ClinicalEvidence

Head lice

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ABSTRACT

INTRODUCTION: Head louse infection is diagnosed by finding live lice, as eggs take 7 days to hatch (but a few may take longer, up to 13 days) and may appear viable for weeks after death of the egg. Infestation may be more likely in school children, with risks increased in children with more siblings or of lower socioeconomic group. Factors such as longer hair make diagnosis and treatment more difficult. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of physically acting treatments for head lice? We searched: Medline, Embase, The Cochrane Library, and other important databases up to March 2014 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found six studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review, we present information relating to the effectiveness and safety of the following interventions: 1,2-octanediol, dimeticone, herbal and essential oils, and isopropyl myristate.

QUESTIONS

INTERVENTIONS

Key points

- Head louse infestation is diagnosed by finding live lice. Most eggs take 7 days to hatch (but a few may take longer, up to 13 days), and may appear viable for weeks after death of the egg.

  Infestation may be more likely in school children, with risks increased in children with more siblings or of lower socioeconomic group. Factors such as longer hair make diagnosis and treatment more difficult.

  Anecdotal reports suggest that prevalence during the 1990s has increased in most communities in Europe, the Americas, and Australasia. However, considerable differences are found between countries in terms of the number of products available, dosage form, and active substances used in treatment products.

- For this review, we have focused on the evidence for the efficacy of some of the physically acting topical treatments for head lice and compared these with each other and some of the insecticides. There is interest in this type of treatment as resistance to one or more insecticides that act on the insect nervous system is now common in most developed countries.

  In the US, there are no registered physically acting treatments for head lice (nearly all products being based on insecticides of one form or another), whereas in some countries in Europe (e.g., the UK) almost all treatments sold are currently based on physically acting principles.

  In other European countries, there are varying mixes of physically acting and insecticide-based products available. In Australia, the majority of products are based on plant extracts and essential oils.

  Generally the evidence for physically acting topical head lice treatments is weak. All of the RCTs we found were small and were sponsored by industry.

  Interpretation of the results presents challenges due, for instance, to the variations in the formulations of products containing the same active treatment (e.g., lotions *v* mousses *v* shampoos; other included constituents, such as alcohols and conditioning agents; differing application procedures), reducing the quality of the evidence. Furthermore, there is some question about what exactly constitutes 'physically acting', as different authors describe the actions of some materials in different ways.

- Dimeticone is a silicone and is a physically acting topical treatment working by occlusion. It does not act on the insect nervous system and is unlikely to be affected by resistance to older insecticides.

  Dimeticone seems to be more effective at eradicating head lice compared with malathion or permethrin.

- 1,2-octanediol is a detergent that dissolves some components of the lipid waterproofing layer of the louse cuticle, reducing the ability of the louse to prevent water loss through the cuticle, and resulting in dehydration.

  We found no direct information from RCTs meeting *Clinical Evidence* inclusion criteria on the effectiveness of any commercially available formulation of 1,2-octanediol in people with head lice infestation.

- In general, we don't know whether herbal and essential oils (we evaluated evidence on eucalyptus oil, tea tree oil, and tocopheryl acetate only) are effective at eradicating head lice compared with other treatments, as we found few RCTs. Efficacy is likely to depend upon the compound(s) or extracts used and the mode of action is unclear.
- Isopropyl myristate (a physically acting treatment that may work by occlusion or by dissolving cuticle wax) may be more effective at eradicating head lice than permethrin, pyrethrum, or malathion, although the evidence is weak from a small number of trials.

Clinical context

GENERAL BACKGROUND

Head lice are obligate ectoparasites of socially active humans that infest the scalp and attach their eggs to the hair shafts. Conclusive diagnosis is made by finding live lice. Infestation occurs most frequently in school children and is largely harmless, although sensitisation reactions to louse saliva and faeces may result in localised irritation and erythema and secondary infection of scratches may occur.

FOCUS OF THE REVIEW

There are many different treatment options for head lice. Resistance to one or more insecticides, which have been traditionally used to manage head louse infestation, is now common in most developed countries. Therefore, for this review, we have focused on the evidence for some physically acting topical treatments, for which chemical resistance is not a concern. These treatments kill head lice by a physical rather than a chemical means, such as by occlusion of the louse respiratory system and prevention of excretion of water taken up when lice feed on blood. We have compared these physically acting treatments with each other and with some of the insecticides.

COMMENTS ON EVIDENCE

Generally, the evidence we found was weak. All of the RCTs we found were small and were sponsored by industry. There are variations in the formulations of products containing the same active treatment (e.g., lotions *v* mousses *v* shampoos; other included constituents, such as alcohols and conditioning agents; differing application procedures), which reduces the quality of the evidence. Furthermore, there is some question about what exactly constitutes 'physically acting', as different authors describe the actions of some materials in different ways.

SEARCH AND APPRAISAL SUMMARY

The literature search was carried out in March 2014. For more information on the electronic databases searched and criteria applied during assessment of studies for potential relevance to the review, please see the Methods section. Searching of electronic databases retrieved 71 studies. After deduplication, 28 records were screened for inclusion in the review. Appraisal of titles and abstracts led to the exclusion of 18 studies and the further review of 10 full publications. Of the 10 full articles evaluated, no systematic reviews and six RCTs were included.

ADDITIONAL INFORMATION

The availability of different treatments varies widely between countries. Guideline recommendations in different countries also differ. In the UK, there is a difference in which treatments for head lice are available on prescription compared with over the counter.

DEFINITION

Head lice are obligate ectoparasites of socially active humans. They infest the scalp and attach their eggs to the hair shafts. Itching, resulting from multiple bites, is not diagnostic, but may increase the index of suspicion. Most eggs take 7 days to hatch (but a few may take longer, up to 13 days) and may appear viable for weeks after death of the egg. [1] Therefore eggs glued to hairs, whether hatched (nits) or unhatched, are not proof of active infection. A conclusive diagnosis is made by finding live lice. One observational study compared two groups of children with lice eggs but no lice at initial assessment. [2] Over 14 days, more children with five or more eggs within 6 mm of the scalp developed infestations compared with those with fewer than five eggs. Adequate follow-up examinations using detection combing are more likely to be productive than nit removal to detect and identify the need for treatment of any re-infestation. Infestations are not self-limiting. Various treatment options have been used that can broadly be divided into five groups as follows: topically applied insecticides; topically applied, physically acting agents; topically applied, homeopathic, plant formulations and other remedies; oral drugs; mechanical agents (combs, electronic devices, heating devices). This review focuses on the topically applied, physically acting agents.

INCIDENCE/ PREVALENCE

We found no studies on incidence and few recently published studies of prevalence in resource-rich countries. Anecdotal reports suggest that prevalence has increased during the early 1990s in most communities in Europe, the Americas, and Australasia. A cross-sectional study from Belgium (6169 children aged 2.5–12.0 years) found a prevalence of 8.9%. [3] An earlier pilot study (677

children aged 3–11 years) showed that, in individual schools, the prevalence was as high as 19.5%. [4] One cross-sectional study from Belgium found that head lice were significantly more common in children from families with lower socioeconomic status (OR 1.25, 95% CI 1.04 to 1.47), in children with more siblings (OR 1.2, 95% CI 1.1 to 1.3), and in children with longer hair (OR 1.20, 95% CI 1.02 to 1.43), although hair length may primarily influence the ability to detect infestation. The socioeconomic status of the family was also a significant influence on the ability to treat infestations successfully — the lower the socioeconomic status, the greater the risk of treatment failure (OR 1.70, 95% CI 1.05 to 2.70). [3]

AETIOLOGY/ RISK FACTORS Observational studies indicate that infestations occur most frequently in school children, although there is no evidence of a link with school attendance. [5] [6] We found no evidence that lice prefer clean hair to dirty hair.

PROGNOSIS The infestation is largely harmless. Sensitisation reactions to louse saliva and faeces may result in localised irritation and erythema. Secondary infection of scratches may occur. Lice have been identified as primary mechanical vectors of scalp pyoderma caused by streptococci and staphylococci usually found on the skin. [7]

AIMS OF INTERVENTION To eliminate infestation by killing or removing all head lice and their eggs.

OUTCOMES **Eradication rate** treatment success is given as the percentage of people completely cleared of head lice. This may be reported as proportion of people lice/louse-free at any point in time, or with no live lice present after last treatment. There are no standard criteria for judging treatment success or what constitutes infestation. Trials used different methods, and in some cases the full methodology was not reported. Few studies were pragmatic. **Adverse effects.**

METHODS *Clinical Evidence* search and appraisal March 2014. The following databases were used to identify studies for this systematic review: Medline 1966 to March 2014, Embase 1980 to March 2014, and The Cochrane Database of Systematic Reviews 2014, issue 2 (1966 to date of issue). Additional searches were carried out in the Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA) database. We also searched for retractions of studies included in the review. Titles and abstracts identified by the initial search, run by an information specialist, were first assessed against predefined criteria by an evidence scanner. Full texts for potentially relevant studies were then assessed against predefined criteria by an evidence analyst. Studies selected for inclusion were discussed with an expert contributor. All data relevant to the review were then extracted by an evidence analyst. Study design criteria for inclusion in this review were: published RCTs and systematic reviews of RCTs in the English language, at least single-blinded, and containing 20 or more individuals (10 in each arm), of whom more than 80% were followed up. There was no minimum length of follow-up. We excluded all studies described as 'open', 'open label', or not blinded unless blinding was impossible. We included RCTs and systematic reviews of RCTs where harms of an included intervention were assessed, applying the same study design criteria for inclusion as we did for benefits. In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the MHRA, which are added to the reviews as required. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 15). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the Clinical Evidence population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of physically acting treatments for head lice?

OPTION 1,2-OCTANEDIOL New

- For GRADE evaluation of interventions for Head lice, see table, p 15 .
- We found no direct information from RCTs meeting *Clinical Evidence* inclusion criteria on the effectiveness of any commercially available formulation of 1,2-octanediol in people with head lice (see Comments).

Benefits and harms

1,2-octanediol versus malathion:

We found one three-armed RCT comparing 1,2-octanediol lotion (20% alcohol vehicle) with 0.5% malathion liquid in people with head louse infestation. [8] However, the preparation of 1,2-octanediol used in this trial is a non-standard preparation that is not commercially available (see Comments). An aqueous preparation of 1,2-octanediol is commercially available, but we found no direct information from RCTs meeting *Clinical Evidence* inclusion criteria on the effectiveness of aqueous 1,2-octanediol in people with head lice.

Comment:

We found two RCTs reported in the same paper. [8] The first RCT was a three-armed trial (520 people with confirmed head lice infestation, aged 4 years and older) comparing 1,2-octanediol lotion (in a 20% alcohol vehicle; 2.0–2.5 hour application) with 1,2-octanediol lotion (in a 20% alcohol vehicle; 8 hours/overnight) versus 0.5% malathion liquid (overnight application). [8] We have not extracted data from this RCT in the benefits and harms section because the preparation of 1,2-octanediol used in this study is a non-standard preparation that is not commercially available, but we have included the following comments.

Treatment success was defined in this RCT as elimination of head lice using two applications of treatment 7 days apart, cure, or re-infestation after cure. [8] Both arms using 1,2-octanediol were associated with more successful treatment compared with 0.5% malathion liquid (RR 1.50, 97.5% CI 1.22 to 1.85, at least P <0.025 with 1,2-octanediol lotion left on for 2.0–2.5 hours *v* 0.5% malathion liquid; RR 1.86 97.5% CI 1.54 to 2.26, P <0.0005 with 1,2-octanediol lotion left on for 8 hours/overnight *v* 0.5% malathion liquid). The RCT reported treatment-related adverse events in 21/175 (12%) people with 1,2-octanediol lotion left on for 2.0–2.5 hours compared with 2/171 (2%) people with 0.5% malathion liquid (P = 0.001), and 26/174 (15%) people with 1,2-octanediol lotion left on for 8 hours/overnight, compared with 2/171 (2%) people with 0.5% malathion liquid (P <0.0005). Treatment-related adverse events were described as primarily application site reactions, in which participants experienced some form of short term irritation, variously described as an itchy and 'hot' paraesthesia-like sensation. Such events all passed within 15 to 20 minutes. No serious treatment-related adverse events were reported.

This trial was conducted at three geographically separate study sites in the UK. [8] The success rates for malathion varied at these different sites. The authors commented that this indicates different sensitivities to malathion in the different regions. The second RCT (121 people), reported in the same paper, was another three-armed trial comparing 1,2-octandiol in an alcohol-free aqueous basis (applied for 8 hours/overnight) *v* 1,2-octandiol in an alcohol-free aqueous basis (applied for 2.0–2.5 hours) *v* 1,2-octandiol in 20% alcohol lotion (applied for 2.0–2.5 hours). [8] The aqueous (mousse) formulation applied for 8 hours/overnight was shown to be more effective, with lice eliminated from 31/40 (78%) compared with 24/40 (60%) for the 20% alcohol-based lotion (RR = 1.29, 95% CI 0.95 to 1.75; NNT –5.7). The aqueous (mousse) formulation applied for 2.0–2.5 hours eliminated lice in 17/41 (42%) people compared with 24/40 (60%) for the 20% alcohol-based lotion (RR = 0.69, 95% CI 0.44 to 1.08). Treatment-related adverse events were similar to those recorded in the first RCT and were reported as more frequent with the 20% alcohol-based lotion compared with the aqueous-based mousse (P <0.045). [8]

Both RCTs in this paper were industry sponsored. [8] The competing interest statement reports that the industry sponsors played no active role in the design of the studies, data collection and analysis, interpretation of the results, decision to publish, or the writing of the manuscript itself.

Clinical guide:

Octanediol is essentially a detergent that dissolves some components of the lipid waterproofing layer of the louse cuticle. This reduces the ability of the louse to prevent water loss through the cuticle, resulting in dehydration. [8] Resistance to one or more insecticides is now common. [9] [10] [11] (See Comments for dimeticone, p 4 .) As with many of the treatments for head lice, availability will vary between countries.

OPTION DIMETICONE

- For GRADE evaluation of interventions for Head lice, see table, p 15 .
- Dimeticone seems to be more effective at eradicating lice compared with malathion or permethrin.

- We found no evidence from RCTs about the effects of dimeticone compared with herbal and essential oils, isopropyl myristate, octanediol, spinosad, ivermectin, or pyrethrum.

Benefits and harms

Dimeticone versus malathion:

We found no systematic reviews but we found one RCT comparing dimeticone with malathion. [12] The RCT compared two applications of malathion 0.5% aqueous (applied for 8 hours or overnight) 7 days apart with two applications of dimeticone 4% lotion (applied for 8 hours or overnight) 7 days apart. See Further information on studies.

Eradication rate

Dimeticone compared with malathion Dimeticone seems to be more effective compared with malathion at increasing the proportion of people who are lice-free after the second treatment or with no re-infestation after cure at 14 days (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Eradication rates					
[12] RCT	73 children and adults	**Proportion of lice-free people after the second treatment, or no re-infestation after cure , 14 days** 30/43 (70%) with dimeticone 10/30 (33%) with malathion	ARR –36% 95% CI –60% to –13% P <0.01	○○○	dimeticone

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[12] RCT	73 children and adults	**Adverse effects** with dimeticone with malathion The RCT reported no adverse effects associated with dimeticone 2/30 (7%) people reported itching or irritation of the neck or scalp during treatment with malathion			

Dimeticone versus permethrin:

We found no systematic reviews but we found two RCTs comparing dimeticone with permethrin. [13] [14] The first RCT compared dimeticone 92% lotion applied for 8 hours with permethrin 1% alcoholic lotion applied for 30 minutes (both groups used 2 applications 7 days apart). [13] The second RCT compared 4% dimeticone liquid gel (applied once for 15 minutes) with 1% permethrin creme rinse (applied for 10 minutes, repeated after 7 days). [14]

Eradication rate

Dimeticone compared with permethrin Dimeticone lotion (2 applications, 7 days apart) or liquid gel (single application) seem to be more effective at increasing head lice eradication compared with permethrin alcoholic lotion or creme rinse (2 applications, 7 days apart) following completion of treatment schedule (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Eradication rate					
[13] RCT	145 children aged 5–15 years with head lice	**Proportion louse-free , 7 days (before second treatment)** 47/73 (64%) with dimeticone 43/72 (60%) with permethrin	RR 1.22 95% CI 0.59 to 2.52 P = 0.5 See Further information on studies	⟷	Not significant
[13] RCT	145 children aged 5–15 years with head lice	**Proportion louse-free , 9 days** 70/72 (97%) with dimeticone 48/71 (67%) with permethrin	RR 1.44 95% CI 1.22 to 1.70 P <0.0001 See Further information on studies	●○○	dimeticone
[14] RCT	90 children and adults with confirmed head lice infestation	**Elimination of infestation after completion of treatment regimen , by 14 days** 30/43 (69.8%) with dimeticone liquid gel 7/47 (14.9%) with permethrin creme rinse 'Elimination of infestation after completion of treatment regimen' included cure or cure followed by re-infestation Result for dimeticone comprised 26 cure, 4 re-infestation Result for permethrin comprised 6 cure, 1 re-infestation	OR 13.19 95% CI 4.69 to 37.07 P <0.001 See Further information on studies	●●●	dimeticone

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[13] RCT	145 children aged 5–15 years with head lice	**Ocular irritation due to product running into eyes** 2 people with dimeticone 0 people with permethrin	Significance not reported		
[14] RCT	90 children and adults with confirmed head lice infestation	**Adverse effect considered possibly related to treatment** 1 person with dimeticone 1 person with permethrin Adverse effect reported for dimeticone was dry skin following treatment Adverse effect reported for permethrin was rash on the back of the neck following treatment No adverse effects considered to be serious were reported	Significance not reported		

Further information on studies

[12] This trial was industry sponsored but the competing interest statement reports that the industry sponsors played no active role in the design, execution, or interpretation of the study.

[13] This study was terminated for logistical reasons following the assessment on day 9, which was 5 days fewer than the normal primary endpoint assessment day. This study used 'wet combing with conditioner', which can be used as a treatment intervention, to evaluate efficacy between applications of treatments. It is possible that some of the effect attributed to the combing element of 'bug busting' may actually be caused by the activity of conditioners on head lice and their eggs. A non-RCT has indicated that a conditioner-like formulation was an effective pediculicide if allowed to dry on the hair. [15] A similar effect could occur if combing during 'bug busting' takes long enough. Wet combing with conditioner may cause adverse reactions, which have been observed during normal cosmetic use. [16] [17] [18] [19]

[14] Due to a concern about re-infestation because of contact with another member of the same household who had been randomised to receive a different treatment, a randomisation model was used that ensured all members of the same household were allocated to receive the same treatment. Dry detection combing was used as the assessment method.

[14] This trial was industry sponsored but the acknowledgement statement reports that the industry sponsors played no active role in the design, execution, interpretation of the data, or the preparation of the manuscript.

Comment: Common practice is to treat with two applications of treatment 7 days apart, to ensure elimination of louse nymphs emerging from eggs that were not killed by the first treatment. Most investigators agree that a final examination after 14 days is necessary to determine cure.

Clinical guide:
Dimeticone is a silicone and a physically acting treatment for head lice. It occludes the louse respiratory system and prevents excretion of water taken up when lice feed on blood. [20] It does not act on the insect nervous system and is unlikely to be affected by resistance to insecticides. Resistance to one or more insecticides is now common. [9] [10] [11] All the RCTs were conducted in areas where resistance to insecticides is widespread. [12]

OPTION HERBAL AND ESSENTIAL OILS (EUCALYPTUS OIL, TEA TREE OIL, AND TOCOPHERYL ACETATE)

- For GRADE evaluation of interventions for Head lice, see table, p 15 .
- For this review we evaluated herbal and essential oils containing eucalyptus oil, tea tree oil, and tocopheryl acetate.
- In general, we don't know how effective herbal and essential oils (eucalyptus oil, tea tree oil, and tocopheryl acetate) are at eradicating lice compared with other treatments.
- Herbal and essential oil treatment containing eucalyptol may be more effective at eradicating lice compared with malathion, although we only found one RCT.
- Herbal and essential oil treatment containing tea tree oil (plus lavender oil 1%) may be more effective at eradicating lice compared with pyrethrum (synergised with piperonyl butoxide), although we only found one RCT.
- Herbal and essential oil treatment containing tocopheryl acetate (in a cyclomethicone carrier) may be more effective at eradicating lice compared with permethrin 1% (creme rinse), although we found only one RCT.

Benefits and harms

Herbal and essential oils versus malathion:

We found no systematic review but found one RCT. [21] This RCT (216 children) compared eucalyptol-based shampoo applied for 15 minutes with 1% malathion foam (shampoo) massaged into scalp for 5 minutes and then washed out after 30 minutes. Both were applied on three occasions 1 week apart.

Eradication rate

Herbal treatments compared with malathion Eucalyptol may be more effective than malathion at eradicating head lice at 21 days, although evidence is weak from one RCT. We found no evidence on other herbal products versus malathion (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Eradication rate					
[21] RCT	216 children aged 4–14 years	**Louse free , day 21** 66/106 (62.3%) with eucalyptol 42/104 (40.4%) with malathion	Unadjusted P value = 0.002 Adjusted P value = 0.003 See Further information on studies	○○○	eucalyptol

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[21] RCT	216 children aged 4–14 years	**Adverse events** with eucalyptol with malathion 8/216 children reported adverse events, with similar numbers in both groups; these effects were all mild, transient, and limited to itching or stinging No severe adverse events associated with treatment	P value not reported		

Herbal and essential oils versus permethrin:

We found one RCT (45 people with confirmed head louse infestation), which compared tocopheryl acetate 20% spray (in a cyclomethicone carrier) with permethrin 1% creme rinse. [22] The tocopheryl acetate spray was applied to dry hair, massaged, and left on for 20 minutes, after which time it was washed out with shampoo and the hair was rinsed. The 1% permethrin creme rinse was applied to hair that had been washed and towel-dried, massaged into the hair, and left on for 10 minutes before it was rinsed off with water. Each treatment was repeated after 7 days.

Eradication rate

Herbal treatments compared with permethrin Tocopheryl acetate 20% spray may be more effective than permethrin at eradicating head lice at 14 days, although evidence is weak from one small RCT. We found no evidence on other herbal products versus permethrin (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Eradication rate					
[22] RCT	45 people with confirmed head louse infestation (aged 2–45 years)	**Treatment success , day 14** 13/23 (56.5%) with tocopheryl acetate 5/22 (22.7%) with permethrin Successful treatment was defined as no lice found on days 9 and 14 Analysis was by worst-case analysis (see Further information on studies)	OR 4.42 95% CI 1.21 to 16.21 P = 0.033	●●○	tocopheryl acetate

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[22] RCT	45 people with confirmed head louse infestation (aged 2–45 years)	**Treatment-related adverse events** 1/23 with tocopheryl acetate 1/22 with permethrin Both events were application site events (stinging, itching)			

Herbal and essential oils versus pyrethrum:

We found no systematic review but found one RCT. [23] The RCT (123 primary school-aged children) compared tea tree oil 10% plus lavender oil 1% with pyrethrum 1.65 mg/g synergised with piperonyl butoxide 16.5 mg/g aerosol mousse, both applied for 10 minutes. Tea tree and lavender oil was applied on three occasions 1 week apart. Pyrethrum mousse was applied on two occasions, with 1 week between applications. Lavender oil at 1% is unlikely to have any real effect and is probably included as a fragrance. See Further information on studies.

Eradication rate

Herbal treatments compared with pyrethrum Tea tree oil may be more effective than pyrethrum (synergised with piperonyl butoxide) at eradicating head lice after final treatment, although evidence is weak from one small RCT. We found no evidence on other herbal products versus pyrethrum (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Eradication rate					
[23] RCT **3-armed trial**	123 primary school children aged 4–12 years	**Louse free , day after final treatment** 41/42 (97.6%) with tea tree oil 10/40 (25.0%) with pyrethrum The remaining arm assessed a suffocation product containing benzyl alcohol, mineral oil, polysorbate 80, sorbitan monooleate, Carbopol 934, water, and triethanolamine (n = 45)	P <0.0001	○○○	tea tree oil

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[23] RCT **3-armed trial**	123 primary school children aged 4–12 years	**Treatment-related adverse events** stinging (13 children, 30.2%), flaky scalp/dry scalp (8 children, 18.6%), erythema (4 children, 9.3%) with tea tree oil flaky scalp/dry scalp (3 children, 6.8%), erythema (1 child, 2.3%) with pyrethrum The remaining arm assessed a suffocation product containing benzyl alcohol, mineral oil, polysorbate 80, sorbitan monooleate, Carbopol 934, water, and triethanolamine (n = 45)	P value not reported		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		No severe adverse events associated with treatment			

Further information on studies

[21] This RCT reported adjusted and unadjusted P values. The adjusted P values have taken into account the clustering effect of including participants within families, as siblings were screened and enrolled if found to have head lice.

[21] The conflict of interest statement for this RCT includes that the authors are employed by the pharmaceutical company that sponsored the trial and also manufactures the eucalyptol-containing herbal head lice shampoo being studied.

[22] A worst-case analysis was performed because the randomisation resulted in a high proportion of households in which both treatments were used, resulting in an unexpectedly high level of re-infestation of people receiving the more effective treatment with tocopheryl acetate. This RCT was industry funded. The sponsor played no role in design, interpretation of results, or writing of the manuscript.

[23] This RCT was industry funded. The competing interest statement declares that the funding company had no active role in the design, study management, data analysis, interpretation of results, or manuscript writing.

Comment: **Clinical guide:**
Alcohol and other essential oil based preparations have the potential to cause irritation of excoriated skin. Several essential oil components are considered to be sensitising agents. [24]

A potential for toxic effects has been recognised for several essential oils. [25]

OPTION ISOPROPYL MYRISTATE

- For GRADE evaluation of interventions for Head lice, see table, p 15 .
- Isopropyl myristate may be more effective at eradicating lice compared with permethrin, pyrethrum, and malathion, with similar rates of adverse events, although the evidence is weak from a small number of trials.
- We don't know whether isopropyl myristate is beneficial compared with dimeticone, herbal treatments, 1,2-octanediol, ivermectin, or spinosad, as no RCTs have been found.

Benefits and harms

Isopropyl myristate versus malathion:

We found no systematic review but found one RCT. [26] The RCT compared an occlusive treatment containing isopropyl myristate (IPM), laureth-3, butylene/ethylene/styrene, copolymer, carthamus tinctorius (safflower), and butylated hydroxytoluene with a malathion foam (shampoo) product. Both treatments were administered on three occasions (days 0, 7, and 14) following the manufacturer's recommendations regarding application techniques.

Eradication rate

Isopropyl myristate compared with malathion We don't know if isopropyl myristate is more effective at eradicating head lice compared with malathion foam, as the evidence is weak from a single, small RCT, and almost half the children still had head lice detected at 21 days (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Eradication rate					
[26] RCT	216 primary school-aged children	**Louse free , at day 1** 42/97 (43%) with isopropyl myristate	Unadjusted P value = 0.116 Adjusted P value = 0.143	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		55/101 (55%) with malathion	See Further information on studies		
[26] RCT	216 primary school-aged children	**Louse free , at day 21** 55/102 (54%) with isopropyl myristate 42/104 (40%) with malathion	Unadjusted P value = 0.052 Adjusted P value = 0.024 See Further information on studies	○○○	isopropyl myristate

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[26] RCT	216 primary school-aged children	**Severe adverse events** 1/108 with isopropyl myristate 0/108 with malathion Severe adverse effects associated with isopropyl myristate were erythema, swollen ears, and rash; affected participant was withdrawn from study	P value not reported		
[26] RCT	216 primary school-aged children	**All non-severe adverse events** 2/108 with isopropyl myristate 5/108 with malathion These events included all non-severe adverse effects considered at least remotely or possibly related to study treatment Adverse effects associated with isopropyl myristate were stinging eyes and/or scalp Adverse effects associated with malathion included stinging, dizziness, and pruritus	P value not reported		

Isopropyl myristate versus permethrin:

We found no systematic review but found one RCT. [27] The RCT (168 people) compared IPM 50% (isopropyl myristate/cyclomethicone) with permethrin 1% creme rinse, both applied for 10 minutes on two occasions 7 days apart. See Further information on studies.

Eradication rate

Isopropyl myristate compared with permethrin Isopropyl myristate lotion may be more effective at eradicating head lice compared with permethrin at 14 days, but the evidence is weak from a single, small RCT (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Eradication rate					
[27] RCT	168 people (141 children, 27 adults)	**Eradication rate , 14 days** 91/111 (82%) with isopropyl myristate (IPM) 11/57 (19%) with permethrin	Difference 63% 95% CI 50% to 75% P <0.001	○○○	IPM

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[27] RCT	168 people (141 children, 27 adults)	**Adverse effects** with IPM with permethrin All adverse events considered possibly or probably related, or with an unknown relationship to product, were mild and included rash, nausea, dry skin, eye pain, eczema, headache All events occurred in the IPM/C group	Reported as no significant difference between groups in frequency, duration, or severity of adverse effects	⟷	Not significant

Isopropyl myristate versus pyrethrum:

We found no systematic review but found one RCT. [28] The RCT (60 people) compared isopropyl myristate (IPM) 50% with pyrethrum 0.33% synergised with piperonyl butoxide 4% shampoo, both applied for 10 minutes. IPM was applied on up to three occasions 1 week apart, depending on whether lice were present at an assessment. Pyrethrum shampoo was applied on two occasions with 1 week between applications.

Eradication rate

Isopropyl myristate compared with pyrethrum Isopropyl myristate may be more effective at eradicating head lice compared with pyrethrum shampoo at 14–21 days, but the evidence is weak and from a single, small RCT (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Eradication rate					
[28] RCT	60 children and adults with head lice	**Eradication rate , 7 days** with isopropyl myristate (IPM) with pyrethrum Absolute results reported graphically	P = 0.5 See Further information on studies	⟷	Not significant
[28] RCT	60 children and adults with head lice	**Eradication rate , 14 days** with IPM with pyrethrum Absolute results reported graphically	P = 0.0236 See Further information on studies	○○○	IPM
[28] RCT	60 children and adults with head lice	**Eradication rate , 21 days** with IPM with pyrethrum Absolute results reported graphically	P = 0.0021 See Further information on studies	○○○	IPM

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[28] RCT	60 children and adults with head lice	**Adverse effects** with IPM with pyrethrum All adverse events were reported as being mild, and to have resolved by completion of the study	22 events reported, both treatments "showed similar profiles consistent with those observed for other pediculicides" Significance and P value not reported		

Further information on studies

[26] The published author information includes the name of a pharmaceutical company that is also the name in the paper next to the isopropyl myristate-containing intervention used in the trial.

[26] This RCT reported adjusted and unadjusted P values. The adjusted P values have taken into account the clustering effect of including participants within families, as siblings were screened and enrolled if found to have head lice.

[27] This study reported two smaller RCTs with similar methods analysed as one. The randomisation of the first trial (74 participants) was 1:1 (IPM:permethrin) and that of the second (94 participants) was 4:1 (IPM:permethrin). However, the second RCT was terminated prematurely for commercial reasons.

[27] This RCT was industry funded. The competing interest statement declares that the funding company had no active role in the design, study management, data analysis, interpretation of results, or manuscript writing.

[28] In this RCT all participants were treated on day 0, but were re-treated on either day 7 or day 14, or both, only if lice were found, which made understanding of the outcomes difficult. Six of 60 (10%) people left the study before the endpoints. This study also reported results of a non-RCT proof of concept trial using IPM plus combing.

[28] The published author information includes the name of a pharmaceutical company.

Comment: The RCT comparing isopropyl myristate with pyrethrum [28] mainly reported outcomes as reductions in louse numbers per assessment rather than elimination of infestation. We have only reported people who were free of adult and nymphal lice.

GLOSSARY

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Pragmatic RCT An RCT designed to provide results that are directly applicable to normal practice (compared with explanatory trials that are intended to clarify efficacy under ideal conditions). Pragmatic RCTs recruit a population that is representative of those who are normally treated, allow normal compliance with instructions (by avoiding incentives and by using oral instructions with advice to follow manufacturers' instructions), and analyse results by 'intention to treat' rather than by 'on treatment' methods.

Scalp pyoderma Scalp pyoderma involves impetigo-like bacterial infections that result from scratching. In most cases they are caused by streptococci, with some staphylococcal involvement. Scalp pyoderma of this type is closely associated with long-term louse infestation.

SUBSTANTIVE CHANGES

1,2-octanediol: New option. Categorised as 'unknown effectiveness'.

Dimeticone One RCT added. [14] Categorisation unchanged (likely to be beneficial).

Herbal and essential oils (eucalyptus oil, tea tree oil, and tocopheryl acetate) Title clarified (evidence focused on eucalyptus oil, tea tree oil, and tocopheryl acetate). Three RCTs added. [21] [22] [23] Categorisation unchanged (unknown effectiveness).

Isopropyl myristate One RCT added. [26] Categorisation unchanged (likely to be beneficial).

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Competing interests: IFB is the -author of a number of references cited in this review, all of which were industry sponsored. IFB has been a consultant to various makers of pharmaceutical products, alternative therapies, and combs for treating head louse infections. PS is a Clinical Trials Consultant at the Insect Research & Development/The Medical Entomology Centre at Cambridge.

Disclaimer

GRADE **Evaluation of interventions for Head lice.**

Important outcomes			Eradication rate						
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of physically acting treatments for head lice?									
1 (73) [12]	Eradication rate	Dimeticone versus malathion	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
2 (235) [13] [14]	Eradication rate	Dimeticone versus permethrin	4	–1	0	0	0	Moderate	Quality point deducted for early termination of one of the RCTs at 9 days
1 (216) [21]	Eradication rate	Herbal and essential oils versus malathion	4	–1	0	–1	0	Low	Quality point deduced for weak methods (all of the authors were employees of the pharmaceutical company that funded the trial); directness point deducted for unclear generalisability of the single specific essential oil
1 (45) [22]	Eradication rate	Herbal and essential oils versus permethrin	4	–1	0	–1	0	Low	Quality point deducted for sparse data; directness point deducted for unclear generalisability of the single specific essential oil
1 (123) [23]	Eradication rate	Herbal and essential oils versus pyrethrum	4	–1	0	–1	0	Low	Quality point deducted for sparse data; directness point deducted for unclear generalisability of the single specific essential oil
1 (216) [26]	Eradication rate	Isopropyl myristate versus malathion	4	–1	0	–1	0	Low	Quality point deducted for weak methods (published author information includes the name of a pharmaceutical company that is also the name next to the isopropyl myristate-containing intervention used in the trial); directness point deducted due to intervention containing various other chemicals
1 (168) [27]	Eradication rate	Isopropyl myristate versus permethrin	4	–1	0	–1	0	Low	Quality point deducted for sparse data; directness point deducted for early termination of 1 RCT
1 (60) [28]	Eradication rate	Isopropyl myristate versus pyrethrum	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results

We initially allocate 4 points to evidence from RCTs, and 2 points to evidence from observational studies. To attain the final GRADE score for a given comparison, points are deducted or added from this initial score based on preset criteria relating to the categories of quality, directness, consistency, and effect size. Quality: based on issues affecting methodological rigour (e.g., incomplete reporting of results, quasi-randomisation, sparse data [<200 people in the analysis]). Consistency: based on similarity of results across studies. Directness: based on generalisability of population or outcomes. Effect size: based on magnitude of effect as measured by statistics such as relative risk, odds ratio, or hazard ratio.