

Efficacy of the *Peganum harmala* oil versus 1% permethrin shampoo on the treatment of head louse infestation

Abstract

Introduction: Head louse infestation is one of the major public health problems among children worldwide. Several drugs have been developed to treat the infestation. Side effects and drug resistance associated with these drugs limit their applicability. Increasing attention of scientific committees to alternative drugs along with greater effects and lower complications and costs, increase the hope of success for alternative drugs.

Materials and methods: 93 participants (11 men and 82 women) with positively diagnosed with head lice infestation were allocated into two groups using the stratified randomization method. The intervention in one group comprised of *Peganum harmala* oil applied onto the patient's hair and scalp and the hair and scalp being washed after 20 minutes once a day. The procedure was performed on the first three days of week one of intervention (phase 1) and reiterated on the subsequent week (phase 2) in a similar manner. The other group applied permethrin shampoo once in the first week of intervention and once in the second week.

Results: Permethrin shampoo recovered 7 (29.2%) in day 1, 2 (15.4%) in day 2, 2 (25.0%) in day 3 and 28 (73.7%) in day 11 but *Peganum harmala* oil recovered 17 (70.8%) in day 1, 11 (84.6%) in day 2, 6 (75.0%) in day 3 and 10 (26.3%) in day 11 (P-value <0.005).

Conclusion: The clearing effects and side effects of *Peganum harmala* oil and permethrin shampoo are approximately similar in the two-phase application although the oil's clearing and protective effect is greater than that of the shampoo with its effect occurring earlier than that of the shampoo.

Key words: *Peganum harmala*, Persian medicine, Permethrin, Pediculosis.

1- Introduction

Head louse (*Pediculus humanus capitis*) infestation is one of the major public health problems among children worldwide [1]. It affects 6 million to 20 million people annually and approximately costs US\$ 400 million. [2]. At its peak, the disease will be of a far greater prevalence, where the widespread prevalence rate is reported up to 80% in different parts of the world which increases progressively [3-5].

The head louse is a parasite of humans whose adult insects can survive for up to 10 days and fertile eggs up to 3 weeks away from the host. Three types of lice may infect humans: *Pediculus capitis*, *Pediculus corporis*, and *Pediculus pubis*.

Allergic reactions to the poison, stool, or body parts of the lice can continue for 3 to 8 months and cause itching. Itching leads to inflammation and secondary bacterial infections associated with pustules and cervical lymphadenopathy. The primary source of transmission is direct contact with an infested person, but transmission is also common through contaminated devices (e.g., hat or scarf, comb, brush, headset, bed, carpet, etc.).

When a patient complains of pruritus in a certain area without a clear rash, she/he can be suspected of lice infestation. Diagnosis is through locating lice or its eggs in the back of the head. Finding eggs does not suggest an active infestation because the eggs may persist for months after a successful treatment. Nevertheless, living eggs are located about a quarter inch (6.5 mm) from the scalp and are easily detectable through wood light examination [6].

Thus far, several drugs or drug categories have been developed to treat the disease, including dichlorodiphenyltrichloroethane (DDT), lindane, malathion, carbaryl, permethrin, etc. However, the side effects and drug resistance associated with these drugs limit their applicability [7].

In many societies, permethrin 1% stands as the first-line treatment for lice infestation and the most effective lousicide over-the-counter medication, which operates by paralyzing the

respiratory nerves of the lice. Growing eggs do not have a nervous system on the first four days. Insecticides that act on the nervous system tissues should have sustained activity to kill the nits. Permethrin does not eliminate 100% of the nits, and more treatment is achieved by re-administration one week after the first administration [6]. Permethrin 1% has a clinical efficacy of 65% to 95% [6, 8]. However, resistance to all topical drugs, including permethrin, has been demonstrated. Some head lice in the United States are resistant to lindane 1% and Pyrethrins [6].

Ineffective pediculicide compositions, improper use of effective compositions, toxicity considerations, and increased pesticide-resistance of the head lice are among the reasons for the high prevalence of the lice [9]. The severe hardship and difficulty associated with the selection of common local pediculicide drugs have led to an unexpected and emergency situation as well as the spread of resistance in many parts of the world [1]. Increased resistance of the head lice to chemical pediculicide drugs have encouraged communities to replace them with herbal anti-lice drugs for the same purpose [1].

Increasing attention of scientific committees, the World Health Organization, and public attention to alternative drugs and complementary therapies, along with greater effects and lower complications and costs, increase the hope of success for alternative drugs [1]. Therefore, in some countries, research has been initiated to find herbal alternatives. For example, in the Philippines, research was conducted on the *Anona squamosa* leaves, which is easily accessible and inexpensive in the region [10]. Therefore, low cost and availability of the treatment are two important factors in medications.

A significant medicinal herb found in Persian medicine sources is *Peganum harmala*. This plant is termed “*esfand*” and “*espan*” in Persian and “*harmal*” in the Persian medicine books. It is of the family Zygophyllaceae and the scientific name of *Peganum harmala* L. In some scientific sources, it is posited in the family of Rutaceae [11].

Peganum harmala dries moisture and acts as its resolvent (Mohallel in Persian medicine) [12]. It has been described as an effective and experienced remedy for the removal of lice and their eggs [13,14].

Among *Peganum harmala* products, its oil was selected in this study, since it is both recommended in Persian medicine [15] and is a mechanical assistant in the disposal of eggs given the slippery surface it creates. It also enjoys the two main contributors of acceptability, i.e., inexpensiveness and availability.

Therefore, this clinical study was designed to compare the efficacy of permethrin shampoo and *Peganum harmala* oil so that in the event of an appropriate effect for the oil, it can be recommended as an inexpensive and low-risk local therapy for head lice infestation.

2- Materials and methods

2-1- Study population:

People referred to the healthcare centers in Karaj city were examined by the health care provider and physician of each center for the presence of head lice. Those whose diagnosis was positive were re-examined and confirmed by the researcher and if they met the inclusion criteria were enrolled upon signing the written informed consent.

2-2- Sample size calculation:

The sample size was determined as $n=43$ per group, using the comparison of two proportions formula, and considering the pilot study results, type I error of 0.05, power of 80%, and the attrition rate of 20%.

2-3- Inclusion and exclusion criteria:

Inclusion criteria comprised of the presence of adult lice or nymphs at a maximum distance of 1.5 cm from the scalp, no drug or therapeutic treatment applied for the lice in the past four weeks, and the consent of the patient or his/her parents for participation. Pregnant women, children below two years, and individuals with skin lesions on the scalp were excluded. Moreover, the patients were excluded in case they were not available for follow-up, if they used the drugs irregularly, or had an infection or lesion in the head area, or suffered from a cutaneous allergy to *Peganum harmala* oil or permethrin shampoo during the study. According to the severity of the problem, the patients were categorized into three groups:

1. Mild: There are no adult lice and only nits are observable.

2. Moderate: There are fewer than 5 adult lice.
3. Severe: There are more than 5 adult lice.

2-4- Treatment procedure:

Participants were allocated into two groups using the stratified randomization method.

1- *Peganum harmala* oil groupe:

The intervention in one group comprised of *Peganum harmala* oil applied onto the patient's hair and scalp and the hair and scalp being washed after 20 minutes once a day. The procedure was performed on the first three days of week one of intervention (phase 1) and reiterated on the subsequent week (phase 2) in a similar manner.

2- Permethrin shampoo group:

The other group applied permethrin shampoo once in the first week of intervention and once in the second week.

2-5- Prescribing method:

This method of prescribing *Peganum harmala* oil was due to the fact that the response to treatment by this method was very good in the pilot study. Also, the method of prescribing *Peganum harmala* oil was similar in Persian medicine sources. But permethrin shampoo was prescribed according to the common standard pattern of prescription.

2-6- General recommendations:

It was emphasized to both group members that the drug should be used on dry and clean hair. Family members of the participants were also treated with the respective procedure of phase 1 in order to reduce the risk of re-infestation in both groups. Other health cares that were needed to accelerate the treatment process (including rinsing and exposing the tools to sunshine, combing the hair, etc.) were instructed and emphasized to both groups.

2-7- Patient Follow-up:

The efficacy of the intervention was evaluated on days 1, 2, and 3 from the onset of the initial application and one day after the last application through face-to-face examination. The length of the study period was 11 days in both groups.

The number of adult insects and the presence or absence of eggs were controlled in an exact and direct examination of the entire head, especially the back of the head and ears. The result was recorded as complete cure or mild, moderate, and severe infestation.

2-8- Data analysis:

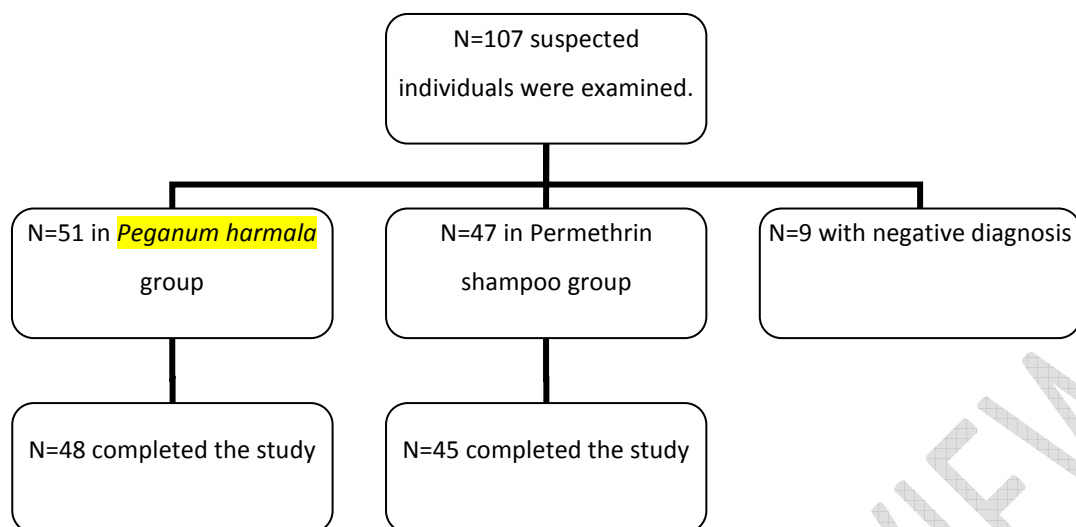
Data were analyzed by SPSS software. Quantitative variables were described using the mean values and standard deviation, and qualitative data using frequency. Quantitative analysis of the variables was performed by independent t-test or paired t-test, and qualitative analysis of the data using Chi-square test. The statistical significance level was considered at 5%.

2-9- Ethics statement:

This clinical trial was carried out in Karaj, Iran, from May to December, 2018. After the protocol of the study was approved in the Ethics Committee affiliated to Iran University of Medical Sciences in 2017 (Number: 93210309006), the study was registered in the clinical trial registry (identifier: IRCT20170825035890N1).

3- Results

In this study, 107 people referred to the health centers and identified as positive or suspected head lice infested victims by the health care provider were examined. Of these, 9 were negative and 98 were positively diagnosed with head lice infestation and thus included in the study. Of the participants, five were excluded from the study for reasons such as travel and migration. In total, 93 patients were enrolled of whom n=45 (48.4%) were in the Permethrin shampoo group and n=48 (51.6%) were in the *Peganum harmala* oil group.



The two groups did not have a significant difference in terms of demographic characteristics and were highly similar. The frequency values of age, gender, and education of the participants are displayed in Table 1. Participants ranged in age from 2 to 52 years with an average of 16.3 ± 12.33 years. Of them, 11 (11.8%) were male and 82 (88.2%) were female.

Table 1. Comparison of frequency of gender, and age range in Peganum harmala oil and permethrin shampoo groups

Variable		Permethrin shampoo group Mean \pm SD	Peganum harmala oil group Mean \pm SD	P-value
Age (year)		15.3 \pm 10.82	18 \pm 13.57	0.295
Gender	Men	6	5	0.754
	Women	39	43	

At baseline, 39 (41.9%) of the patients suffered from mild, 42 (45.2%) from moderate, and 12 (12.9%) from severe head lice infestation. Changes in the disease severity one days before the onset of the intervention, on the first, second and third days of intervention, and one day after the completion of the intervention are shown in Table 2.

Table 2. Comparison of changes in the disease severity in Peganum harmala oil and permethrin shampoo groups

Group	Time point	Baseline	Day 1	Day 2	Day 3	One day after treatment completion
	Status	N (%)	N (%)	N (%)	N (%)	N (%)
Permethrin shampoo	Mild	20(44.4%)	35(77.8%)	35(77.8%)	34 (75.6%)	5 (11.1%)
	Moderate	20(44.4%)	3(6.7%)	1(2.2%)	1 (2.2%)	1 (2.2%)
	Severe	5(11.1%)	0	0	0	0
	Cure	0	7(15.6%)	9(20.0%)	10 (22.2%)	39 (86.7%)
Peganum harmala oil	Mild	19(39.6%)	25(52.1%)	20(41.7%)	15 (31.3%)	3 (6.3%)
	Moderate	22(45.8%)	3(6.3%)	1(2.1%)	1 (2.1%)	1 (2.1%)
	Severe	7(14.6%)	0	0	0	0
	Cure	0	20(41.7%)	27(56.3%)	32 (66.7%)	44 (91.7%)
P-value		0.836	0.02	0.001	0.000	0.703

According to the results of Table 3, the number of cured persons in the oil group is significantly more than that of the shampoo group.

Table 3. Comparison of the frequency of treated and untreated individuals in the first and second weeks in Peganum harmala oil and permethrin shampoo groups

Time point	Status	Peganum harmala oil N (%)	Permethrin shampoo N (%)	P-value
Week 1	Cured	32 (66.7%)	10 (22.2%)	< 0.001
	Uncured	16 (33.3%)	35 (77.8%)	
Week 2	Cured	44 (91.7%)	39 (86.7%)	0.515
	Uncured	4 (8.3%)	6 (13.3%)	

According to Table 4, the greatest efficacy of oil was on day 1 and for the shampoo, in the second week. Moreover, in the oil group, the number of sessions required for treatment was significantly less than that of the shampoo group.

Table 4. Frequency of recovered subjects per day in Peganum harmala oil and permethrin shampoo groups

	Day 1	Day 2	Day 3	Day 11
Peganum harmala oil	17 (70.8%)	11 (84.6%)	6 (75.0%)	10 (26.3%)
Permethrin shampoo	7 (29.2%)	2 (15.4%)	2 (25.0%)	28 (73.7%)
P-value	<0.005			

The mean treatment time in the oil group was 2.2 ± 1.19 days, and in the shampoo group, it was 3.3 ± 1.19 days.

The symptoms of the patients, including itching and burning, were compared before and after intervention in the two groups (Table 5). The difference between the symptoms of the patients in the two groups was not statistically significant before (pv:0.772) and after (pv:0.609) intervention.

Table 5. Comparison of symptoms of patients in Peganum harmala oil and permethrin shampoo groups before and after intervention

	Peganum harmala oil				Permethrin shampoo				P-value
	Asymptomatic	Burning	Itching	Burning and itching	Asymptomatic	Burning	Itching	Burning and itching	
Before intervention	23 (47.9%)	3 (6.3%)	17 (35.4%)	5 (10.4%)	23 (51.1%)	1 (2.2%)	15 (33.3%)	6 (13.3%)	0.772
After intervention	47 (97.9%)	0	1 (2.1%)	0	43 (95.6%)	0	2 (4.4%)	0	0.609

One participant of the *Peganum harmala* oil group mentioned complications such as burning and headache, which was not severe enough to discontinue the drug, and in the shampoo group, two participants suffered from head burning, in both of whom the severity was not significant enough to stop the medication.

4- Discussion

In terms of chemical composition, there are four alkaloids, namely, harmine, harmaline, harmalol, and peganin or vasicine in the root and seeds of *Peganum harmala*. Alkaloid peganin is extracted from the blossoms and stem of *Peganum harmala*. These alkaloids are not toxic in ordinary contact. However, when applied as vapor and smoke, they are effective and can affect aquatic organisms in high concentrations. *Peganum harmala* ripe seeds have about 3.8 to 5.8 percent of the major four alkaloids. Alkaloids in *Peganum harmala* have shown poisonous impacts on a number of lower animals, especially worms and unicellular organisms. Various studies have demonstrated different anti-parasitic effects of alkaloids derived from *Peganum harmala*, including the anti-mildew, antifungal, antibacterial, and insecticidal properties, which are especially found in the root and seeds of the plant [11,16,17].

Oral overdose can have side effects such as abortion, hallucinations, neurosensorial syndromes, bradycardia, and gastrointestinal disorders such as nausea and vomiting, as well as tremor and colonic seizures [11], but no side effects have been reported for its topical application.

According to the Persian medicine literature, a drug to treat lice infestation should be both siccative and resolvent [18] so that it can eliminate skin moisture, which is the essence of the disease, and thus the potential of infestation can be suppressed. *Peganum harmala* is of a hot and dry temperament and is a medicine that cuts abnormal humor off the organ without altering its consistency and a medicine which, due to its moderate heat, serves to dilute thick humor. The temperament of *Peganum harmala* oil is as same as *Peganum harmala*. As the oil also has the above-mentioned properties, it is described as an effective and experienced treatment for the removal of lice and their eggs. Similarly, the root of the plant is beneficial

for the removal of the lice [13,14,18]. Given the fact that this plant is native to Iran and available in different parts of the country [19], it can be used as a suitable treatment for the disease.

Since there are no reports concerning the effectiveness of *Peganum harmala* oil or other products on lice infestation as far as the literature indicates, it is not possible to juxtapose the results of this study and those of other studies. However, in a study by Abdolhosseini et al., the effect of local application of *Squill vinegar* on lice infestation was investigated. In five cases, the problem was completely disappeared; in two cases, the disease was clearly reduced on the seventh and fourteenth days of intervention (75%); and in all cases, itching was relieved [1]. In our study, *Peganum harmala* oil was of a greater impact.

Hucklebach et al. evaluated two products, a combination of *coconut, fennel, and ylang-ylang* oil, and a shampoo containing soy bean oil in a randomized controlled trial. The efficiency rates of the medications were 82% and 62%, respectively [20]. Other studies have investigated the effects of *neem* extract, *Melia azedarach* L oil, *paw paw* herbal shampoo, and *Annona squamosa* seed extract, all of which were found beneficial [21-24].

In this study, the efficacy of *Peganum harmala* oil treatment - as described in Persian medicine books - was compared with standard treatment with permethrin. In future studies, the same dose of the two drugs can be compared.

5- Conclusion

It can be concluded that the **clearing** effects and side effects of *Peganum harmala* oil and permethrin shampoo are approximately similar in the two-phase **application and** also the oil's **preventive** effect is greater than that of the shampoo with its effect occurring earlier than that of the shampoo. However, given the significant difference in the **clearing** effect of *Peganum harmala* oil on the first, second, and third visits, it can be concluded that it is of a higher **clearing** rate and a greater effect on the removal of lice eggs, as the important contributor to the transmission and longevity of lice. Hence, it can reduce the risk of transmission to other people and the re-emergence of the disease in patients undergoing treatment. With regard to the results of the study, it seems that *Peganum harmala* oil can be recommended as a

pediculosis treatment medication, which is effective, more efficient in a shorter time period, and accompanied with fewer complications. Considering the local effects of this medication, it can be speculated that it can also have preventive effects, such that it can be recommended for individuals who are prone to recurrent pediculosis. This hypothesis, however, requires to be tested in a clinical trial and other studies.

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