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Comparison of the effect of acetaminophen and licorice-based traditional medicine on reducing pain of patients undergoing adenotonsillectomy, a pilot randomized clinical trial study

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***Abstract*---**Introduction: Adenotonsillectomy is one of the common surgeries specifically performed in children. The major complication of this surgery is post-surgery pains. The present study compared the effect of acetaminophen and licorice-based traditional medicine for the

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alleviation pain in patients with adenotonsillectomy. Materials and Method: This single-blinded pilot clinical trial study was carried on 3–15-year-old patients who had undergone tonsillectomy. After the surgery patients of both groups received 10 mg/kg syrup of acetaminophen every six hours for 24 hours. In addition, in the patients of the experimental group, licorice lozenges (with doses of 1000 mg) were administered. Wong-Baker's Faces Pain Scale was used to measure the level of pains. Results: A total of 40 patients were assessed. Friedman test demonstrated that the mean pain of the two groups showed significant reduction (p=0.001). Also, the MannWhitney-U test revealed that the mean pain severity in the licoricereceiving group in 6 (p=0.056), 12 (p=0.02) and 18 (p=0.006) hours after the surgery significantly decreased compared to that of the control group. Conclusion: The level of pain reduction after adenotonsillectomy in the licorice group was significantly higher than that in the control group.

***Keywords*---**adenotonsillectomy, licorice, acetaminophen, pain.

Introduction

Tonsillectomy or adenotonsillectomy is one of the common surgeries specifically carried out in the age group of children (1). This type of surgery is, nowadays, carried out in different forms, each having its own specific complications. The problems that may engender following tonsillectomy or adenotonsillectomy are pains, laryngospasm, airway obstruction, nausea, vomiting and aspiration (2). The major complication of this surgery is post-surgery pains. Pains from tonsillectomy or adenotonsillectomy have been reported in 20-50% of the children who have undergone this surgery (3). Severity of post-surgery pain can increase the consumption of painkillers and cause longer duration of hospitalization, thus affecting the patient's oral swallowing and daily activities. Thus, reducing postsurgery pain can help improve the patient's quality of life (4). Measures to reduce the post-surgery pains may involve local anesthesia or intravenous steroids (5), use of high-dose steroids (6) and diclofenac suppositories (7).

Use of complementary medicine is one of the ways to reduce pain. Licorice is a traditional medicine product which has long been used as a pain-relieving agent because of its sedative, local *anesthetic* and anti-inflammatory properties. Licorice is characterized by anti-inflammatory, anti-bacterial, anti-oxidant and anti-viral as well as expectorant properties (8-10). Licorice compounds apply their antiinflammatory properties by inhibiting the migration of white blood cells to the inflamed region and inhibiting the production of inflammatory intermediaries in the neutrophiles. The use of licorice inhibits the enzyme 11-beta dehydrogenase and increases the blood cortisol levels. This substance may help reduce pain through reducing inflammation (11).

The study by Zareian et al. on the effects of licorice extract on chronic and acute pain in rats concluded that the licorice root had analgesic effects similar to those of the analgesic properties of non-steroid anti-inflammatory drugs, including

Salicylate (12). Other studies have also examined the use of the licorice extract in reducing the pain of patients with irritable bowel in defecation and of those with aphthous ulcer (13, 14). Considering the importance of pain mitigation in patients with tonsillectomy, the present study compared the pain reduction effects of acetaminophen and licorice-based traditional medicine in patients with adenotonsillectomy.

Materials and Procedures

This is a single-blinded pilot clinical trial study which was carried out at the Bu Ali Sina Hospital in 2021. The research population consisted of 3–15-year-old patients who had undergone tonsillectomy. The exclusion criteria were the patients who required re-intubation, bleeding, failed first attempt tracheal intubation, bleeding disorders, systemic diseases such as diabetes, congenital disorders such as developmental delay and drug intolerance, history of taking aspirin 2 weeks before tonsillectomy, history of peritonsillar abscesses, and acute tonsillitis 4 weeks before tonsillectomy.

After giving information of administering the study and acquiring written consent forms from the parents of the qualified patients, the sampling procedures was performed. Initially, demographic and medicinal data were gathered through a questionnaire. Initially, demographic and medicinal data were gathered through a questionnaire. Measured variables were gender, age, weight and presence of postsurgery clinical symptoms such as sore throat, nausea, vomiting and headaches. To examine the level of pains, Wong-Baker's Faces Pain Scale was used. This tool measures the severity of pain in such areas of no hurt (0), hurts little bit (1), hurts little more (2), hurts even more (3), hurts whole lot (4) and hurts worst (5). The Wong-Baker Faces Pain Scale has a numerical and a facial part. The numerical part was used for the children aged 7 and above, while its facial pertained to children who were yet to understand the meaning of a number (children under the age of 7 years) (15). Using the simple random method, the studied samples were randomly placed in two groups: 1) licorice-based traditional medicine group and 2) control group. The patients received no food or liquid for at least half an hour before being examined for pains. The pain examiner was a trained and fixed expert who had no knowledge of the type of the groups. After the surgery and when the patients could eat (usually 6 hours after the surgery), the intervention was carried out by feeding the patients of both groups 10 mg acetaminophen syrup per each kilogram of weight every six hours for 24 hours. In addition, in the patients of the experimental group, licorice lozenges (with doses of 1000 mg) were administered every six hours, with one licorice lozenge pill given to patients with less than 30 kgs and two pills to patients with higher than 30 kgs. This administration was repeated for up to three doses. The licorice lozenge used in this study had been manufactured at an Iranian Faculty of Pharmacy.

The surgery technique in all the patients was the same and the anesthetization technique included nitrous oxide and isoflurane. Tonsillectomy was performed by 24W monopolar suture and electrocautery. All patients received venous dexamethasone of 0.5 to 12 mg/kg. Following the surgery, the patients were asked to use liquids to prevent dehydration. The Wong-Baker Faces Pain Scale was used to measure the pains of the patients after being discharged from

recovery in 6, 12, 18 and 24 hours after the surgery. Data were analyzed with SPSS (Statistical Package for Social Science, Version21) using descriptive statistics (mean, standard deviation and percentage), and analytical tests (MannWhitney-U and Friedman and Kolmogorov-Smirnov test). The confidence level in all statistical tests was 95%.

Wong-Baker Faces Pain Scale

Results

The number of 40 patients, including experiential and control groups, entered this study. Results showed that the mean ages of the experimental and control groups were 10.60±2.63 and 8.65±3.81 years, respectively. The statistical independent t-test did not show a significant difference between the two groups in term of age (p=0.063). However, the girls were the most patients in the two groups. The statistical Chi-Square test did not show a significant difference between the two groups in term of gender (p=0.514). The mean weight of the patients in the experimental and control groups were 38.05±11.36 and 35.15± 16.24 kg, respectively. The statistical independent t-test did not show a significant difference of weight in the two groups (p=0.517). Results showed that although the control group reported the most post-surgery symptoms, the statistical chi-square tests did not show a significant difference of post-surgery in the two groups (Table 1).

Friedman test also demonstrated that the mean pain of the two groups in the studied hours saw a significant reduction (p=0.001). Also, the statistical MannWhitney-U test revealed that the mean pain severity in the licorice-receiving group in 6 (p=0.056), 12 (p=0.02) and 18 (p=0.006) hours after the surgery significantly decreased compared to that of the control group. Meanwhile, in terms of pain severity, the licorice-receiving group and the control group did not show a significant difference in 24 hours following the surgery (p= 0.512) (Table 2).

Table 1: Frequency of post-surgery clinical symptoms in experimental and control groups

Clinical symptoms	Experimental group (n=20) (Number %)	Control group (n=20) (Number %)	P value
Sore throat	0	3(15)	0.107
Nausea	2(10)	1(5)	

Headache	2(10)	0
Sore throat and nausea	0	2(10)
Sore throat and headache	0	3(15)
Nausea and Vomiting	7(35)	4(20)
Sore throat+ nausea + vomiting	0	1(5)
None	7(35)	7(35)

Table 2: Comparison of pain severity of the two groups in 6,12, 18, and 24 hours following the surgery

Group		No.	Mean ± SD	P value
6 hours	Experimental	20	3.25± 0.71	0.056
	Control	20	3.8±0.83	
12 hours	Experimental	20	2.45±0.68	0.02
	Control	20	2.90±0.55	
18 hours	Experimental	20	1.8±0.61	0.006
	Control	20	2.40±0.68	
24 hours	Experimental	20	1.35±0.58	0.512
	Control	20	1.50±0.51	

Discussion and Conclusion

Findings of the present study showed that although pain in both groups saw a reduction in the hours under study, the patients of the experimental group experienced significant reduction of pain in 6, 12 and 18 hours after the surgery compared to the control group. Zareian et al. (2003) studied the analgesic effects of the hydroalcoholic extract of the licorice root in acute and chronic pains. This study which was conducted on rats compared the analgesic effects of the licorice and the analgesic effects of sodium salicylate.

To examine pains, two types of tests, i.e., the tail flick test (to examine the acute pain) and formalin test (to examine the chronic pain) were used. The analgesic effects of 100, 200- and 300-mg/kg concentrations of the body weight, hydroalcoholic extract of the licorice extract with analgesic effects of 300 mg/kg concentrations of the body weight and sodium salicylate were compared as positive control. The findings suggested that the licorice extract and sodium salicylate had reduced the pains in the second stage of the formalin test; however, in the tail flick test, they did not show significant analgesic effects as compared to the control group. A comparison of the analgesic effects of the extract and the analgesic effects of the sodium salicylate indicated the lack of a significant difference between these two substances. It was also found that the analgesic effects of the licorice root were similar to those of the non-steroid antiinflammation drugs, including salicylate (12).

In another study, Rahimian et al. (2011) investigated the effects of licorice on pains and defecation in patients with irritable bowel syndrome. In this doubleblinded randomized controlled clinical trial study, 90 patients with the disease were randomly placed in experimental and control groups. The experimental patients received Nortriptyline tablets and D-reglis tablets (6 tablets in three shifts on a daily basis for 8 weeks), while the control patients received Nortriptyline tablets and placebo, as their defecation was registered by using a questionnaire.

Pain severity was measured by Visual Analog Scale (VAS). Study findings demonstrated that pain severity in both groups (experimental and control) had seen a reduction trend within 8 weeks. However, no significant difference was noted in any of the stages in the two groups (13). Consistent with the present study, results by Rahimian et al. suggested a reduction of pain in the two groups under study. Our study results, however, showed the greater effects of licorice extract in experimental patients. This difference of result can be due to the difference of patients under study and type of their pains. The quality of pain in patients with irritable bowel syndrome, which is a chronic pain, may differ from that of the patients undergoing tonsillectomy, which is an acute pain, and this has made the efficacy of the licorice different. As stated, tonsillectomy is one of the most common surgeries which is carried out by ENT specialists. Post-surgery pains are the serious complications of this disease (5,6, 12).

Post-tonsillectomy and its treatment can be a challenge, as the level of pain and stress the patient suffers from is often underestimated. For this, various traditional methods are usually used to reduce post-tonsillectomy pains. To reduce pains, various chemical drugs are used; however, their undesirable side effects require finding new analgesic compounds, especially medicines of herbal origin. These medicines not only have analgesic effects and produce less unwanted complications, but they are also economical.

Limitations

A limitation of this study was the low volume of the samples due to the outbreak of the COVID-19. It is proposed to do a study with higher sample volumes to examine pain from swallowing and taking rest in patients. To better measure the effects of licorice, it is proposed to give only licorice to one group and only acetaminophen to the other, and to compare the effects of the licorice with other pain-relieving drugs after surgeries.

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

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