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Original Article

Black mulberry syrup on reducing tonsillar hypertrophy and its clinical symptoms: A randomized, double-blind, controlled trial

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Abstract

Background: Chronic tonsillitis can lead to various complications in childhood. Various treatment methods, including pharmaceutical treatments, surgery, and complementary medicine, have been used to treat it. Iranian traditional medicine has mentioned the effects of black mulberry on tonsillitis. Hence, this study aimed to investigate the effects of black mulberry syrup on tonsil hypertrophy.

Methods: This controlled clinical trial study involved 5- to 15-year-old children referred to Bu-Ali Hospital, Sari. First, 76 patients were allocated equally to the intervention or control groups using randomized blocks of four. In a three-week period, the intervention group received black mulberry syrup, whereas the control group received the placebo. Data analysis was done in SPSS Version 20, using Mann–Whitney U and McNemar tests.

Results: The study results revealed significant differences between the intervention and control groups regarding the primary outcomes of the intervention, including the size of the tonsils, oral breathing during sleep, nocturnal snoring, and hypernasal speech (P=0.001). The intervention group showed significant improvement in these symptoms compared to the control group.

Conclusion: The findings of this study suggest that black mulberry syrup effectively alleviated tonsillitis symptoms in the intervention group compared to the control group. In addition, no side effects or drug complications were reported in any study participants.

Keywords: Black mulberry, Tonsillitis, Children, Respiratory, Complementary medicine, Medicinal plants.

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Tonsils, located in the lateral oropharynx, are composed of bundles of lymphatic tissue and serve as a primary defense barrier against pathogens (1, 2). Tonsillitis is a relatively common disease, accounting for 1.3% of childhood visits (3). Often caused by a viral or bacterial infection, this disease has symptoms such as a sore throat before progressing to chronic stages (4). Acute symptoms of tonsillitis include fever, tonsillar exudate, sore throat, and painful anterior cervical lymphadenopathy. Adenotonsillar hypertrophy can cause numerous symptoms and complications, such as mouth breathing, nasal congestion, hypernasal speech, nocturnal snoring, swallowing disturbances, obstructive sleep apnea, sleep disorders, otitis media, and chronic and recurrent sinusitis. In addition, it can lead to complications, such as child growth failure, cardiovascular disease, neurocognitive abnormalities, learning disorders, and behavioral problems in the long run (5). Patients exhibiting signs and symptoms of pharyngitis who are affected by group A streptococci (GAS) based on laboratory tests are typically prescribed antibiotics such as penicillin V (oral), amoxicillin, benzathine penicillin G, and azithromycin (6-8).

Although it is not routinely recommended, tonsillectomy may be considered as a treatment option when the child recurrently suffers from group A streptococcal pharyngitis. Tonsillectomy is usually recommended for pharyngitis, with the frequency of at least 7 episodes in one year or five episodes per year for two years (9). Traditional Iranian medicine, the result of extensive experience accumulated by healers over the centuries, can offer treatment methods for numerous diseases where modern medicine often faces challenges or, in many cases, only provides symptomatic relief (10). Furthermore, the World Health Organization has emphasized the development of traditional medicine (11). In Iranian traditional medicine, there is a vast diversity of medications, and herbal-based pharmaceutical products are generally accessible at relatively low costs within the local area of residence (12).

In addition to antibiotic treatment and surgery, various studies have explored prescribing complementary medicine and herbal remedies to alleviate the symptoms. For instance, in a randomized controlled clinical trial, Di Stadio et al. (13) demonstrated that using Difensil Immuno, containing Sambucus nigra (elderberry), zinc, and vitamins D, E, and C, effectively reduced tonsillitis periods and decreased the size of the tonsils (13). Similarly, Vavilova et al. used an herbal product named Tonsilgon®, composed of marshmallow root, yarrow herb, dandelion flower, chamomile flower, and oak bark, to treat tonsillitis. The results revealed that swollen tonsils decreased in 98% of children of in the intervention group after two weeks of treatment (14). Furthermore, Malapane et al. used lactose tablets containing Atropa belladonna L., calcium sulfide, and calcium phosphate and demonstrated a decrease in tonsil size within six days of treatment (15). The results of another study conducted by Popovych et al. revealed that using an herbal product called BNO1030, composed of marshmallow root, dandelion herb, walnut leaves, oak bark, chamomile flowers, and yarrow herb, improved tonsillitis in children in the intervention group compared to the control group (16). Although these studies highlight the potential efficacy of herbal products in managing tonsillitis, one cannot mention the positive effect of a single plant or herbal product on tonsillitis symptom improvement.

Traditional medicine texts indicate that black mulberry fruit is an herbal remedy that alleviates respiratory problems. According to references in Persian traditional medicine, the combination of black mulberry paste and linseed can effectively treat nighttime snoring and dyspnea in children (17, 18).

Among the other benefits of black mulberry in Iranian traditional medicine, one can mention its use for treating throat inflammation (19), enlarged tonsils (20), sore throat, mouth ulcers, and tongue inflammation (21, 22). Scientific studies have shown that black mulberry is a good source of phenolics, including flavonoids, anthocyanins, and carotenoids. Phenolics possess a wide range of biochemical activities, such as strong antioxidant, antiproliferative, and anti-inflammatory properties. Therefore, products made from black mulberry extract can be utilized in the treatment or prevention of inflammatory diseases and in inhibiting cell proliferation (23, 24).

Moreover, some other books of traditional medicine schools have mentioned the therapeutic effects of black mulberry syrup on treating oropharyngeal diseases, anorexia, and diarrhea (25). Persian traditional medicine textbooks have stated that using black mulberry and its products can treat pharyngitis (19), enlarged tonsils (20), sore throat, mouth ulcers, and swelling of the tongue (21, 22). Based on a review of the national and international databases, we found no clinical trial study investigating the application of black mulberry products for treating enlarged tonsils in humans. Hence, this study aimed to evaluate the effect of black mulberry on reducing the size of hypertrophic tonsils and alleviating the clinical symptoms associated with enlarged tonsils.

Methods

Study design: This study is a double-blind, randomized, controlled clinical trial conducted on 76 5- to 15-year-old children. This study was conducted on eligible patients referred to a specialized clinic in Bu-Ali Hospital, Sari. The Bu-Ali Hospital ENT Specialty Clinic in Sari serves as the referral center for Mazandaran University of Medical Sciences, attracting patients from across the province for treatment. This clinic represents a good sample of Mazandaran's population. After ensuring the eligibility criteria, the principal investigator talked with the patients' parents about the treatment method and duration. Those willing to participate in the study signed an informed consent form and were included in the study. The patients in the intervention group received black mulberry syrup steadily one hour after meals three times a day for 3 weeks, one dessert spoon (3 cc) for those under 10 and one tablespoon (5 cc) for those over 10. All participants and their parents in the study received the necessary instructions. They were advised to avoid having very cold liquids, ice water, ice cream, and vinegar-based or highly acidic products during the treatment period. In addition, they were instructed to follow health protocols to prevent infections, such as colds and viral respiratory diseases. This

included wearing masks outside the home, at school, or in markets, and washing their hands after returning home. In the placebo group, the eligible patients had oral syrup containing water, glucose, and food color in the same way as the intervention group.

Moreover, they received the necessary training on the precautions above. All participants in the study group were provided with a brochure containing the mentioned instructions, along with the contact number of the principal investigator, so they could reach out with any questions regarding the treatment method or report any potential side effects. During the three-week treatment period, weekly follow-up phone calls were made to the parents of both groups to ensure proper medication use and adherence to dietary restrictions and medical recommendations. Moreover, the patient condition, symptoms, and treatment process were controlled, and the potential drug side effects were monitored. Additionally, parents were interviewed weekly about any signs of skin allergies or gastrointestinal intolerance, and the findings were recorded in the patient's file.

Ethical consideration: This study was conducted after the researchers received ethics approval from the Ethics Committee in Medical Research of Mazandaran University of Medical Sciences with the ethics code MAZUMS.REC.1401.066 and ICT number IRCT20220315054291N1. All procedures were in accordance with the Helsinki Code of Ethics. In addition, the parents of the participating children signed the written informed consent.

Plant material: The black mulberry belongs to the Moraceae family and Morus (mulberry) species. This fruit grows in diverse climatic conditions, from tropical to Mediterranean climates, in southwestern Asia, Europe, and Africa (26). Morus is derived from the Latin word 'mora,' meaning late, because the buds of this tree grow very late. There are 24 species and 100 subspecies of mulberry in the world. Morus negra (black mulberry or BlackBerry), Morus alba (white mulberry), and Morus rubra (red mulberry) are three popular subspecies of mulberry, which have been mentioned in various studies for their various medical properties (24). Voucher specimen (1044) is kept in the Herbarium of the Faculty of Pharmacy, Medicinal Plants Research Center, Mazandaran University of Medical Sciences, Sari, Iran.

Medication preparation: The black mulberry plant samples, confirmed by an expert, were provided from Ken district in the north of Tehran. Then, a herbarium sample was prepared, and a number was assigned to it. (Voucher specimen-1044). Black mulberries were washed and sterilized (without heat) for concentration. The extraction was performed using maceration at a temperature below 65°C. The obtained extract was concentrated using an evaporator, and standardization was conducted based on total phenol content and vitamin C levels. According to the traditional medicine texts, honey should be used as an ameliorator for mulberries to minimize any potential side effects of the mulberry produce (27). Therefore, pure concentrated black mulberry extract was mixed with honey from one source and brand from the Lar region so that plant residuals such as pollens were eliminated. Therefore, thyme honey was provided from Lar region and standardized. An edible product containing black mulberry and natural honey was formulated into a syrup for consumption by patients with tonsil hypertrophy by Giah Essence Phytopharm Co. (Gorgan, Iran) The syrup was prepared in a pharmaceutical company named " Giah Essence " with the economic code 411183351865. A placebo syrup containing glucose and food color without an active agent was produced, similar to the original syrup. Both were produced and packaged in 120 cc bottles by the same medicinal plant company.

Inclusion criteria: The inclusion criteria comprised 5- to 15-year-old children diagnosed with tonsil hypertrophy by an otolaryngologist with no history of adenotonsillectomy, and absence of diabetes or severe neurological conditions.

Exclusion criteria: The exclusion criteria included children with acute tonsillitis, tonsil abscess, unstable clinical conditions and use of systemic corticosteroids or antibiotics in the last 4 weeks, allergy to black mulberry, lack of ability to communicate, and unwillingness to cooperate

Sample size calculation: According to the values obtained by Lazim et al. (28), at the confidence level of 0.95, the power test of 0.90, σ1=6.3, σ2=5.7, μ1=98.1, μ2=93.23, and using the following formula the sample size was estimated to be 32 patients in each group. Considering a 20% drop-out rate, the final sample size in each group was determined to be 38.

$$n_i = \frac{[z_{1-\frac{\alpha}{2}} + z_{1-\beta}]^2 (SD_1^2 + SD_2^2)}{(\mu_1 - \mu_2)^2} \quad i = 1,2$$

Instrumentation: To collect the data, we used a demographic-medical information checklist, Brodsky grading scale, and Visual Analog Scale (VAS). The demographic-medical information checklist comprised variables such as age, gender, parent's occupation, and place of residence. The medical information included symptoms onset, tonsil size grade, asymmetry, and redness, purulent secretions, hypernasal speech, nocturnal snoring, and oral breathing during sleep, swallowing disturbance, sore throat, daytime sleepiness, earache, halitosis, cough, and history of

chronic diseases and drug history. Brodsky grading scale was employed to classify the size of the palatine tonsils (29). Table 1 shows the criteria in this scale. The tonsil size in this scale is a clinical grading determined through observation and clinical examination of the oropharynx by an ENT specialist. The evaluation of tonsil size, which is theoretically useful and applicable in estimating tonsil volume, is based on assessing the extent to which the tonsils occupy the oropharyngeal space. In grade zero, the tonsils are located within the tonsillar fossa and do not occupy any space of the oropharyngeal orifice. In grade 1, the tonsils are outside the mentioned fossa but occupy less than 25% of the oropharyngeal orifice's width. In grade 2, the tonsils occupy between 26 to 50% of the oropharyngeal orifice's width, while they occupy between 51 to 75% of the oropharyngeal orifice's width in grade 3. Finally, the tonsils occupy more than 75% of the oropharyngeal orifice's width in grade 4 (29).

The severity of the clinical symptoms, including mouth breathing during sleep, hypernasal speech, nocturnal snoring, and swallowing disturbance, was assessed using the VAS. The intensity was reported by the patient's parents before and after the intervention based on a numerical scale ranging from 0 (least severity) to 10 (highest severity). They marked the score for the severity of each symptom on a continuum of values from 0 to 10 for each variable after follow-up. On this scale, 0 stands for no clinical complaints, 1-3 for mild, 4-6 for moderate, 7-9 for severe, and 10 for extreme complaint for each variable. The assessments were conducted in person at the clinic and recorded in the patient's file.

Table 1. Grading of tonsil size based on the Brodsky scale

Grade	Brodsky Grading scale of tonsillar enlargement
Grade 0	The tonsils are located within the tonsillar fossa
Grade 1	The tonsils extend beyond the tonsillar fossa but occupy < 25% of the oropharyngeal width
Grade 2	The tonsils occupy 26–50% of the oropharyngeal width
Grade 3	The tonsils occupy 51–75% of the oropharyngeal width
Grade 4	The tonsils occupy > 75% of the oropharyngeal width

Random allocation and blinding: The study samples were randomly assigned using random numbers generated by computer software. A total of 19 blocks of 4 participants were created, ensuring that each block included 2 individuals from the intervention group and 2 from the control group. Overall, 76 envelopes were prepared, each containing a designation based on the computer-generated information: the letter "A" (intervention group) and "B" (control group). The envelopes were sequentially numbered from 1 to 76, and the participants were enrolled in the study in sequence, starting with the first eligible patient who met the inclusion criteria and provided written informed consent, continuing until the 76th participant. Allocation to the intervention and control groups was conducted using a double-blind design, so neither the participants nor the treating physician was aware of the type of treatment (medication or placebo). Patients who had the letter "A" were assigned to the intervention group and received mulberry syrup, while those who had the letter "B" were placed in the control group and received the placebo.

Outcomes: In this study, the patient's tonsil grade was considered the primary outcome, and their clinical complaints, such as swallowing disturbance, hypernasal speech, oral breathing during sleep, and nocturnal snoring, were evaluated as the secondary outcome on two occasions (before the intervention and 3 weeks after the intervention). Then, the participants were asked about tonsillectomy surgery on two occasions, i.e., 3 and 12 weeks after starting the intervention. The clinical symptoms of the patients were evaluated twice in person at the clinic (before the intervention and three weeks after the start of the intervention) by an ENT specialist, and the results were recorded in the patients' files. Additionally, inquiries about the decision to undergo tonsillectomy were made at two time points (three weeks and 12 weeks after the start of the intervention), and the outcomes were recorded in the patients' files. Finally, the patients who did not consume more than 10% of the medicine or placebo were excluded from the study. In this study, patient's compliance with drug consumption was assessed by determining the number of remaining products at the end of the third week.

Data analysis: Quantitative variables were described using mean and standard deviation, while the qualitative ones were described using frequency and percentage. To compare the mean size of tonsils in the two groups, we first checked the normality of data distribution using the Shapiro-Wilk test, and the homogeneity of variances was established using Levene's Test. Then, the Mann-Whitney U test was employed to compare the mean size of tonsils in the two groups. In addition, the McNemar test was utilized to compare pre/post-intervention within groups. Data analysis was done using SPSS 20 with a significance level of 0.05 according to the per-protocol method.

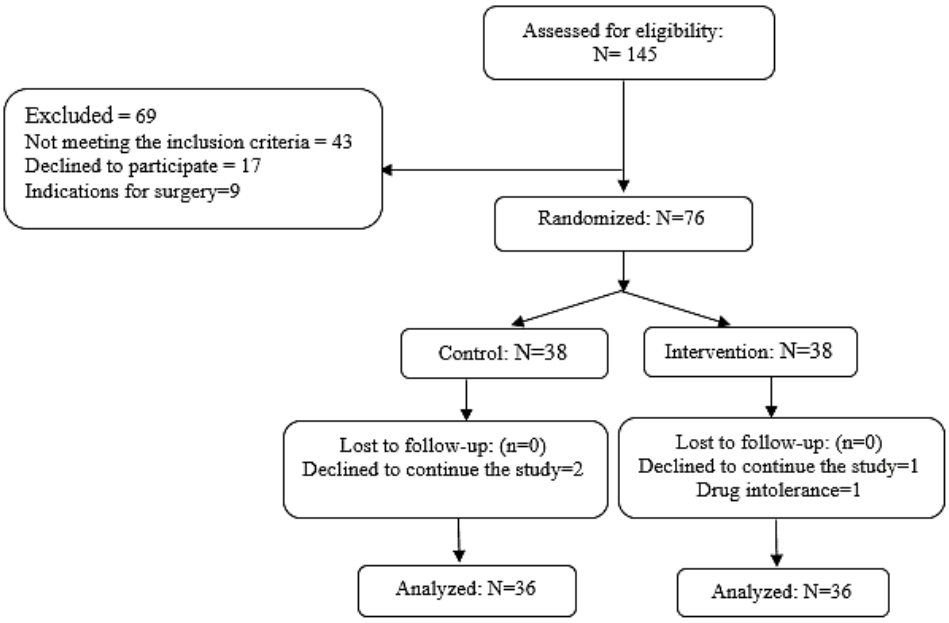

Figure 2. The process of screening, allocation, follow-up, and data analysis

Results

According to the findings, the mean age of the patients was 6.93±2.39 in the intervention group, and 7.47±2.15 in the control group, indicating no statistically significant difference between the two groups (P=0.102). Regarding gender distribution, 23 boys were in the intervention group and 22 in the control group, showing no statistical difference between the two groups (P=0.808). Correspondingly, the mean duration of the disease in the intervention (18.25±20.003) and control (15.63±11.32) groups did not show a significant difference (P = 0.865). According to table 2, there is no statistical difference in the tonsil size between the groups before the intervention, with the mean size of tonsils in the intervention and control groups being 2.69 and 2.58 (P=0.524), respectively. However, after the intervention, a significant difference in tonsil size is observed between the two groups; that is, in the intervention group, the value is 1.92, while it is 2.33 in the control group (P=0.032). A comparison of the changes in the tonsil size before and after the intervention demonstrates a significant difference in the two groups (P=0.001).

Similarly, no statistically significant difference is observed in mouth breathing during sleep between the intervention (7.89) and control (7.81) groups (P=0.794) before the intervention. However, these values have changed to 4.75 and 6.89 in the intervention and control groups after the intervention, showing a significant difference between the two groups (P=0.001). Regarding nocturnal snoring, no statistically significant difference is observed between the intervention and control groups before the intervention; however, after the intervention, a significant difference is noticed (P=0.001). In addition, concerning hypernasal speech, the mean values are 5.58 and 5.39 in the intervention and control groups before the intervention, which does not have a significant difference. On the other hand, these values have changed in the intervention and control groups to 3.08 and 5.47, indicating a more significant decrease in hypernasal speech symptoms in the intervention group. The mean changes in oral breathing, nocturnal snoring, and hypernasal speech after the intervention show a more remarkable change in the intervention group compared to the control, and this difference is significant between the two groups (P=0.001).

On the other hand, no significant difference is observed between the two groups in swallowing disturbance after the intervention (P=0.176).

Similarly, there is no statistically significant difference between them, considering the changes after the intervention compared to before. Table 3 demonstrates that the number of patients in the intervention group experiencing sleepiness has decreased significantly from 16 (44.4%) before treatment to 6 (16.6%) after the intervention (P = 0.002). In the control group, this number has dropped from 18 (50%) to 12 (33.3%) post-intervention (P = 0.031). Regarding fatigue and lethargy, 17 patients (47.2%) in the intervention group experienced these symptoms before treatment, which has decreased significantly to 1 patient (7.2%) afterward (P = 0.001). However, the number has decreased from 15 (41.6%) to 6 (16.6%) in the control group (P = 0.002). In terms of bad breath, 26 patients (72.2%) in the intervention group had reported it before treatment, and this has reduced to 2 patients (5.5%) after the intervention (P = 0.001). In the control group, bad breath has decreased from 25 patients (69.4%) to 16 (44.4%) post-intervention (P = 0.002). Regarding earache, all 11 patients (30.5%) in the intervention group have experienced complete relief after the intervention (P = 0.006), and in the control group, the number decreases from 12 (33.3%) to 1 (2.7%) after intervention (P = 0.001).

The results reveal that the number of patients with dry cough in the intervention group has dropped from 13 (36.1%) before the intervention to 3 (8.3%) afterward (P = 0.012), whereas in the control group, there is a decrease from 8 (22.2%) to 3 (8.3%), though it was not statistically significant. Lastly, regarding cough with phlegm, all 9 (25%) patients in the intervention group experience complete improvement after the intervention (P = 0.021), while the number of cases has decreased from 9 (25%) to 2 (5.5%) in the control group (P = 0.016). The patients were followed up 12 weeks after the start of treatment. According to table 4, a statistically significant difference is observed between the two groups in terms of tonsillectomy rates. In the intervention group, 8 (22.2%) patients have undergone tonsillectomy within 12 weeks, whereas 23 patients (63.9%) in the control group have tonsillectomy (P = 0.001).

Table 2. Comparing the mean tonsil size, mouth breathing, nocturnal snoring, and hyper nasal speech in patients by intervention and control groups

Variable	Stage	Intervention	Control	P-value*
		Mean±SD		
Tonsil size	Before	2.69±0.82	2.58± 0.55	0.524
	After	1.92±0.84	2.33±0.63	0.032
	Before/after changes	-0.78 ± 0.68	-0.25±0.43	0.001
Mouth breathing during sleep	Before	7.89±1.99	7.81±2.57	0.794
	After	4.75±2.47	6.89±2.43	0.001
	Before/after changes	-3.14±2.08	-0.92±1.59	0.001
Nocturnal snoring	Before	7.92±2.46	8.39±2.20	0.325
	After	4.42±2.76	7.44±2.21	0.001
	Before/after changes	-3.50±2.72	-0.94±1.53	0.001
Hypernasal speech	Before	5.58±3.27	5.39±3.32	0.891
	After	3.08±2.72	5.47±3.46	0.001
	Before/after changes	-2.50±2.73	-0.083±0.84	0.001
Swallowing disturbance	Before	1.28±2.35	1.14±2.12	0.918
	After	0.33±1.14	0.89±1.93	0.176
	Before/after changes	0.94±1.95	0.25±1.05	0.130

* Mann Whitney U Test

Table 3. Comparison of the frequency distribution of drowsiness, fatigue and lethargy, halitosis, earache, dry cough, and cough with phlegm before and after the intervention in patients by intervention and control groups

Variable	Intervention group (n=36)		McNemar Test	Control group (n=36)		McNemar Test
	Before	After	P-Value	Before	After	P-value
	Number (percentage)			Number (percentage)		
Sleepiness	16 (44.4)	6 (16.6)	0.002	18 (50)	12 (33.3)	0.031
Fatigue and lethargy	17 (47.2)	1 (2.7)	0.001	15 (41.6)	6 (16.6)	0.002
Halitosis	26 (72.2)	2 (5.5)	0.001	25 (69.4)	16 (44/4)	0.002
Earache	11 (30.5)	0 (0)	0.006	12 (33.3)	1 (2.7)	0.001
Dry cough	13 (36.1)	3 (8.3)	0.012	8 (22.2)	3 (8.3)	0.063
Cough with phlegm	9 (25)	0 (0)	0.021	9 (25)	2 (5.5)	0.016

Table 4. Comparison of tonsillectomy frequency between intervention and control groups 12 weeks after treatment onset

Variable		Group		Total	P-value
		Intervention	Control		
Tonsillectomy 12 weeks after intervention onset	No	28 (77.8)	13 (36.1)	41 (56.9)	0.001
	Yes	8 (22.2)	23 (63.9)	31 (43.1)	
	Total	36 (100)	36 (100)	72 (100)	-

*Chi Square Test

Discussion

The primary approach to treating tonsil hypertrophy typically involves conservative therapies aimed at reducing the severity of symptoms and clinical complaints. These treatments include using corticosteroids (both topical and systemic), decongestants, mucolytics, anti-allergic medications, and antibiotics in more severe cases accompanied by bacterial infection (30). Tonsillectomy should be considered if these treatments prove ineffective or if the patient's symptoms worsen and the size of the tonsils increases despite medical treatments. Tonsillectomy or tonsil removal, as an invasive treatment option, is one of the most common surgical procedures performed in childhood, associated with various complications (31). Sore throat, otalgia, fever, dehydration, and uvular edema are more common postoperative complaints. Less common complications include atlantoaxial subluxation, mandible condyle fracture, infection, eustachian tube injury, and psychological trauma (32). Thus, utilizing an effective herbal product to alleviate the symptoms of tonsil hypertrophy can reduce the need for tonsillectomy, helping to avoid its associated complications, minimize risks, and reduce healthcare costs. The study findings demonstrated a significant relationship between the use of black mulberry products and a decrease in tonsil size in the intervention group. Additionally, treatment with this herbal product led to significant improvement in hypernasal speech problems and a decrease in mouth breathing during sleep and nocturnal snoring in the intervention group compared to the control group.

Regarding the effect of the black mulberry products on the tonsil size, the results of this study showed a decrease in the tonsil size in the intervention group. Although it was observed in both groups, it was greater in the intervention group. Similarly, Vavilova et al. (14) used Tonsilgon® to treat tonsilitis and presented a reduction in tonsil swelling in 98% of children after using it for two weeks. Moreover, Malapane et al. (15) observed a decrease in tonsil size in the intervention group who took lactose tablets for 6 days. Likewise, the findings of the study conducted by Popovych et al. (16) showed that BNO 1030 could improve symptoms caused by swollen tonsils in children in the intervention group. Finally, Bereznoy et al. (33) demonstrated a reduction in swollen tonsils in 6-10-year-old children in the

intervention group after six days of using Pelargonium sidoides for tonsillopharyngitis treatment. All studies mentioned above are in line with the present study.

Different herbal combinations have been used for tonsillitis treatment, and each has positively improved the symptoms of swollen tonsil. However, studies have yet to work on one single herbal product to find its effects on tonsillitis. What distinguishes the present study from other studies is that this study used the black mulberry product to treat tonsillitis without combining it with other herbal or mineral supplements, even vitamins, which is the positive point of this study. Regarding mouth breathing during sleep, this study demonstrated a significant decrease in the intervention group's complaints following the use of black mulberry syrup, supporting the effectiveness of this product in improving oral breathing during sleep. Correspondingly, Klimova et al. (34) used tonsilgon N for a pharyngeal tonsil treatment in children and revealed that nasal breathing at night improved after five days of intervention by 1.4 times in comparison to the control group. In addition, they showed that daytime mouth breathing in the intervention group improved by 15%, 30%, and 73% on days 5, 7, and 9 from the beginning of the intervention, respectively.

This study revealed that swallowing disturbance decreased in both groups after intervention. Although the change in the intervention group was more remarkable, it was not statistically significant. Popovych et al. (16) used BNO 1030 and reported that 16% of the intervention group after 2 days and 77.5% after 10 days of treatment had no pain during swallowing, indicating a statistically significant difference between the two groups. In addition, Malapane et al. (15), who used a lactose tablet to treat tonsilitis symptoms, showed a decrease in swallowing disturbances in the intervention group after 6 days of treatment. Adhvaryu et al. (35) also used the herbal product Kanchnara (a combination of orchid flower, gooseberry, pepper, cashew nut, and ginger) to relieve the symptoms of tonsilitis. They found that this product could improve swallowing disturbances in 77% of study participants in the intervention group. A comparison of the results of these studies and the present study shows that black mulberry syrup was not as effective as herbs, such as BNO 1030 and lactose tablets, in improving swallowing disturbances in patients with tonsillitis.

Finally, 8 (2.22%) patients in the intervention group and 23 (9.63%) patients in the control group underwent tonsillectomy, showing a statistically significant difference between the two groups. However, no similar studies that intervened in the treatment of tonsilitis have specifically investigated the impact of the intervention on tonsillectomy rate. According to the study results, it can be concluded that black mulberry syrup can diminish the symptoms caused by tonsillar hypertrophy in three weeks. The intervention group that received black mulberry syrup experienced a significantly more significant drop in symptoms compared to the control group that used the placebo. Additionally, no adverse effects were reported in the intervention group, indicating the safety of black mulberry syrup in complementary medicine for alleviating symptoms of tonsillar hypertrophy.

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Authors' contribution: All the authors participated in conducting the study. MA. Pourabbasi designed the study, drafted the initial manuscript, obtained the patient consent form, collected data, filed the patient case, prepared a herbarium, and approved the final manuscript. MH. Soleimani, from Giah Essence Phytopharm Co. (Gorgan, Iran), standardized and prepared the black mulberry product. N. Behnampour randomized the patients, analyzed the data, and revised the manuscript. M. Nikkhah confirmed the diagnosis of tonsil hypertrophy in patients, determined the tonsil size, and revised the manuscript. S.S. Yousefi supervised various stages of the study and revised and approved the final manuscript. All authors have confirmed the submitted manuscript and are responding to the study.

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