Nasiri and Hoshang Akbari; drafting of the manuscript: Hosnieh Raoufian and Ebrahim Nasiri; critical revision of the manuscript for important intellectual content: Ebrahim Nasiri, Hosnieh Raoufian, Reza Ghafari, and Hoshang Akbari; statistical analysis: Ebrahim Nasiri and Hoshang Akbari; approval of final manuscript: all authors read and approved the final manuscript.

Clinical Trial Registration Code: The study was registered in the Iranian Registry of Clinical Trials (Code: IRCT.20190113042346N1).

Conflict of Interests: The authors declare they have no conflict of interest.

Ethical Approval: The study was approved by the Ethics Committee of the University (Code: IRAN.MAZUMS.REC.1397.3485).

Funding/Support: This paper was supported by the Deputy of Research and Technology of Mazandaran University of Medical Sciences.

References

1. Tuhanioglu B, Erkan SO. Tonsillectomy pain control with IV dexamethasone, infiltrated dexamethasone and infiltrated bupivacaine; a randomised, double-blind, placebo controlled, prospective clinical trial. *J Pak Med Assoc.* 2018;**68**(7):1002-8. [PubMed: 30317291].
2. Cheraghi F, Almasi S, Roshanaee G, Behnud F, Hasan Tehrani T. [Effect of parents training on controlling of pain due to tonsillectomy in hospitalized children: A randomized clinical trial study]. *Avicenna J Nurs Midwifery Care.* 2014;**22**(2):52-63. Persian.
3. Zalzal HG, Makary CA, Evans R, Giardina S, Underwood T, Rowlands A, et al. Using clinical indicators to reduce perianesthesia recovery time following outpatient tonsillectomy. *Ann Otol Rhinol Laryngol.* 2018;**127**(9):620-4. doi: 10.1177/0003489418783226. [PubMed: 29925253].

4. Plunkett A, McCoart A, Howard RS, Dennison E, Bartoszek M. A randomized, single-blind, prospective trial of auricular 'battlefield' acupuncture for the reduction of postoperative tonsillectomy pain in adults. *Pain Manag.* 2018;**8**(4):287-95. doi: [10.2217/pmt-2018-0007](https://doi.org/10.2217/pmt-2018-0007). [PubMed: [29898645](https://pubmed.ncbi.nlm.nih.gov/29898645/)].
5. Meo SA, Al-Asiri SA, Mahesar AL, Ansari MJ. Role of honey in modern medicine. *Saudi J Biol Sci.* 2017;**24**(5):975-8. doi: [10.1016/j.sjbs.2016.12.010](https://doi.org/10.1016/j.sjbs.2016.12.010). [PubMed: [28663690](https://pubmed.ncbi.nlm.nih.gov/28663690/)]. [PubMed Central: [PMC5478293](https://pubmed.ncbi.nlm.nih.gov/PMC5478293/)].
6. Raggio BS, Barton BM, Grant MC, McCoull ED. Intraoperative cryoanalgesia for reducing post-tonsillectomy pain: A systematic review. *Ann Otol Rhinol Laryngol.* 2018;**127**(6):395-401. doi: [10.1177/0003489418772859](https://doi.org/10.1177/0003489418772859). [PubMed: [29776324](https://pubmed.ncbi.nlm.nih.gov/29776324/)].
7. Ruan X, Salinas OJ, Kaye AD. Peritonsillar morphine infiltration to prevent early postoperative pain after tonsillectomy. *Eur J Anaesthesiol.* 2017;**34**(1):47-8. doi: [10.1097/EJA.0000000000000478](https://doi.org/10.1097/EJA.0000000000000478). [PubMed: [27191921](https://pubmed.ncbi.nlm.nih.gov/27191921/)].
8. Sarafraz M, Derakhshandeh V, Nesioonpour S, Araghi S. Efficacy of peritonsillar infiltration of ketamine, tramadol, and lidocaine for prevention of post tonsillectomy pain. *Niger J Med.* 2016;**25**(1):49-52. [PubMed: [29963818](https://pubmed.ncbi.nlm.nih.gov/29963818/)].
9. Moeen SM. Reply to Xin, Juan; Zhang, Yabing; Zhou, Xiaoshuang; Liu, Bin, regarding their comment 'Acupuncture may be an effective supplement treatment for dexamethasone in pediatric tonsillectomy'. *Paediatr Anaesth.* 2017;**27**(2):212. doi: [10.1111/pan.13043](https://doi.org/10.1111/pan.13043). [PubMed: [28101980](https://pubmed.ncbi.nlm.nih.gov/28101980/)].
10. Fayoux P, Wood C. Non-pharmacological treatment of post-tonsillectomy pain. *Eur Ann Otorhinolaryngol Head Neck Dis.* 2014;**131**(4):239-41. doi: [10.1016/j.anorl.2014.07.002](https://doi.org/10.1016/j.anorl.2014.07.002). [PubMed: [25104640](https://pubmed.ncbi.nlm.nih.gov/25104640/)].
11. Mayer A, Slezak V, Takac P, Olejnik J, Majtan J. Treatment of non-healing leg ulcers with honeydew honey. *J Tissue Viability.* 2014;**23**(3):94-7. doi: [10.1016/j.jtv.2014.08.001](https://doi.org/10.1016/j.jtv.2014.08.001). [PubMed: [25187187](https://pubmed.ncbi.nlm.nih.gov/25187187/)].
12. Shahanipour K, Sadeghi M. [The therapeutic effects of Aloe vera and honey on burn wounds in rats]. *J North Khorasan Univ Med Sci.* 2016;**8**(1):71-81. Persian. doi: [10.29252/jnkums.8.1.71](https://doi.org/10.29252/jnkums.8.1.71).
13. Abdullah B, Lazim NM, Salim R. The effectiveness of Tualang honey in reducing post-tonsillectomy pain. *Kulak Burun Bogaz Ihtis Derg.* 2015;**25**(3):137-43. doi: [10.5606/kbbihtisas.2015.00008](https://doi.org/10.5606/kbbihtisas.2015.00008). [PubMed: [26050853](https://pubmed.ncbi.nlm.nih.gov/26050853/)].
14. Frotan R, Saadaty A, Wafaie SM, Reiecy F. [A comparative study on impact of topical cooling and manual pressure before intramuscular injection on pain severity in 5-12 years old children]. *Fez J Kashan Univ Med Sci.* 2006;**10**(3):52-5. Persian.
15. Shin JM, Byun JY, Baek BJ, Lee JY. Effect of cold-water cooling of tonsillar fossa and pharyngeal mucosa on post-tonsillectomy pain. *Am J Otolaryngol.* 2014;**35**(3):353-6. doi: [10.1016/j.amjoto.2014.01.005](https://doi.org/10.1016/j.amjoto.2014.01.005). [PubMed: [24508083](https://pubmed.ncbi.nlm.nih.gov/24508083/)].
16. Alebouyeh MR, Imani F, Golsokhan H, Entezari SR, Sayarifard A. [The analgesic effect of topical tramadol in controlling postoperative pain in children undergoing tonsillectomy or adenotonsillectomy]. *Anesthesiol Pain.* 2015;**4**(3):21-9. Persian.
17. Amani S, Kheiri S, Ahmadi A. Honey versus diphenhydramine for post-tonsillectomy pain relief in pediatric cases: A randomized clinical trial. *J Clin Diagn Res.* 2015;**9**(3):SC01-4. doi: [10.7860/JCDR/2015/9784.5635](https://doi.org/10.7860/JCDR/2015/9784.5635). [PubMed: [25954673](https://pubmed.ncbi.nlm.nih.gov/25954673/)]. [PubMed Central: [PMC4413123](https://pubmed.ncbi.nlm.nih.gov/PMC4413123/)].
18. Ma J, Zheng M, Mu JW, Cui P. The role of hypertonic saline in monopolar tonsillectomy in pediatric patients. *Indian J Otolaryngol Head Neck Surg.* 2018;**70**(2):180-3. doi: [10.1007/s12070-014-0774-7](https://doi.org/10.1007/s12070-014-0774-7). [PubMed: [29977837](https://pubmed.ncbi.nlm.nih.gov/29977837/)]. [PubMed Central: [PMC6015567](https://pubmed.ncbi.nlm.nih.gov/PMC6015567/)].
19. Kalrozi F. [A clinical case report for normal honey wound treatment]. *J Army Nurs Fac.* 2009;**4**(4). Persian.
20. Mohebbi S, Nia FH, Kelantari F, Nejad SE, Hamedi Y, Abd R. Efficacy of honey in reduction of post tonsillectomy pain, randomized clinical trial. *Int J Pediatr Otorhinolaryngol.* 2014;**78**(11):1886-9. doi: [10.1016/j.ijporl.2014.08.018](https://doi.org/10.1016/j.ijporl.2014.08.018). [PubMed: [25193590](https://pubmed.ncbi.nlm.nih.gov/25193590/)].
21. Samdariya S, Lewis S, Kauser H, Ahmed I, Kumar D. A randomized controlled trial evaluating the role of honey in reducing pain due to radiation induced mucositis in head and neck cancer patients. *Indian J Palliat Care.* 2015;**21**(3):268-73. doi: [10.4103/0973-1075.164892](https://doi.org/10.4103/0973-1075.164892). [PubMed: [26600693](https://pubmed.ncbi.nlm.nih.gov/26600693/)]. [PubMed Central: [PMC4617032](https://pubmed.ncbi.nlm.nih.gov/PMC4617032/)].
22. Lavaf M, Simmer M, Mojab F, Majd HA, Samimi M. [Comparison of the effect of honeybee cream and phenytoin cream on severity of episiotomy ulcers in primiparous women]. *J Tradit Med Islam.* 2015;**6**(3). Persian.
23. Moghimi Hanlani S, Mehdizadeh Tourzani Z, Tajvidi M, Baheri B, Lilabadi Asl MP. [The effect of topical cryotherapy on labor pain in primiparous women]. *Iran J Obstet Gynecol Infert.* 2018;**21**(5):14-21. Persian.
24. Gharehbagh R, Najaf Yarandi A, Rezi M, Kamali P. [Cold therapy! How does it effect pain after knee surgery]. *Iran J Nurs.* 2000;**13**(24):33-40. Persian.