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Interventions for treating headlice

Ciara S Dodd¹

¹Cardiff School of Biosciences, Cardiff University, Cardiff, UK

Contact address: Ciara S Dodd, Cardiff School of Biosciences, Cardiff University, PO Box 915, Cardiff, CF10 3TL, UK.
DoddCS@cardiff.ac.uk.

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ABSTRACT

Background

Infection with head lice is a widespread condition in developed and developing countries. Infection occurs most commonly in children, but also affects adults. If left untreated the condition can become intensely irritating and skin infections may occur if the bites are scratched.

Objectives

The aim of this review was to assess the effects of interventions for head lice.

Search methods

Cochrane Infectious Diseases Group specialized trials register (July 2002); The Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 2, 2002); MEDLINE and TOXLINE (1966 to July 2002); EMBASE (1980 to May 2002); LILACS (July 2002); Science Citation Index (1981 to July 2002); BIOSIS (1985 to July 2002); reference lists of relevant articles; pharmaceutical companies producing pediculicides (published and unpublished trials); UK and US Regulatory Authorities.

Selection criteria

Randomised trials (published and unpublished) or trials using alternate allocation were sought which compared pediculicides with the same and different formulations of other pediculicides, and pediculicides with physical methods.

Data collection and analysis

Of the 71 identified studies, only four met the inclusion criteria. Two reviewers independently assessed trial quality. One reviewer extracted the data.

Main results

We found no evidence that any one pediculicide has greater effect than another. The two studies comparing malathion and permethrin with their respective vehicles showed a higher cure rate for the active ingredient than the vehicle. Another study comparing synergised pyrethrins with permethrin showed their effects to be equivalent. A comparative trial of malathion lotion vs combing, showed combing to be ineffective for the curative treatment of head lice infection. Adverse effects were reported in a number of trials and were all minor, although reporting quality varied between trials.

Authors' conclusions

Permethrin, synergised pyrethrin and malathion were effective in the treatment of head lice. However, the emergence of drug resistance since these trials were conducted means there is no direct contemporary evidence of the comparative effectiveness of these products. The 'best' choice will now depend on local resistance patterns. Physical treatment methods (BugBusting) were shown to be ineffective to treat head lice. No evidence exists regarding other chemical control methods such as the use of herbal treatments, when used in the curative treatment of head lice. Future trials should take into account the methodological recommendations that arise from this review.

PLAIN LANGUAGE SUMMARY

Synopsis pending.

BACKGROUND

Infection with head lice is widespread and is common in children, but also affects adults, in both developed and developing countries. Head lice infections can be unpleasant as they become intensely irritating, and if left untreated, skin infections may occur if the bites are scratched. Social attitudes to head lice infection vary greatly between societies and even within different segments of a community. In many western societies, parents are often ashamed if their children have lice, because of the common misconception that the infection is associated with being unclean. In some other societies, infection with lice is seen as normal.

The cost of treating head lice infections is high. It has been estimated that in the USA the annual cost is \$367 million, which includes the amount spent on over the counter pediculicides as well as the cost to the school system (Clore 1990). In developed countries, these OTC pediculicides are expensive, which may cause difficulties for low income earners, especially if several members of the family need to be treated at the same time. In developing countries products are often not available, and when they are, they are often prohibitively expensive. In these circumstances, people may use cheaper or traditional treatments instead; in some cases, people have used low grade agricultural insecticides, which can be fatal (Wohlfahrt 1982).

NATURAL HISTORY

Human head lice (*Pediculus humanus capitis*) are external parasites of man with an obligatory blood-feeding habit, which requires them to feed on their host's blood several times each day. They are normally found on the scalp, but have also been known to occur on the eyebrows. Infection is spread from one person to another only by relatively prolonged head to head contact and so typically occurs between people who know each other well. Burgess (1996) estimates that it takes at least 30 seconds for lice to move from

one head to another, therefore fleeting contact will be insufficient for lice to be transferred between heads. Lice which are observed on chair backs, pillows, hats and other locations are either dead, sick, elderly or are cast skins of lice, all of which are incapable of infecting a person.

Diagnosis of head lice infection is by the presence of live lice on the scalp. Simply finding eggs is insufficient for a diagnosis as these may not be viable. In addition, the nits (hatched and empty egg shells) may be mistakenly identified by the untrained eye as viable embryonated eggs.

Once a person has contracted head lice, the infection develops steadily if left unchecked. The female louse mates within a couple of days of moulting to an adult and begins egg laying soon after. The eggs are deposited on a hair, and attached close to the scalp by a glue-like glandular discharge secreted by the female louse. The eggs hatch in 6-9 days and the nymphs feed soon after emergence. There are three nymphal instars, each of which is completed in three to five days, so within 9 to 15 days of hatching adult lice appear and begin laying eggs. Nymphs are juvenile lice and in appearance look like the adults, only smaller. It is only third instar nymphs and adult lice which are capable of spreading from one person to another. First and second instar nymphs and eggs are not infectious.

PREVALENCE and MANIFESTATION

The highest prevalence of head lice infection occurs in children between the ages of 4 and 11, although, due to their social behaviour (playing in small groups with close head to head contact), girls tend to show a higher incidence of infection than boys. Previously it has been argued that head lice are a school rather than a community problem, however it is now known that head lice are spread into schools from the community and that children of school age are the group most likely to contract this infection.

Prevalence does not vary significantly with season, and any variation seen is probably due to an alteration in social behaviour rather than climatic conditions (Wickenden 1985).

Maunder (1993) states that most cases of head lice infection are symptomless. Any itching caused by the insect bites is an allergic reaction to the saliva of the lice, which is injected during feeding. The patient's response to this passes through the classical range of immune responses, from no reaction through delayed and immediate reactions to tolerance (Mumcuoglu 1991, Burgess 1995a). This pruritus (itching) can take up to 3 months to develop (Roberts 1988), which means that most people may not know that they have lice up until this point.

As well as itch, other symptoms can be associated with head lice infection. Head lice are one of the commonest causes of impetigo of the scalp in developed countries (Burgess 1995a) and Taplin and Meinking (1988) have suggested that head lice may be the only cause of pyoderma (bacterial skin infection) of the scalp in many societies. In exceptional circumstances, if the infection is caused by a nephritogenic strain of streptococci it may cause glomerulonephritis (kidney inflammation) (Mumcuoglu 1991). Pyoderma can occur when bite lesions are excoriated. Bites may also become infected by the bacteria carried on the bodies or limbs of the lice or in their faeces. In some cases, infected bites have led to lymphadenopathy (Chung 1991, Mumcuoglu 1991). The ability of head lice to act as vectors of disease is unknown, although they have been infected in the laboratory with *Rickettsia prowazekii* (Murray 1975). This organism causes typhus, although in the field, transmission of the *R. prowazekii* has only been observed by clothing lice (*Pediculus humanus corporis*), not head lice (*Pediculus humanus capitis*).

In cases of severe louse infection which have persisted for 12-18 months, the sufferer develops secondary sensitisation causing a general systemic reaction in which the patient experiences a feeling of malaise and generally feels 'lousy' (Mumcuoglu 1991, Maunder 1983).

SOCIAL IMPACT

In western societies, there is generally a reaction of shock and revulsion by parents when they discover that their children have head lice. This entomophobic reaction is common in most people and sometimes also occurs in the professionals dealing with the problem. The association of having head lice and being unclean and dirty is common although misfounded, as lice are equally likely to be found on clean or dirty hair. These reactions lead to difficulties when contact tracing because parents often do not want to admit to other members of their family and friends that their children have lice because of the embarrassment and social stigma attached. However in other parts of the world, contracting head lice does not provoke such extreme reactions, so in theory contact tracing may be performed.

INTERVENTIONS

It is believed that time spent curing an individual is wasted unless infectious contacts are also traced and treated. By doing this the risk of reinfection to the patient will be reduced as will the degree of transmission of lice on a wider scale. As most infections have existed for weeks rather than days before they are discovered, contacts over the last month should be traced.

Historically louse control was achieved by physical means such as combing, picking out lice by hand or by shaving the hair. These physical means were also sometimes coupled with the use of naturally occurring medicines, which are still used extensively in poorer parts of the world, as modern alternatives are often too expensive or not available. In the UK, a combing method known as "Bug-Busting" is also used to control head lice. This method requires the hair to be wet combed for 30 minutes every third or fourth day using a special, fine toothed "louse detection" comb. However this method has been criticised as unfeasible because "too few people have sufficient motivation or skill" to implement this method effectively, and success is most likely "if an infection is found in the earliest stages when few lice are present" (Burgess 1997).

Before the advent of modern insecticides, chemical treatments were either of botanical origin unique to each geographical region or based on inorganic poisons and petroleum based organics (Burgess 1995a).

After the second world war, DDT was widely used for louse control, although the development of DDT resistant lice and environmental concern has led to its replacement with newer, more rapidly acting insecticides. However, some DDT powder and lotion preparations are still used in some countries which do not have a well developed consumer supply for louse control products. Other pediculicides which have been used previously, but whose use has been discontinued include benzyl benzoate, crothamiton, lindane (gamma benzene hexachloride). Pediculicides which are still in use in Europe are malathion, permethrin, carbaryl, d-phenoethrin, bioallethrin and synergised pyrethrins. Two other pediculicides are still known to be used for the treatment of head lice; deltamethrin, which is only used in Chile and Brazil, and pirimiphos-methyl in the Czech Republic. There have been a number of incidental reports that the systemic use of ivermectin for the treatment of onchocerciasis has effectively controlled head lice (Dunne 1991), as has topical application (Youssef 1995, Glaziou 1994), although it is not registered for use against human lice.

Formulation

The way in which these insecticides are formulated into the marketed products may have a pronounced effect on their efficacy and acceptability. In some cases the vehicle for the pediculicide may also have some degree of pediculicidal effect which will enhance the performance of the insecticide. This must be taken into account when comparing products, which may have the same active ingredient (insecticide), but different formulation. Formulation can also affect the acceptability of the pediculicide to the public.

The products which become the most popular and hence used most frequently, are those which in general tend to be the easiest to use, with the shortest application time and the most pleasing cosmetic attributes (such as smell). This can lead to single product domination of the market which in turn may mean an increased rate of resistance development.

Safety

Concerns regarding the toxicity of some of the insecticides used to treat head lice infection have been expressed by members of the public and recorded in the popular press. Isolated incidents of toxicity have also been reported in the scientific literature (Lewis 1977, Lee 1976, Scowen 1995, Shuster 1996, Culver 1988). One insecticide has been withdrawn from OTC and is now only available in the UK on prescription. This is not the case in other countries.

RESISTANCE

Resistance to permethrin is already widespread in Britain (Burgess 1995c), and where it occurs may render any products containing related compounds ineffective. Resistance to permethrin has also been documented in Israel and the Czech Republic as well as in anecdotal reports from several other European countries and elsewhere (Burgess 1995b). A study by Chosidow et al (1994) conducted in elementary schools in Paris, concluded that some resistance had developed in head lice to phenothrin. Resistance in head lice to malathion has been reported in a few individual cases (Silverton 1972, Goldsmid 1990) in Tasmania and is widespread in the UK (Burgess 1996). To date there have been no published reports of resistance to carbamates (carbaryl) in head lice, although Burgess has recorded isolated pockets of resistance to carbaryl in the UK (Burgess pers. comm. August 1998).

To delay resistance, a policy of rotating recommended insecticides was implemented by the majority of health authorities in the UK on an annual or triennial basis. The monopoly that school health clinics held on the supply of pediculicides ended in 1992. Since then, the increasing availability of pediculicides over the counter means rotation is unenforceable (Burgess 1998), and, coupled with existing resistance, is rendered ineffective. The current recommendation is a mosaic model in which the same product is used for a course of treatment (2 applications spaced 7 days apart) and then a different insecticide from another resistance group is used for a course of treatment if the first insecticide fails.

COMPARISONS

This review will examine the existing evidence, using randomised controlled trials, of the effectiveness and safety of the preparations and methods used in the curative treatment of head lice infection on humans. This review will concentrate on placebo (vehicle) controlled and comparative trials as these are the most useful types of study to show comparisons between efficacy of different active ingredients and formulations. In vitro studies will be excluded from

the review because the methods used and the results obtained from these investigations do not give an accurate representation of the effectiveness of a product when used in the field on people infected with head lice. The susceptibility of laboratory lice to insecticides may be greater than that of field collected lice, as they will not have been subject to the same selection pressures as the lice from the field. Also, in in-vitro studies insecticide is often applied directly onto the louse which is not representative of a real life situation.

To determine ovicidal effect in field trials, it may be necessary to collect viable eggs before and immediately after the participant has been treated and incubate them in the laboratory. The results will provide a quantifiable evaluation of ovicidal effect (% mortality of eggs). Using this method will eliminate any confounding factors such as the effect of sebum, hair washing etc, but may not be practical in all circumstances. Determining ovicidity in vitro and to a lesser extent from field results is important as a non- or partially ovicidal product will require a second application at day 7 to kill any newly hatched lice from eggs surviving the first treatment. Failure to determine ovicidal effect may result in treatment failure when the product is marketed.

A previous systematic review (not a Cochrane review) was conducted in 1995 by Vander Stichele (Vander Stichel 1995a). However this review was criticised in a number of publications (Burgess 1995b, Stallbaumer 1995), which indicated that the review was weak in certain areas, including the choice of some inappropriate quality criteria, such as time/season of study and swimming. Some trials which were deemed of suitable quality, upon closer inspection were found to be seriously flawed in their methodological quality. The author agreed that analysis using stricter criteria would be appropriate and should be conducted as a Cochrane Review (Vander Stichel 1995b).

To minimise bias in this review, the inclusion criteria for RCT's were pre-specified as follows:

- i) participants should have live lice or 'lice and eggs', present on their head before enrolment on the study, not just eggs alone;
- ii) participants should not have used any other pediculicide in the month preceding enrolment on the trial;
- iii) lice and eggs should not be removed by combing following treatment with a pediculicide, except during detection combing at follow-up, when the number and stages of lice caught should be recorded.

The overall aims of this review are to determine which pediculicide is the most effective (gives the highest cure rate) for the treatment of head lice, to assess the effect of formulation and to compare physical and chemical control methods.

OBJECTIVES

1. to determine which topical (or oral/systemic) intervention results in the highest cure rate for the treatment of pediculosis capitis, and whether this is influenced by concurrent contact tracing and/or an education programme.

2. to determine which formulation is most effective.

3. to determine which pediculicide is the safest in terms of toxicity and ADR and is the most acceptable

4. to ascertain whether chemical control methods (pediculicides) are more effective than physical control methods (combing).

The above objectives will be tested using the following hypotheses (where data is available):

effectiveness of permethrin, d-phenothrin, malathion, carbaryl and synergised pyrethrin is equivalent.

different formulations (lotion vs. shampoo vs. creme rinse vs. mousse) of the same insecticide are equivalent.

different vehicles (aqueous vs. alcoholic) of the same formulation (lotion, shampoo, creme rinse, mousse) of the same insecticide are equivalent.

treatment with pediculicide is equivalent to herbal/ethnic treatments.

treatment is less effective when contacts are not concurrently treated than when they are treated.

effectiveness of any single pediculicide is not altered by resistance of lice to the insecticide.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (published and unpublished) comparing pediculicides with the same and different formulations of other pediculicides, and pediculicides with physical methods have been included in this review. Alternate allocation studies have been included in addition to randomised studies.

In a separate summary of toxicity, any report from controlled and uncontrolled studies was included, including cohort and case controlled designs, or case reports or case series.

Types of participants

Ideally, children who have not achieved their fourth birthday should not be enrolled on a trial. This is because some treatments

may be stressful for children under this age and therefore may result in some form of non-compliance. Also if any adverse events occur they are unlikely to be able to communicate them to the investigator.

For this review studies were included if participants were children of any age or adults diagnosed as being infected with head lice as determined by the presence of live lice not just eggs.

In the efficacy analysis, participants should be excluded from the trial if: they were exposed to pediculicides less than one month before the start of the study; a louse detection comb was used to remove lice following treatment with pediculicide, unless: a) used to detection comb for the presence of lice, with documentation of the number and stages of lice removed at each follow-up or; b) where combing was being assessed as a treatment in its own right. In the effectiveness analysis, we modified this exclusion criteria so that children who had been exposed to pelliculicides less than two weeks were included.

Types of interventions

Any topical (or oral/systemic) treatment used to attempt to cure infestation with head lice including traditional herbal treatments. Physical control methods such as "BugBusting" (combing) have also been included.

The value of health education combined with treatment.

Contact tracing vs. single patient treatment

Types of outcome measures

Efficacy

1. pediculicidal effect (ability to kill lice) measured by primary cure by day two, as determined by detection combing; and
2. ovicidal effect (ability to kill eggs) determined by the need for re-treatment at day 7; and
3. patient should be completely free from lice by day 14

Adverse Reactions

1. minor - defined as: causing no limitation of normal activities.
2. moderate - defined as: causing some limitation of normal activities.
3. major - defined as: causing inability to carry out usual activities. This includes: fatal, life-threatening, disabling, incapacitating, hospitalisation or prolonged hospitalisation, overdose, newly diagnosed cancer.

Acceptability

acceptability of compound and formulation to patient and parents, including ease of use, and percentage dropouts.

Search methods for identification of studies

The Cochrane Infectious Diseases Group specialized trials register was searched for relevant trials up to July 2002. The topic search terms used were: head lice; head louse; pediculosis; pediculus humanus capitis; pediculosis capitis. Full details of the Cochrane Infectious Diseases Group methods and the journals hand searched are published in The Cochrane Library in the section on Collaborative Review Groups.

The reviewer searched The Cochrane Controlled Trials Register, published on The Cochrane Library (2002, Issue 2). Full details of the sources and methods used are published in The Cochrane Library.

The following databases were also searched using the topic search terms in combination with the search strategy developed by the Cochrane Collaboration and detailed in the Cochrane Reviewers' Handbook (Clarke 2002):

- (1) MEDLINE and TOXLINE (1966 to July 2002) (Table 1);
- (2) EMBASE (1980 to May 2002) (Table 1);
- (3) LILACS (La Literatura Latinoamericana y del Caribe de Informacion en Ciencias de Salud) www.bireme.br; accessed July 2002;
- (4) Science Citation Index (1981 to July 2002); and
- (5) BIOSIS 1985 to July 2002).

The topic search terms used were: head lice; pediculosis; pediculus; pediculosis capitis; malathion; permethrin; pyrethrin; carbaryl; insecticide; and shampoo.

Unpublished trials were sought by contacting as many pharmaceutical companies which produce pediculicides as possible. A total of 35 companies were contacted, including: Warner Lambert; Seton; Hogil; Dell Laboratories; Pfizer; Block Drug; Instituto Candioli; Eduard Gerlach; Laboritos Cusi; SCAT; Proctor and Gamble; Bayer.

External referees were asked to check the completeness of the search strategy, and to identify any additional unpublished, on-going or planned trials.

The reviewer also checked the citations of all the trials identified by the above methods.

In addition a broader search strategy for identifying trials and reports of insecticide toxicity and safety was conducted. The search terms used were: names of all identified drugs limited to 'adverse effects', 'drug therapy' or 'drug toxicity' (e.g. lindane/ae, lindane/dt, lindane/to); head louse, pediculosis or the selected indexed keyword limited to drug therapy or drug effects (e.g. pediculosis/dt, pediculus/de); insecticides/tu (therapeutic use); pyrethrins/tu; adverse drug reaction/; drug safety/; drug toxicity/; convulsion/; side effect(s)/tw (text word). The selection and combination of search terms had to be modified to suit the particular database.

The Medicines Control Agency (MCA) in the UK, and the Federal Drug Administration (FDA) in the USA, were contacted for details of any reports of adverse effects relating to the use of pediculicides. The data collected by the MCA is collated from the yellow card reporting scheme. Reports of adverse effects made to the FDA for OTC products are published in the Federal Register, but reports concerning POM products are reported separately.

Data collection and analysis

The titles and abstracts of all trials identified from the searched databases and other sources were screened by two independent reviewers. These reviewers independently selected trials which met previously defined inclusion criteria. Where agreement was not reached, a third reviewer settled any debate.

Methodological quality was assessed against general and (louse) specific parameters.

General

Randomisation; assessor blinding; loss to follow-up; dropouts; intention to treat (at least one follow-up); inclusion and exclusion criteria; formal statement of statistics used including power of study and confidence level.

Specific

Formulation detailed; identity of applicants and investigators; application procedure (which is formulation dependent); documentation of pediculicidal effect by day 2, and on day 4, day 7, day 10 and day 14 and ovicidal effect on days 7 and 14.

Ovicidal effect

Some of the pediculicides available on the market kill both lice and their eggs. Therefore, the ovicidal effect of these products was compared to determine which had the greatest ovicidal effect.

Ovicidal effect is calculated as:

pre-treatment hatch rate (%) - post-treatment hatch rate (%) = % mortality (of eggs)

RESULTS

Description of studies

Seventy-one studies were identified and included on the trials register. Only four studies met the inclusion criteria, and for one further information from the authors is needed before a decision about its inclusion can be made. The other 66 studies were excluded (see list).

The two main reasons for exclusion were: a) no attempt at randomisation, or randomisation inadequate; b) inadequate diagnostic criteria for head lice infection. Trials were excluded if participants had infection diagnosed on eggs alone, which does not prove infection. Studies were also excluded: a) if participants had been treated with pediculicide less than one month prior to enrolment on the trial; b) if lice/eggs were combed from the hair following treatment.

Taplin et al conducted two trials in a community in Panama where the prevalence was >90%. The first trial (1982) examined malathion versus placebo. The placebo arm received the vehicle base (isopropyl alcohol) used to deliver the malathion in the treatment arm. A mixture of adults and children with infection (N=119) were enrolled, most of whom reported long-term infection

with lice. Only 115 were included in the analysis. Four participants (2 from each group) were excluded due to missing results or protocol violation. All subjects reported pruritis of the scalp before treatment; 11 reported dermatitis; 7 reported pyoderma; 8 reported excoriation; and 4 reported eczema. Ovicidal effect of the two treatments was assessed by collecting ten shafts of hair with viable ova attached from each participant before and immediately after treatment. These were incubated in individual petri-dishes for 14 days at 30 Celsius and 70% RH. Percentage mortality of the ova was then calculated.

The second trial (1988) examined permethrin versus placebo (as above). Again a mixture of children and adults with infection (N=93) were enrolled. Only 63 of these were randomised into treatment and placebo groups. A further 30 non-randomised subjects (children) were treated with lindane to act as a positive control. Ovicidal effect of the two treatments (permethrin and placebo) was assessed by collecting shafts of hair with viable ova attached from each participant before and immediately after treatment and incubating them in individual containers. Percentage mortality of the ova was then calculated.

Burgess et al (1994) conducted a two centre trial which took place in a school and a childrens home in Dhaka, Bangladesh where the prevalence of infection was 75% and 100% respectively. This study compared the effectiveness of synergised pyrethrin (pyrethrin plus piperonal butoxide synergist, to enhance the effect of the insecticide) with permethrin. A mixture of children and adults with infection (N=52) was enrolled on the trial. Ovicidal effect of the two treatments was assessed by collecting viable ova from each participant before and immediately after treatment. These were incubated in individual petri dishes for 14 days at 30 Celcius and 50% RH. Percentage mortality of the ova was then calculated.

The fourth, most recent trial (Roberts et al 2000) compared BugBusting (a physical treatment) with malathion. The participants in this study were schoolchildren with infection (N=81), aged between 3-14 years from two counties in North Wales, UK. All other family members found to be infected were concurrently treated with malathion, but were not included in the study. In both groups treatment was parentally applied. For treatment with malathion this consisted of two applications spaced seven days apart in accordance with the manufacturers instructions. Treatment with the BugBusting kit involved applying conditioner, in excess, to wet hair, then combing thoroughly with a detection comb until no more lice were found. This procedure was repeated every 3-4 days for at least two weeks.

All the trials identified were from the published literature. Thirty-six companies which produce head louse products were contacted for published and unpublished material, but those which replied did not identify any unpublished work. Seven replies were received, which identified several other RCTs and descriptive studies. No companies offered to provide unpublished data. A second letter is being sent to those companies which may have unpublished studies, to inquire whether they will provide the material for inclusion

in the Review.

Safety information was extracted from the RCTs, whether included or excluded, as well as from references identified in a separate literature search and data provided by MCA and FDA. These results are presented in narrative form in the results, and we intend to make the tables available through the Cochrane Infectious Diseases Group Web Site (<http://www.liv.ac.uk/evidence>).

Risk of bias in included studies

RANDOMISATION AND ALLOCATION CONCEALMENT

Participants in 3 studies were individually randomised into the test groups, but details of the method of allocation concealment are not given. In Roberts et al (2000) allocation was concealed in marked envelopes.

GENERATION OF ALLOCATION SEQUENCE

The method of generation of the allocation sequence is given by Taplin et al (1982; 1986). Personal communication with Burgess has shown the allocation sequence to be in blocks of 3 (1 permethrin:2 synergised pyrethrins). In the study by Roberts et al (2000) the allocation sequence was generated by random numbers.

REPORTING OF EXCLUSION/INTENTION TO TREAT ANALYSIS

Taplin et al (1982) reported four exclusions from the analysis, two from the treatment group (inadvertently treated with lindane as well) and two from the control group (not seen at follow-up). A further three subjects in the malathion group were unavailable for the 7 day evaluation.

No subjects were excluded or lost to follow-up in the Taplin et al (1986) trial.

In the third study (Burgess 1994) no patients were excluded. However, many were lost to follow-up due to a public holiday (pers. comm.). For the pyrethrin treatment group, three were lost on day 2, eighteen on day 4, 23 on day 6, 37 on day 8, and 38 on day 14. From the permethrin treatment group, two were lost on day 2, two on day 4, seven on day 6, eight on day 8, and none were available on day 14.

Roberts et al (2000) reported four exclusions and one loss to follow-up in the BugBusting arm of the trial and two exclusions in the malathion treatment arm. Of these, two were excluded as they were simultaneously treated with both interventions.

BLINDING

Both the studies by Taplin et al (1982; 1986) were double blind. The studies by Burgess et al (1994) and Roberts et al (2000) were single blind. This was because different formulations of pediculicide and different treatments were being compared which had different application procedures.

INFORMED CONSENT

Informed consent was obtained in all four studies, from parents, guardians or a suitable responsible person in the native language of the participants.

INCLUSION CRITERIA

To be included in the study, adult lice and nymphs plus at least 20 viable ova not more than 1.5 cm from scalp (Taplin 1982 & Taplin 1986), or live lice (Burgess 1994 & Roberts et al 2000) were required.

EXCLUSION CRITERIA

In all four studies appropriate exclusion criteria were chosen and reported. Taplin et al (1982) made no comment about prior pediculicide use, but it is known to the author that no pediculicides were available in the San Blas Islands. Also most subjects reported a long-standing history of infection with lice, over a lifetime or many years which indicates that prior treatment had not been used or that products were unavailable; no hair grooming aids were used during the study. Taplin et al (1986) excluded participants if pediculicide had been used less than 3 months before commencement of the trial; no antibacterial shampoos/soaps or hair grooming aids could be used less than one week prior to or during the study; people receiving antibiotic therapy were also excluded.

Burgess et al (1994) did not comment on previous pediculicide use, but no products were available in the study area (pers comm). Roberts et al (2000) excluded patients who had received pediculicide treatment two weeks prior to the commencement of the study. However, of the 72 patients included in the analysis, 42 of them retrospectively reported that they had not used pediculicides in the four weeks before trial entry. In this subgroup, the difference in the effectiveness of treatments did not reach significance.

FORMULATION AND MANUFACTURER

Taplin et al (1982) used 0.5% malathion (Prioderm lotion) and its alcoholic vehicle base (70% isopropyl alcohol with terpenoids), which were supplied by Robert Grandy, The Purdue Frederick Co., Norwalk, Conn. USA.

Taplin et al (1986) used 1% permethrin (Nix creme rinse) and its vehicle base (20% isopropyl alcohol) supplied by Burroughs Wellcome Co., Research Triangle Park, NC, USA, and 1% lindane (Kwell) purchased in the USA.

Burgess et al (1994) used 0.165% synergised pyrethrin mousse (Banlice) and 1% permethrin creme rinse (Nix) supplied by Soltec Research Pty Ltd.

Roberts et al (2000) used 0.5% malathion (Suleo-M lotion or Derbac-M liquid). No mention was made regarding the supplier of these preparations for the study.

APPLICANTS/INVESTIGATORS

In three trials, the treatments were provider applied and assessor blinded at follow-up. In the trial by Roberts et al (2000) the treatments were parentally applied and assessed professionally at follow-up.

APPLICATION PROCEDURE

Details of the application procedure are given in all four studies.

TREATING CONTACTS

In one study, family contacts were treated with lindane shampoo to prevent reinfection of the test subjects (Taplin 1982). In the trial by Roberts et al (2000) all other family members found to be

infected were concurrently treated with malathion, but were not included in the study. In the other two studies contacts were not treated (Taplin 1986; Burgess 1994).

FOLLOW-UP

Taplin et al (1982) followed up patients at 24 hours and 7 days post-treatment. Lice collected from the hair washings were assessed at 2 and 24 hours post-treatment. In 1986, Taplin et al observed participants at 1, 2, 4, 6, 24 hours, 7 and 14 days post-treatment, but only reported the results at days 7 and 14. Burgess et al (1994) followed up patients at 2, 4, 6, 8, and 14 days after treatment. Follow-up was carried out by combing at 7 and 14 days in Roberts et al (2000)

OVICIDAL EFFECT

Ovicidal effect was assessed in all three trials at day 7 and/or day 14. Two trials (Taplin 1986; Burgess 1994) give details of the pre and post treatment hatch rates, but Taplin et al (1982) only reports the final ovicidal effect. Ovicidal effect was not measured by Roberts et al (2000).

DETECTION COMB

In two studies (Burgess 1994 & Roberts et al 2000) detection combing was used to assess for the presence of lice at follow-up. Taplin et al 1982 and 1986 visually inspected patients for the presence of lice at follow-up.

At the final assessment, Taplin et al (1982) rubbed the patients head with isopropyl alcohol and then rubbed with a loosely woven cotton towel to remove any lice.

CURE OF PRURITIS

A number of patients had concomitant scalp disease (probably due to infection with lice) prior to enrolment on the study, 29 of which were improved or unchanged when study ended (Taplin 1982). The three remaining studies made no comment (Taplin 1986; Burgess 1994; Roberts et al 2000).

SAFETY/SIDE EFFECTS

Investigators from all three studies sought information on adverse reactions and side effects of treatment. One patient complained of stinging (6 minutes duration) in the malathion group when the preparation was applied, due to a reaction of the pyoderma lesions on scalp to the alcoholic vehicle (Taplin 1982). One patient complained of the strong smell of Suleo-M and switched to Derbac-M for the second application (Roberts et al 2000). No other effects were observed. No effects were recorded from any patient when treated with permethrin (Taplin 1986) or synergised pyrethrins or permethrin (Burgess 1994).

Effects of interventions

EFFECTIVENESS

Drug treatment vs. placebo

Two trials compared treatment with placebo (Taplin 1982; Taplin 1986). Both trials clearly showed an effect on cure rates, with fewer lice found following application of malathion and permethrin than before treatment. In the malathion trial (Taplin 1982)

68/68 patients treated with malathion and 42/47 with the vehicle were free from lice by day 2. The primary cure could not be assessed at day 2 for the permethrin study (Taplin 1986) as patients were not followed up until day 7.

At day 7 both treatments significantly reduced the number of lice. The results for permethrin showed that 29/29 patients were free from lice compared to 3/34 treated with the vehicle. When participants were treated with malathion (Taplin 1982) 62/65 were free from lice at day 7 compared to 21/47 treated with the vehicle. At day 14 28/29 participants were free from lice in the permethrin treatment group compared to only 2/34 of those receiving the vehicle. There was no day 14 follow-up in the malathion vs. vehicle trial (Taplin 1982).

The ovicidal effect (determined by incubating eggs collected from treated participants before and after application of pediculicide) of both permethrin and malathion was greater than that of their respective vehicle bases. However, the difference was not as great between malathion 85.8% and its vehicle 47.8% (Taplin 1982) as it was between permethrin 62% and its vehicle 8% (Taplin 1986). This indicates that the vehicle for malathion is not totally inert, but has some degree of pediculicidal and ovicidal effect. Overall malathion was more ovicidal than permethrin in absolute terms. Synergised pyrethrin vs. permethrin

One trial compared synergised pyrethrins plus PBO with permethrin (Burgess 1994). At all follow-up investigations, both treatments were shown to be highly effective, in most cases resulting in complete cure. Although the number of follow-up investigations conducted was suitable, the number of participants assessed at each follow-up, except the first, was poor and steadily decreased at each subsequent assessment. No results were collected on day 7. No comparison could be made on day 14 as no data was available for the permethrin treatment group.

A direct comparison between permethrin and synergised pyrethrin in terms of ovicidal effect, showed that synergised pyrethrin (34.2% mortality of ova) was significantly more ovicidal than permethrin (8% mortality of ova).

Chemical vs. physical

One trial compared chemical vs physical treatments (Roberts et al 2000). This trial met the inclusion criteria for the effectiveness analysis. Using an intention to treat analysis, the cure for those allocated to BugBusting was 12/33, compared to 33/42 for Malathion (RR 2.10, 95% confidence intervals 1.30 to 3.37). The cure rate at 7 days was not reported.

In a sub-group of 42 participants who had not used pediculicides in the four weeks prior to enrollment, the cure rate was 58% for BugBusting and 78% malathion, with the BugBusting Group 1.9 times more likely to have lice at the end of treatment than those who received malathion (difference not statistically significant).

Comparison of formulations

No RCTs were identified of suitable quality which compared different formulations of the same insecticide.

Comparison of vehicles

No RCTs have been conducted to compare the effect of different vehicles on formulation or effectiveness.

Concurrent treatment of contacts

No trials specifically addressed this, although Taplin et al 1986 treated family contacts as a matter of course to prevent test subjects becoming re-infected.

Exploring data using less stringent quality criteria

In order to explore whether useful data were contained in the excluded trials, we conducted a separate analysis of trials using less stringent quality criteria. The aim of this was to determine whether potentially useful data were actually being discarded as a result of the review's prespecified entry criteria being too stringent, following comments from our referees.

The analysis relaxed the inclusion criteria for trials in relation to diagnostic criteria at entry and prior pediculicide use. This analysis examined trials where the diagnosis of headlice was made on the basis of "either lice or eggs"-allowing the inclusion of patients who do not actually have a headlice infection. The analysis also examined trials where prior pediculicide use within 2 weeks of enrolment onto study could not be excluded. The trials examined were those identified in the main search strategy but excluded (n=66).

Nineteen trials met the "relaxed" inclusion criteria, as of January 1999. They are summarised in a table on the Cochrane library web site. The results obtained from this analysis broaden the variety of pediculicides included, with variable cure rates for each. The data, if examined observationally, show that various treatments appear to work but we were not able to identify any additional data that contributed to the review objectives. This analysis indicates further work summarising data from such studies is probably not worthwhile, so this analysis will not be extended or updated.

ADVERSE REACTIONS

Toxicity was systematically summarised in all trials identified for this review. This data set included a) trials included in the cure review; b) trials identified but subsequently excluded from the cure review; c) other studies as identified by the methods section describing the additional toxicity search. From a) and b) above, 43 sought data on the safety of the products tested by recording any adverse events reported by the participants following application of the test products. Data from the MCA and Federal Register is still being processed, and the author is still awaiting information relating to adverse effects for Prescription Only Medicines from the Federal Drug Administration in USA.

No major adverse effects were reported with malathion (studies=12, total participants =803); with carbaryl (studies =6, total participants =247); with permethrin (studies=5, total participants =1236); with phenothrin (studies=6, total participants =296); with synergised pyrethrins (studies=10, total participants =942); with lindane (studies=6, total participants =749).

Malathion lotion was tested in 7 studies, shampoo in one, and unspecified formulation in 5. In the seven studies of lotion, minor effects were noted in two studies (8/310 participants), giving a

total of 8/803 reactions. No adverse effects were reported in the one study of shampoo (0/7 participants); and none in the five studies where the formulation was unspecified (0/486). The side effects reported were all minor. They included: stinging/tingling of scalp; red eyes; erythema of the scalp; increase in dandruff. Carbaryl lotion was tested in 3 studies, shampoo in 2, and unspecified formulation in 2. In the three studies of lotion, minor effects were noted in all three studies (15/101 participants), giving a total of 15/247 reactions. No adverse effects were reported in the two studies of shampoo (0/75 participants); and in none in the two studies where the formulation was unspecified (0/71). The side effects reported were all minor and those which were reported were erythema of scalp; itching; rash; stinging scalp; skin irritation on hands/scalp; flaking skin; stinging on contact; eye irritation due to fumes.

All the studies using permethrin were with creme rinse which was tested in 5 studies. In 3 of these studies, minor effects were observed, giving a total of 66/1236 reactions. The side effects reported were all minor and those which were reported were pruritus; pain; burning/stinging; tingling; oedema; erythema; rash. Phenothrin lotion was tested in 3 studies, and shampoo in 3. In the three studies of lotion, minor effects were noted in 2 studies (14/204 participants), giving a total of 14/296 reactions. No adverse effects were reported in the 3 studies of shampoo (0/92 participants). The side effects reported were all minor. They included: itching; dermatitis; cough; stinging; greasy hair; shortness of breath; red blotches on neck; skin staining; skin irritation.

Synergised pyrethrin lotion was tested in 5 studies, shampoo in 7, spray in 1, and unspecified formulation in one. In the 5 studies of lotion, minor effects were noted in 2 studies (35/288 participants), giving a total of 35/942 reactions. No adverse effects were reported in the 7 studies of shampoo (0/571 participants) or in the one study on spray (0/50 participants); and none in the study where the formulation was unspecified (0/33). The side effects reported were all minor. They included: pruritus; erythema; rash; dry scaly patches; slight oedema.

Lindane lotion was tested in 1 study, and shampoo in 6. In the 1 study of lotion, no reactions were observed (0/9 participants). Adverse effects were reported in 3 of the studies using shampoo (46/740 participants), giving a total of 46/749 reactions. The side effects reported were all minor. They included: pruritus; pain; burning/stinging; numbness; tingling; erythema; rash; slight oedema. The Committee on Safety of Medicines/Medicines Control Agency have received a number of suspected adverse drug reaction reports associated with pediculicides. To 4 August 1998 they had received 43 reports (73 reactions) associated with malathion, 27 reports (43 reactions) associated with permethrin, 21 reports (38 reactions) associated with phenothrin and 16 reports (25 reactions) associated with carbaryl through the 'Yellow Card Scheme'. They had received no reports of a suspected adverse drug reaction with a fatal outcome (CSM - personal communication).

DISCUSSION

The published literature relating to the treatment of head lice includes a reasonable number of clinical trials. However, the majority of these RCTs did not meet the inclusion criteria, failing mainly on poor methodological quality, leaving only 4 studies which could be included in the analysis. Since so many RCTs have been rejected, it may appear, on first impressions, that this review has been over-selective in the choice of inclusion criteria. However, the criteria chosen are fundamentally important when designing trials for the treatment of head lice. If these criteria are not adhered to when designing a trial, bias will be introduced into the results and the outcome may be altered. Unfortunately, it seems that the majority of researchers conducting trials in this subject area have overlooked these points when designing and conducting trials. Although such bias could be reduced in these studies when patients are allocated randomly into treatment groups, there may still be a dramatic effect on the outcome if the effect sizes of the treatments are small. By prespecifying a strict design for a trial any bias should be minimised and a more accurate assessment of effect, no matter how small, should be possible. The three main criteria required to minimise bias, which have been pre-specified in this review, are discussed below.

HOW DO WE DESIGN BETTER TRIALS?

i) DIAGNOSIS REQUIRES THE PRESENCE OF LIVE LICE BEFORE THE STUDY, NOT JUST EGGS.

Any study in which participants were selected by the presence of eggs alone or, "lice or eggs", was rejected. The presence of live lice (not eggs) is the clinical diagnosis for infection and guidelines exist which recommend that treatment should not be applied unless live lice are actually discovered ([Aston 1998](#)). Before enrolment on a trial, a participant must be found to have live lice present on their head. It is not possible to test the ability of a pediculicide to kill juvenile and adult lice, if no lice are present on the head of the participant prior to treatment. If only eggs are found then the subject should not be enrolled. Relying on the presence of eggs alone is insufficient as these may be non-viable, remaining from an earlier infection or having hatched. Even if the eggs are present close to the scalp, which may indicate an active infection, it is still necessary to find live lice before enrolment. A good example of this can be seen in a trial by [Kyle 1990](#), in which a total of 77 patients had only eggs and only 4 had lice and eggs prior to treatment.

ii) PATIENTS SHOULD NOT HAVE USED PEDICULICIDE ONE MONTH PRIOR TO ENROLMENT ON THE STUDY.

In this review, the efficacy analysis including only participants had been treated with another pediculicide less than one month before enrolment on the study was rejected. The reasons for this are two-fold. Firstly, some insecticides have a residual effect on hair, and may remain active for a number of days or weeks. Therefore the residues could interfere with the activity of other insecticides being

tested. After 4 weeks, any remaining residues are likely to have diminished to a low enough level not to interfere with subsequent applications of insecticide. Secondly, the baseline metabolism of any lice surviving treatment may be “primed” on a short term basis to detoxify insecticides more efficiently than lice which have not been treated. This will mean that the treated lice may have an increased chance of surviving another treatment due to more active detoxification. However any lice remaining after 4 weeks will be more likely to have a metabolism which is back to its normal resting base level.

In the effectiveness analysis, we were more permissive with the inclusion criteria, limiting it to two weeks. A sub-group analysis was conducted of the participants that had not been treated with pediculicides in the preceding four weeks and no significant difference between cure rates for the two groups was found.

iii) LICE SHOULD NOT REMOVED FROM THE HEAD FOLLOWING APPLICATION OF PEDICULICIDE BY COMBING (OTHER THAN FOR DETECTION COMBING).

Trials in which lice/eggs were removed as part of the treatment process from the heads of the participants following treatment were excluded, because removal of these lice and eggs introduces a bias into the results. If a pediculicide is being tested for effectiveness, no other intervention should be used until the participant has completed the trial, even if the product being tested is marketed with a nit removal comb and recommends using the comb following application of the pediculicide. Combing the hair removes lice and eggs which may not have been immediately killed by the insecticide. As these have the potential to survive they should not be removed from the head unless fully documented as to number and stage of development, because their survival affects the pediculicidal outcome (effectiveness) of the product. More importantly eggs should not be removed as they may not have been killed by treatment and may subsequently hatch. Removing the lice and eggs therefore gives a false indication of the cidal activity of the product being tested.

For products with a packaged nit removal system, trials should assess the chemical and physical elements of the product separately, using each as an individual treatment. The only benefit in testing the two together is to the manufacturer in that the use of the comb could make their pediculicide appear more effective than may be the case.

iv) ASSESSMENT TIMES

Only one of the included studies (Burgess 1994) attempted a satisfactory number of follow-up investigations, although the number of patients seen at each follow-up was far from satisfactory. The other three studies (Taplin 1982, Taplin 1986, Roberts 2000) were inadequate for the number of follow-up visits conducted. There was no measurement of primary cure reported in two (Taplin 1986,

Roberts 2000), and although in one of these trials (Taplin 1986), patients were observed at 1, 2, 4, 6 and 24 hours post-treatment the results were not presented. In one study (Taplin 1982) the final inspection was conducted after only 7 days.

Ideally, follow-up should be: 24 hours after treatment has finished removed and at days 4, 7 10 and 14. If there are not regular follow-ups early on, it becomes impossible to be certain whether any lice which are found are due to treatment failure or to reinfection. “First and second stage nymphs which are found up to one week post-treatment are hatched from surviving eggs. Adults and third stage nymphs can only be from reinfection unless there is complete treatment failure, when they should have been found at the first follow-up after treatment” (Burgess 1995). If the product is not ovicidal then one would expect to see a reasonable number of first and second stage nymphs from day 4 onwards, although some may appear earlier than this. Studies which finish at day 7 are inadequate because it is not possible to ascertain overall pediculicidal or ovicidal effect. “Eggs that were not killed by the treatment may need up to 10 days to hatch, and newly emerged nymphs, which are difficult to find, require 2 to 3 days to reach the first moult” (Taplin 1986). The final assessment should be at day 14, which “should be regarded as the definitive evaluation of pediculicidal and ovicidal activity” (Taplin 1986).

In order to obtain a quantifiable evaluation of ovicidal effect (i.e. % mortality of ova), hairs with attached ova should be collected before and immediately after treatment and incubated in the laboratory for 14 days. If a product is highly/totally ovicidal, then the field results will show complete cure by day 14, with only a single application, provided the patient is not reinfected. However, if the product is not, or is only partially ovicidal then it will be difficult to assess the degree of ovicidity from the field results alone. Once the product is marketed the field and laboratory results will help to determine the need for a second application of pediculicide at day 7 if the product is non- or partially ovicidal, so that complete cure can be achieved by day 14.

PLACEBO CONTROLLED TRIALS

In the two placebo controlled trials, malathion (Taplin 1982) and permethrin (Taplin 1986) were compared with their respective vehicle bases, which were assumed to be inert and therefore to have no cidal effect on the lice. In these two trials, the pediculicides tested in the treatment groups produced high cure rates, 29/29 for permethrin and 62/65 for malathion. However in the placebo groups for these two trials, a degree of cure was obtained in one study, but not the other. The malathion vehicle resulted in a 21/47 (c. 50%) cure rate. The difference between the activity of these two vehicles was due to a formulation effect. In the permethrin product, the vehicle is 20% isopropyl alcohol alone, which has little effect on lice, whereas in the malathion product, terpenoids are contained in the isopropyl alcohol vehicle (PDR 1990) which are also pediculicidal.

In conclusion both pediculicides tested in the placebo controlled trials are effective. Both permethrin and malathion result in high cure rates. The three failures at day 7 in the malathion trial (Taplin 1982) are accounted for by missing data or protocol violation.

Direct comparison of the effectiveness of the two products in these trials is not possible because the groups will not be randomised. For this reason, it could be argued that placebo-controlled trials are not especially useful when attempting to make an informed decision about the effectiveness of a product. The only real benefit of such placebo-controlled trials is to determine the activity of the vehicle, but usually all that is demonstrated is that the active ingredient is much more effective at controlling lice than the vehicle. In practical terms, comparative trials are more useful in helping to make an informed decision about which is the most effective product.

In comparative studies (the vast majority of trials), it is possible to compare similar products, formulations and active ingredients and the results will more clearly indicate which product is preferable. Unfortunately, all but one of the comparative studies identified for this review were of unsuitable quality for inclusion in the review, although some useful information can be gleaned from them such as safety data and patient acceptability, which will be discussed later.

RESISTANCE

All three acceptable studies were conducted in third world countries in which the participants had no prior exposure to pediculicide and hence were infested with fully susceptible lice. In countries where pediculicide is freely available, head lice are not always fully susceptible to the insecticides with which they are being treated. It is well documented that head lice have become resistant to DDT and lindane. Resistance to these was first reported in 1971 in the UK (Maunder 1971). However, head lice are now becoming resistant to other pediculicides as well.

Since the introduction of pyrethroids, and more specifically permethrin, into the pediculicide market there have been reports of resistant head lice in the UK (Burgess et al 1995), Israel (Mumcuoglu et al 1995), Czech Republic (Rupes 1995) and France (Chosidow et al 1994). Resistance to permethrin (and phenothrin) has developed very quickly, in as little as 2 ½ years in Israel (Mumcuoglu et al 1995) and 4 years in the UK (Burgess et al 1995), but not so quickly to phenothrin in France (Chosidow et al 1994). Although not on the same scale, resistance to malathion has been recorded in Tasmania (Goldsmid 1990) and is widespread in the UK (Burgess 1996), with carbaryl resistance occurring in isolated pockets (Burgess pers comm).

One must therefore err on the side of caution when interpreting the Meta-Analysis, as the results presented do not take into account the subsequent development of resistance to pediculicides in head lice. Consequently, any conclusions which may be drawn from these data, obtained in trials performed in developing countries

alone, will be misleading because the effectiveness of the products may be exaggerated. In some parts of the world, where localised pockets of resistance do occur, a product other than that suggested by the analysis may be the most appropriate.

SENSITIVITY ANALYSIS

The sensitivity analysis which was conducted does not yield any different results to the meta-analysis or any indication of the relative effectiveness of any particular pediculicide. However this analysis has permitted a more detailed criticism of the excluded papers. The reviewers comments on these papers are included in the table which can be found on the web site. It is clear that it was appropriate to exclude these studies from the main analysis because their overall quality is very poor. Many of the papers are direct copies of previous papers, only comparing different pediculicides and with no consideration of the suitability of the methodology used. The number of mistakes and inaccuracies (such as the methods of identifying viable eggs, conducting follow-up assessments at inappropriate times and removing lice at follow-up with a potentially pediculicidal compound) in some of these papers indicates that the researchers in question have little appreciation or understanding of the subject and have limited experience of working with lice. It is essential to have a full understanding of a subject before good quality work can be produced, especially when the results of such work may influence the quality of health care/treatment received by patients. Many of the inaccuracies in these papers have been perpetuated throughout the literature, resulting in a body of research with dubious and sometimes uninterpretable results.

QUALITY OF PRODUCTS

In countries where adequate regulatory authorities already exist, all the components of pediculicides are reviewed for safety as well as efficacy. Therefore the risk from using products developed under these authorities should be minimal. However, in countries without such stringent regulation, off licence products may be available and their use should be regarded with caution.

The safety data gathered from the trials indicated that side effects relating to the use of the various pediculicides were all minor reactions. It is difficult to interpret this type of data quantitatively, as the reporting methods varied in each investigation, as did the sensitivity of the reporting. In many cases the data was gathered from reports of effects recorded by the participants which may introduce bias into the results by being too subjective. It is not always clear from the reports whether the reported reactions were due to the active ingredients or to the vehicle, but it is suspected that in many instances, the reactions were due to the vehicle base.

Although data obtained from the Committee on Safety of Medicines/Medicines Control Agency show a number of suspected adverse drug reactions associated with pediculicides, the reactions have not necessarily been caused by the drug. Many factors have to be taken into account in the assessment of casual relationships,

such as the temporal relationship, concomitant medication and underlying disease. In addition, the number of reports received cannot be used as a basis for determining the incidence of a reaction as neither the total number of reactions occurring, nor the number of patients using the drug is known (CSM - pers. comm. 1998).

AUTHORS' CONCLUSIONS

Implications for practice

REVIEWER'S OPINION

All the chemical products tested in the analysis (permethrin; synergised pyrethroid; malathion) were shown to be effective in the treatment of pediculosis capitis. However, the development of resistance since the trials by Taplin (1982 & 1986) and Burgess (1994) were conducted means that the comparative effectiveness of these products, in the absence of direct evidence of effects, means that the 'best' choice will depend on local resistance patterns. In the study by Roberts et al (2000), two formulations of malathion were shown to provide reasonably effective treatment of head lice in a region with an intermediate level of resistance to malathion.

The first three trials were conducted in third world countries using fully susceptible lice. I would argue that, in the current climate, it is more useful to conduct trials in populations which have been previously exposed to pediculicides and therefore may possess lice which are not fully susceptible and may even be resistant to one or more insecticide. It is of little value conducting a trial to test the effectiveness of a pediculicide in a population that is not representative of the target market for the product. Most people living in developing countries are unable to afford these products developed in the West as they are prohibitively expensive, if they are available at all. It is consumers in western countries who purchase the vast majority of pediculicides.

The results of the trial by Roberts et al (2000) indicate that physical control methods, such as combing/'BugBusting' are ineffective as a means of curing head lice infections. This type of method of intervention is very labour intensive and requires a certain level of skill to be effective, which makes the treatment inappropriate as a primary treatment against head louse infection.

Similarly, no evidence in the form of trials exists to indicate the effectiveness of other chemical control methods such as herbal treatments to cure pediculosis capitis.

Implications for research

REVIEWER'S OPINION

As a result of conducting this review, a number of recommendations can be made regarding any future RCT's in this field.

1. All future trials should be randomised, comparative trials, but not placebo controlled, for the reasons outlined in the discussion. Appropriate inclusion/exclusion criteria should be chosen, i.e.:

i) participants should have live lice or 'lice and eggs' present on the head before enrolment on the study, not just eggs alone;

ii) for an efficacy analysis, participants should not have used any other pediculicide in the month preceding enrolment on the trial;

iii) lice and eggs should not be removed by combing following treatment with a pediculicide, except during detection combing at follow-up, when the number and stages of lice caught should be recorded.

2. An adequate number of follow-up investigations should be conducted, ie, 24 hours after treatment has finished and at days 4, 7 and 14. At each follow-up, effectiveness should be assessed by detection combing as in iii) above, not just visual inspection. If ovicidity is being assessed in vitro, eggs should be collected before and immediately after treatment and incubated for 14 days.

3. All trials should evaluate the safety of the products tested by systematically gathering information about any reported/observed adverse effects, whether treatment related or not.

4. The study should be conducted with enough participants to give adequate power and the statistical methods used should be detailed in the text.

5. Standard exclusion criteria should also be used, in addition to the criteria specific to lice. These are: i) no medication/antibiotics; ii) no pregnant/ nursing women; iii) no-one with known allergies to any specific component of the product being tested, e.g. sensitivity to paraben or chrysanthemum or ragweed etc.

From examining the literature, it is apparent that certain questions remain unanswered. A number of future trials should be conducted to cover the following areas:

1. The localised resistance patterns and the mechanisms by which head lice become resistant to pediculicides need to be determined. This will be beneficial for the development of new products as the results will give an indication of potential areas of cross-resistance.

2. Up-to-date clinical studies need to be conducted in western populations using lice which may not be fully susceptible, so that the effectiveness of the existing products can be accurately assessed. Comparisons which would be useful are: permethrin vs. carbaryl vs. phenothrin vs. synergised pyrethrins vs. malathion. However, in future it may be more prudent to compare new active ingredients which are unlikely to be cross-resistant with those which have been used previously, and to manage these new products in a way that will enable their useful life to be as long as possible.

3. The effectiveness of implementing a mosaic policy has not been investigated in the form of a trial to assess the effect that this has on the speed of the development of resistance.

4. A trial is required to compare the effectiveness of different types of vehicle (aqueous vs. alcoholic lotion; lotion vs. shampoo vs. creme rinse vs. mousse vs. spray).

5. Currently there are no RCTs to determine the effectiveness of herbal/ethnic treatments for head lice, and no comparative studies between these and conventional insecticidal products. Such trials are important as these OTC 'western' pediculicides are often unavailable or prohibitively expensive in developing countries, where people may use traditional/ herbal treatments instead.

6. Further trials comparing the effectiveness of different chemical pediculicides vs. physical control methods (pediculicidal treatment vs. combing/'BugBusting') may be required.

7. The potential of new pediculicides needs to be investigated. These may contain novel active ingredients, formulations and methods of treatment, e.g. oral/systemic treatment; gel; prophylactics containing, for example, Insect Growth Regulators.

8. The effectiveness of contact tracing in reducing the spread of

head lice has not been investigated, nor has the combination of treatment with an education programme.

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REFERENCES

References to studies included in this review

Burgess 1994 {published data only}

Burgess IF, Brown CM, Burgess NA. Synergized pyrethrin mousse, a new approach to head lice eradication: efficacy in field and laboratory studies. *Clinical Therapeutics* 1994;**16**(1):57–64.

Roberts 2000 {published data only}

Roberts RJ, Casey D, Morgan DA, Petrovich M. [Comparison of wet combing with malathion for treatment of head lice in the UK: a pragmatic randomised controlled trial]. *The Lancet* 2000;**356**:540–544.

Taplin 1982 {published data only}

Taplin D, Castillero PM, Spiegel J, Mercer S, Rivara AA, Schachner L. Malathion for treatment of *Pediculus humanus var capitis* infestation. *Journal of the American Medical Association* 1982;**247**(22):3103–3105.

Taplin 1986 {published data only}

Taplin D, Meinking TL, Castillero PM, Sanchez R. Permethrin 1% creme rinse for the treatment of *Pediculus humanus var capitis* infestation. *Pediatric Dermatology* 1986;**3**(4):344–348.

References to studies excluded from this review

Ares Mazas 1985 {published data only}

Ares Mazas E, Casal Porto M, Sela Perez MC, Farquhar JA, Hutchinson DBA. The efficacy of permethrin lotion in pediculosis capitis. *International Journal of Dermatology* 1985;**24**:603–605.

Ares Mazas 1988 {published data only}

Ares Mazas ME, Fandino ML, Silva Villar MJ, Giullan Duran JC. Efficacy of a malathion lotion for the treatment

of pediculosis capitis. *International Journal of Dermatology* 1988;**27**(4):267–268.

Armoni 1988 {published data only}

Armoni M, Bibi H, Schlesinger M, Pollak S, Metzker A. Pediculosis capitis: why prefer a solution to a shampoo or spray?. *Pediatric Dermatology* 1988;**5**(4):273–275.

Bainbridge 1998 {published data only}

Bainbridge CV, Klein GL, Neibert SI, Hassman H, Ellis K, Manring D, et al. Comparative study of the clinical effectiveness of a pyrethrin-based pediculicide with combing versus a permethrin-based pediculicide with combing. *Clinical Paediatrics* 1998;**37**(1):17–22.

Blommers 1978a {published data only}

Blommers L, van Lennep M, van der Kaay HJ. [Gammexaan en malathion bij de behandeling van pediculosis capitis]. *Ned T Geneesk* 1978;**122**(19):664–668.

Blommers 1978b {published data only}

Blommers L, van Lennep M. Head lice in the Netherlands: susceptibility for insecticides in field samples. *Entomologia Experimentia et Applicata* 1978;**23**:243–251.

Blommers 1978c {published data only}

Blommers L. The efficacy of malathion shampoo against head louse infestation. *Acta Leidensia* 1978;**46**:7–8.

Blommers 1978d {published data only}

Blommers L, de Jonge GA, Zwart-Feenstra MC, van der Kaay HJ. [Malathion en de bestrijding van hoofdluis]. *T soc Geneesk* 1978;**56**:735–741.

Blommers 1978e {published data only}

Blommers L. Miscellaneous notes on the toxicity of some insecticides for the head louse, *Pediculus capitis*, De geer (Anoplura). *Acta Leidensia* 1978;**46**:9–15.

- Bowerman 1987** *{published data only}*
Bowerman JG, Gomez MP, Austin RD, Wold DE. Comparative study of permethrin 1% creme rinse and lindane shampoo for the treatment of head lice. *Pediatric Infectious Diseases Journal* 1987;**6**(3):252–255.
- Brandenburg 1986** *{published data only}*
Brandenburg K, Deinard AS, DiNapoli J, Englander SJ, Orthoefer J, Wagner D. 1% permethrin creme rinse vs 1% lindane shampoo in treating pediculosis capitis. *American Journal of Disease in Children* 1986;**140**(9):894–896.
- Brink-Lindroth 1984** *{published data only}*
Brink-Lindroth G, Lundqvist L, Nilsson A. Control of the human head louse with disulfiram and benzyl benzoate emulsions. *Acta Derm Venereol (Stockh)* 1984;**64**:325–330.
- Budak 1996** *{published data only}*
Budak S, Ilhan F, Guruz AY. A comparative study on the efficacy of 0.4% sumithrine and 1% lindane in the treatment of Pediculus humanus capitis in Turkey. *Journal of the Egyptian Society of Parasitology* 1996;**26**(1):237–241.
- Burgess 1990** *{published data only}*
Burgess I. Carbaryl lotions for head lice - new laboratory tests show variations in efficacy. *The Pharmaceutical Journal* 1990;**245**:159–161.
- Burgess 1992** *{published data only}*
Burgess I, Veal L, Sindle T. The efficacy of d-phenothrin and permethrin formulations against head lice: a comparison. *The Pharmaceutical Journal* 1992;**249**:692–693.
- Burgess 1996** *{published data only}*
Burgess IF. Shampoos for head lice treatment - comparative in vitro tests. *The Pharmaceutical Journal* 1996;**257**:188–190.
- Busvine 1942** *{published data only}*
Busvine JR, Buxton PA. A new method of controlling the head louse. *British Medical Journal* 1942;**April 11**:464–466.
- Busvine 1948** *{published data only}*
Busvine JR, Burn JL, Gamlin R. Experiments with DDT and Gamma BHC ("Gammexane") for use against head lice. *The Medical Officer* 1948;**79**:121–4.
- Carson 1988** *{published data only}*
Carson DS, Tribble PW, Weart W. Pyrethreins combined with piperoal butoxide (RID) vs 1% permethrin (NIX) in the treatment of head lice. *American Journal of Diseases in Childhood* 1988;**142**:758–759.
- Chosidow 1994** *{published data only}*
Chosidow O, Chastang C, Brue C, Bouvet E, Izri M, Monteny N, et al. Controlled study of malathion and d-phenothrin lotions for pediculus humanus var capitis-infested school children. *Lancet* 1994;**344**:1724–1727.
- Clore 1993** *{published data only}*
Clore ER, Longyear LA. A comparative study of seven pediculicides and their packaged nit removal combs. *Journal of Paediatric Health Care* 1993;**7**(2):55–60.
- Coates 1971** *{published data only}*
Coates KG. Control of head lice infestation in school children. *Community Medicine* 1971;**126**(10):148–149.
- Cordero 1987** *{published data only}*
Cordero C, Zaia N. Clinical evaluation of pediculicidal and ovicidal efficacy of two pyrethrin-piperonal butoxide formulations. *Clinical Therapeutics* 1987;**9**(5):461–465.
- De Boer 1984** *{published data only}*
De Boer R. Efficacy of malathion and synergised bioallethrine in the treatment of head louse, Pediculus humanus ssp capitis, infestations. *Acta Leidensia* 1984;**52**:53–59.
- De Boer 1985** *{published data only}*
De Boer R, van der Geest LPS. [De werkzaamheid van malathion tegen hoofdluis]. *Ned Tijdschr Geneeskde* 1985;**129**(17):793–796.
- De Felice 1989** *{published data only}*
De Felice J, Rumsfield J, Bernstein JE, Roshal JY. Clinical evaluation of an after-pediculicide nit removal system. *International Journal of Dermatology* 1989;**28**(7):468–470.
- DiNapoli 1988** *{published data only}*
DiNapoli JB, Austin RD, Englander SJ, Gomez MP, Barrett JF. Eradication of head lice with a single treatment. *American Journal of Public Health* 1988;**78**(8):978–980.
- Donaldson 1986** *{published data only}*
Donaldson RJ, Logie S. Comparative trial of shampoos for treatment of head infestation. *Journal of the Royal Society of Health* 1986;**106**(2):39–40.
- Doss 1991** *{published data only}*
Doss S, Powell CA, Miller AJ. Phenothrin lotion the latest recruit in the battle against head lice: the results of two controlled comparative studies. *Journal of the Royal Society of Health* 1991;**111**(2):47–50.
- Dunne 1991** *{published data only}*
Dunne CL, Malone CJ, Whitworth JAG. A field study of the effects of ivermectin on ectoparasites of man. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1991;**85**:550–551.
- Fan 1991** *{published data only}*
Fan PC, Chao D, Lee KM, Chan CH, Liu HY. Chemotherapy of head louse (Pediculus humanus capitis) infestation gamma benzene hexachloride (gamma-BHC) among school children in Szu-Hu District, Yunlin County, Central West Taiwan. *Chinese Medical Journal (Taipei)* 1991;**48**:13–19.
- Fan 1992** *{published data only}*
Fan PC, Chung WC, Kuo CL, Lin CY, Hsu HM, Chuang CH, Chow CY. Evaluation of efficacy of four pediculicides against head louse (Pediculus capitis) infestation. *Kaohsiung Journal of Medical Science* 1992;**8**:255–265.
- Goldsmid 1989** *{published data only}*
Goldsmid JM, Langley JG, Naylor P, Bashford P. Further studies on head lice and their control in Tasmania. *Australian Family Physician* 1989;**18**(3):253–5.
- Gomez Urcuyo 1986** *{published data only}*
Gomez Urcuyo F, Zaia N. Malathion lotion as an insecticide and ovicide in head louse infestation. *International Journal of Dermatology* 1986;**25**:60–62.

- Iannantuono 1997** {published data only}
Iannantuono RF, Devoto F, Saitta MF, del Rosario Valicenti M, Gomez F, Gonzalez C, et al. Pediculicidal activity of an antidandruff shampoo in a 1% copper-oleate formulation. *Advances in Therapy* 1997;**14**(3):134–139.
- Jolley 1991** {published data only}
Jolley JH, Kennedy JP, Miller AJ. A comparison of two insecticidal shampoos in the treatment of head louse infection. *Journal of the Royal Society of Health* 1991;**111**: 90–91.
- Karacic 1982** {published data only}
Karacic I, Yawalkar SJ. A single application of crothamiton lotion in the treatment of patients with pediculosis capitis. *International Journal of Dermatology* 1982;**21**:611–613.
- Kyle 1990** {published data only}
Kyle DR. Comparison of phenothrin shampoo and malathion lotion in the treatment of head louse infection. *Journal of the Royal Society of Health* 1990;**110**:62–63.
- Lange 1980** {published data only}
Lange K, Nielsen AO, Jensen O, Gradual C. Pyriderm Shampoo in the treatment of Pediculosis capitis. *Acta Dermatovenera (Stockholm)* 1980;**61**:91–92.
- Lidror 1965** {published data only}
Lidror R, Lifshitz Y. A new method for lice control in Israel. *Public Health* 1965;**8**(11):1–12.
- Maguire 1972** {published data only}
Maguire J, McNally AJ. Head infestation in school children: extent of the problem and treatment. *Community Medicine* 1972;**128**:374–375.
- Mathias 1984** {published data only}
Mathias RG, Huggins DR, Leroux SL, Proctor EM. Comparative trial of treatment with Prioderm lotion and Kwellada shampoo in children with head lice. *Canadian Medical Association Journal* 1984;**130**:407–409.
- Maunder 1971a** {published data only}
Maunder JW. Use of malathion in the treatment of lousy children. *Community Medicine* 1971;**126**:145–147.
- Maunder 1971b** {published data only}
Maunder JW. Resistance to organochlorine insecticides in head lice, and trials using alternative compounds. *Medical Officer* 1971;**125**(2):27–29.
- Meinking 1986** {published data only}
Meinking TL, Taplin D, Chester Kalter D, Erberle MW. Comparative efficacy of treatments for pediculosis capitis infestations. *Archives of Dermatology* 1986;**122**:267–271.
- Miller 1988** {published data only}
Miller AJ, Miller RB, Simpson MB. Phenothrin lotions in the treatment of head louse infestation. *Journal of the Royal Society of Health* 1988;**108**:11–14.
- Monheit 1986** {published data only}
Monheit BM, Norris MM. Is combing the answer to headlice?. *Journal of School Health* 1986;**56**(4):158–159.
- Morsy 1996** {published data only}
Morsy TA, Ramadan NII, Mahmoud MSE, Lashen AH. On the efficacy of co-trimoxazole as an oral treatment for pediculosis capitis infestation. *Journal of the Egyptian Society of Parasitology* 1996;**26**(1):73–77.
- Pai 1992** {published data only}
Pai KS. Head louse infestation among girls in an orphanage and women in a mental hospital and mass-deloosing with bioallethrin (PARA aerosol). *Korean Journal of Parasitology* 1992;**30**(1):49–52.
- Pitman 1987** {published data only}
Pitman NK, Hernandez A, Hernandez E. Comparison of pediculicidal and ovicidal effects of two pyrethrin-piperonal butoxide agents. *Clinical Therapeutics* 1987;**9**(4):368–372.
- Preston 1977** {published data only}
Preston S, Fry L. Malathion lotion and shampoo: a comparative trial in the treatment of head lice. *Journal of the Royal Society of Health* 1977;**97**(6):291.
- Preston 1979** {published data only}
Preston S. An assessment of two carbaryl preparations. *Journal of the Royal Society of Health* 1979;**99**(4):173.
- Robinson 1980** {published data only}
Robinson DH, Shepherd DA. Control of head lice in school children. *Current Therapeutic Research* 1980;**27**(1):1–6.
- Rousset 1989** {published data only}
Rousset JJ, Agoumi A. [Étude bioclinique d'un shampoing à base de pyrèthrine de synthèse synergisé dans le traitement de la pédiculose]. *Extrait des Comptes Rendus de Thérapeutique et de Pharmacologie Clinique* 1989;**VII**(77): 1–4.
- Rupes 1995** {published data only}
Rupes V, Moravec J, Chmela J, Ledvinka J, Zelenkova J. A resistance of head lice (*Pediculus capitis*) to permethrin in Czech Republic. *Central European Journal of Public Health* 1995;**3**(1):30–32.
- Schuld 1996** {published data only}
Schuld M, Jungen C. Control of lice and nits with NeemAzal-FT. In: Kleeberg H, Micheletti V editor(s). *Practice oriented results on use and production of Neem ingredients and Pheromones IV*. Trifolio-M GmbH, 1996: 103–104.
- Sexton 1991** {published data only}
Sexton C, Miller AJ. A comparison of a single occasion treatment of head louse infestation with phenothrin liquid shampoo or a carbaryl lotion. *Current Medical Research and Opinion* 1991;**12**(7):466–470.
- Shashindran 1978** {published data only}
Shashindran CH, Gandhi IS, Krishnasamy S, Ghosh MN. Oral therapy of pediculosis capitis with cotrimoxazole. *British Journal of Dermatology* 1978;**98**:699–700.
- Sinniah 1982** {published data only}
Sinniah B, Sinniah D. Resistance of head louse (*Pediculus humanus capitis* deGeer) to DDT in Malaysia. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1982;**76**(1):72–74.
- Sinniah 1983a** {published data only}
Sinniah B, Sinniah D. Comparative study of DDT, carbaryl (Sevin) and Actellic (pirimiphos methyl) in the treatment of

- Pediculus humanus capitis. *Public Health (London)* 1983;**97**:3–7.
- Sinniah 1983b** *{published data only}*
Sinniah B, Sinniah D, Rajeswari B. Epidemiology and control of human head louse in Malaysia. *Tropical and Geographical Medicine* 1983;**35**(4):337–342.
- Sinniah 1984** *{published data only}*
Sinniah B, Shekhar C, Rampal L, Senan P. Pediculosis among rural school children in Kelang, Selangor, Malaysia and their susceptibility to malathion, carbaryl, perigen and kerosene. *Journal of the Royal Society of Health* 1984;**104**(3):114–115, 118.
- Sutton 1991** *{published data only}*
Sutton M. Does combing foil head lice?. *Professional Care of Mother and Child* 1991, (October):68.
- Svanasbakken 1982** *{published data only}*
Svanasbakken K, von Hanno T, Kollbaer R, Savonsnick R, Skagseth PA, Skjerven O. Treatment of head lice pediculus humanus capitis with Rinsoderm shampoo - a multicentric investigation. *Pyrethrum Post* 1982;**16**(1):21–22.
- Vermaak 1996** *{published data only}*
Vermaak Z. Model for the control of Pediculus humanus capitis. *Public Health* 1996;**110**:283–288.
- Youssef 1995** *{published data only}*
Youssef MYM, Sadaka HAH, Eissa MM, El-Ariny AF. Topical application of ivermectin for human ectoparasites. *American Journal of Tropical Medicine and Hygiene* 1995;**53**(6):652–653.

References to studies awaiting assessment

- Bingham 2000** *{published data only}*
Bingham P, Kirk S, Hill N, Figueroa J. The methodology and operation of a pilot randomized control trial of the effectiveness of the Bug Busting method against a single application insecticide product for head louse treatment. *Public Health* 2000;**114**:265–268.
- Curiati 1984** *{published data only}*
Curiati WJC. Double-blind study with decamethrin in scabies and head louse [Estudio duplo-cego com decametrina em escabiose e pediculose]. *Rev Bras Med* 1984;**41**(2):81–83.
- Hipolito 2001** *{published data only}*
Hipolito RB, Mallorca FG, Zuniga-Macaraig ZO, Apolinario PC, Wheeler-Sherman J. Head lice infestation: single drug versus combination therapy with one percent permethrin and trimethoprim/sulfamethoxazole.. *Pediatrics* 2001;**107**(3):E30.
- Manrique 2000** *{published data only}*
Manrique T, Cardenas N, Levy J, Mondolfi A. Comparative study with one formula of mineral oil vs. one shampoo with the treatment of the louse infection [Estudio comparativo entre una fórmula de aceite mineral vs. un champú de pediculicida para el tratamiento de la infestación por piojos.]. *Arch venez pueric pediatr* 2000;**63**(1):27–32.

- Ninci 1991** *{published data only}*
Ninci ME. Prophylaxis and treatment of the pediculosis with quassia amara [Profilaxis y tratamiento de pediculosis con cuasia amarga]. *Rev Fac Cienc Med (Cordoba)* 1991;**49**(2):27–31.
- Patrus 1983** *{published data only}*
Patrus OA, Andrade PM, Grossi M. Double-blind therapeutic trial with decamethrin (derived from pyrethroids) in head louse treatment [Ensaio terapeutico duplo-cego com decametrina (derivado piretroide) no tratamento da pediculose do couro cabeludo]. *Rev Bras Med* 1983;**40**(6):221–226.
- Plastow 2001** *{published data only}*
Plastow L, Luthra M, Powell R, Wright J, Russell D, Marshall MN. Head lice infestation: bug busting vs. traditional treatment.. *J Clin Nurs* 2001;**10**(6):775–783.

Additional references

- Aston 1998**
Aston R, Duggal H, Simpson J. Headlice: Report for Consultants in Communicable Disease Control (CCDCs). *The Public Health Medicine Environment Group Executive Committee* 1998, (June 12).
- Burgess 1995a**
Burgess IF. Human lice and their management. *Advances in Parasitology* 1995;**36**:271–342.
- Burgess 1995b**
Burgess IF. Clinical efficacy of treatment for head lice: Authors differ on assessment of flaws in trials. *British Medical Journal* 1995;**311**(7016):1369–1370.
- Burgess 1995c**
Burgess IF, Brown CM, Peock S, Kaufman J. Head lice resistant to pyrethroid insecticides in Britain. *British Medical Journal* 1995;**311**:752.
- Burgess 1996**
Burgess IF. Treatment of head lice. *Maternal and Child Health* 1996;**June**:142–146.
- Burgess 1997**
Burgess IF. The management of head lice infections. *Surgery OTC Review* 1997;**4**(5):15–17.
- Burgess 1998**
Burgess IF. Head lice - developing a practical approach. *The Practitioner* 1998;**242**:126–129.
- Chosidow 1994**
Chosidow O, Chastang C, Brue C, Bouvet E, Izri M, Monteny N, et al. Controlled study of malathion and d-henothrin lotions for Pediculus humanus var capitis infested schoolchildren. *Lancet* 1994;**344**:1724–1727.
- Chung 1991**
Chung RN, Scott FE, Underwood JE, Zavarella KJ. A pilot study to investigate transmission of head lice. *Canadian Journal of Public Health* 1991;**82**:207–208.
- Clarke 2002**
Clarke M, Oxman AD, editors. Optimal search strategy. *Cochrane Reviewers' Handbook* 4.1.6 [updated April

- 2002]; Appendix 5c. In: *The Cochrane Library [database on disk and CDROM]. The Cochrane Collaboration. Update Software: Oxford; 2002, issue 2.*
- Clore 1990**
 Clore ER, Longyear LA. Comprehensive pediculosis screening programmes for elementary schools. *Journal of School Health* 1990;**60**(5):212–214.
- Culver 1988**
 Culver CA, Malina JJ, Talbert RL. Probable anaphylactoid reaction to a pyrethrin pediculicide shampoo. *Clinical Pharmacology* 1988;**7**:846–849.
- Dunne 1991**
 Dunne CL, Malone CJ, Whitworth JAG. A field study of the effects of ivermectin on ectoparasites of man. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1991;**85**:550–551.
- Glaziou 1994**
 Glaziou P, Nyguyen LN, Mouliapelat JP, Cartel JL, Martin PMV. Efficacy of ivermectin for the treatment of head lice (pediculosis capitis). *Tropical Medicine and Parasitology* 1994;**45**(3):253–254.
- Goldsmid 1990**
 Goldsmid JM. Head louse treatment: is there an insecticide resistance problem?. *Medical Journal of Australia* 1990;**153**: 233–234.
- Lee 1976**
 Lee B, Groth P, Turner W. Suspected reactions to gamma benzene hexachloride. *Journal of the American Medical Association* 1976;**236**(25):2846.
- Lewis 1977**
 Lewis RA. Organophosphorous poisoning from preparations used for head lice (proceedings). *West African Journal of Pharmacology and Drug Research* 1977;**4**(1):63–64.
- Maunder 1971**
 Maunder JW. Resistance to organochlorine insecticides in head lice, and trials using alternative compounds. *Medical Officer* 1971;**125**(2):27–29.
- Maunder 1983**
 Maunder JW. An appreciation of lice. *Proceedings of the Royal Institution* 1983;**55**:1–31.
- Maunder 1993**
 Maunder JW. An update on head lice. *Health Visitor* 1993;**66**(9):317–318.
- Mumcuoglu 1991**
 Mumcuoglu KY, Klaus S, Kafka D, Teiler M, Miller J. Clinical observations relating to head lice infestation. *Journal of the American Academy of Dermatology* 1991;**25**(2): 248–251.
- Mumcuoglu 1995**
 Mumcuoglu KY, Hemingway J, Miller J, Ioffe-Uspensky I, Klaus S, Ben-Ishai F, Galun R. Permethrin resistance in the head louse *Pediculus capitis* from Israel. *Medical and Veterinary Entomology* 1995;**9**:427–432.
- Murray 1975**
 Murray ES, Torrey SB. Virulence of *Rickettsia prowazeki* for head lice. *Annals of the New York Academy of Science* 1975;**266**:25–34.
- PDR 1990**
Physician's Desk Reference. 4th Edition. Oradell: Medical economics Co, 1990:999.
- Roberts 1988**
 Roberts C. Head lice. *Pharmacy Update* 1988;**July/August**: 240–242.
- Rupes 1995**
 Rupes V, Moravec J, Chmela J, Ledvinka J, Zelenkova J. A resistance of head lice (*Pediculus capitis*) to permethrin in Czech Republic. *Central European Journal of Public Health* 1995;**3**(1):30–32.
- Scowen 1995**
 Scowen P. Government restricts the use of carbaryl for head lice. *Professional Care of Mother and Child* 1995;**5**(6):163, 165.
- Shuster 1996**
 Shuster J. Lindane-induced CNS effects. *Hospital Pharmacology* 1996;**31**:370,375.
- Silverton 1972**
 Silverton N. Malathion resistant pediculosis capitis. *British Medical Journal* 1972;**3**(827):646–647.
- Stallbaumer 1995**
 Stallbaumer M, Ibarra J. Clinical efficacy of treatment for head lice. Counting head lice by visual inspection flaws trials' results. *British Medical Journal* 1995;**311**(7016): 1369.
- Taplin 1988**
 Taplin D, Meinking T. Infestations. In: Schachner LA, Hansen RC editor(s). *Pediatric Dermatology*. Vol. 2, New York: Churchill Livingstone, 1988:1465–1493.
- Vander Stichel 1995a**
 Vander Stichele RH, Dezeure EM, Bogaert MG. Systematic review of clinical efficacy of topical treatments for head lice. *British Medical Journal* 1995;**311**(7005):604–608.
- Vander Stichel 1995b**
 Vander Stichele RH. Clinical efficacy of treatment for head lice: Authors' reply. *British Medical Journal* 1995;**311** (7016):1369.
- Wickenden 1985**
 Wickenden J. Head lice, schools, teachers and parents. *Health at School* 1985;**1**:18–19.
- Wohlfahrt 1982**
 Wohlfahrt DJ. Fatal paraquat poisonings after skin absorption. *Medical Journal of Australia* 1982;**1**(12): 512–513.
- Youssef 1995**
 Youssef MYM, Sadaka HAH, Eissa MM, El-Ariny AF. Topical application of ivermectin for human ectoparasites. *American Journal of Tropical Medicine and Hygiene* 1995;**53** (6):652–653.

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Burgess 1994

Methods	Two centre, randomised (open-list), comparative, assessor-blind, trial	
Participants	44 children and 8 adults from a school and a childrens home, with an active infection of lice. Age range was 7-15 and adults. No patients excluded from trial. Dhaka, Bangladesh	
Interventions	Pyrethrin (0.165%) plus PBO (1.65%) mousse (Banlice) (42) vs 1% permethrin creme rinse (Nix) (10) . Application time = 10 mins. Pyrethrin applied to dry hair and washed off with shampoo. Permethrin applied to shampooed, towel dried hair and rinsed off with tap water. Five eggs removed from each patient before and after treatment and incubated untill nymphs hatched	
Outcomes	Some patients lost to follow-up in both groups at each follow-up (2, 4, 6, 8, 14 days). 100% cure for evaluated patients in the permethrin group at each follow-up. In pyrethrin group 2 moribund newly hatched nymphs on one patient at day 4; 2 adult lice on another patient at day 6 from reinfestation. No adverse reactions reported by investigators or patients to either product	
Notes	Prevalence of infection 75% at school and 100% at childrens home	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Roberts 2000

Methods	Randomly assigned; assessor blinded; provider applied.
Participants	81 children with an age range of 3-14 years. North Wales, UK
Interventions	Malathion lotion (0.5%) (Suleo-M or Derbac-M) (44) vs BugBusting (37). Malathion lotion was applied to dry hair and allowed to dry naturally; application time = 8-10 hours. For the combing method, the hair was washed and plenty of conditioner applied. The hair was combed straight with a normal comb and then lice were combed out using a detection comb. Treatment was repeated every 3-4 days for up to 27 days. Infected family members of the participants were directed to use malathion lotion to prevent reinfection of the test participants
Outcomes	Patients evaluated at 7 and 14 days. Six participants excluded; one lost to follow-up
Notes	
<i>Risk of bias</i>	

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Taplin 1982

Methods	Assessor blinded; provider applied.
Participants	Children and adults, age range 2-36; 96 males, 23 females San Blas Islands, Panama.
Interventions	Malathion (0.5%) lotion (Prioderm) (50) with isopropyl vehicle vs placebo (isopropyl alcohol) (49). Treatment was applied to dry hair and allowed to dry naturally; application time = 12 hours. Both treatments washed out with neutral shampoo. Ten hairs with viable ova attached were removed from each patient before and after treatment and incubated for 14 days (30°C and 70% RH). Members of the patients' families were directed to use lindane shampoo to prevent reinfection of the test participants.
Outcomes	Patients evaluated at 24 hours, 7 days. Ova evaluated for hatching at 7 and 14 days.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Taplin 1986

Methods	Randomly assigned, placebo controlled, double-blind trial. A non-randomised positive control also used.
Participants	93 children and adults, with an age range of 2-32 years. 55 females and 38 males. All patients infected with lice and eggs. Patients excluded from study if they were being treated with antibiotics. No patients were excluded and none were lost to follow-up. Panama.
Interventions	1% permethrin (Nix) creme rinse (29) vs placebo creme rinse (20% isopropanol vehicle) (34) vs lindane (Kwell) shampoo (30) (non-randomized). After the hair had been shampooed and towel dried permethrin was applied for 10 minutes then rinsed away with clean water. Application procedure for placebo not stated. Lindane was applied to dry hair for 4 mins, then water added to make a lather which was massaged into the scalp for 4-5 mins then rinsed away with clean water. Ten hairs with viable eggs removed from each patient before and after treatment and incubated.
Outcomes	Patients were evaluated at 1, 2, 4, 6, 24 hours, 7 and 14 days after treatment. 100% in the permethrin group, 9% in the placebo group and 67% in the lindane group of patients were free of lice at day 7. By day 14, 97% in the permethrin group, 6% in the placebo group and 43% in the lindane group of patients.

Taplin 1986 (Continued)

	were free of lice. The results for lindane and placebo were attributed to treatment failure. Ovicidal effect as determined by hatch rate at day 14 was 30% for permethrin, 86% for placebo and 55% for lindane, compared to a pre treatment rate of 90%	
Notes	Prevalence of lice >90% in the study area.	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

PBO - piperonal butoxide

BugBusting - combing treatment using conditioner

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Ares Mazas 1985	PRIMARY REASON FOR EXCLUSION: A non-randomised, non-comparative trial. OTHER REASONS FOR EXCLUSION: Inclusion criteria for lice infection not clear, only mentions eggs. Unclear regarding prior pediculicide use and combing following treatment. COMPARISON: None - permethrin lotion
Ares Mazas 1988	PRIMARY REASON FOR EXCLUSION: A non-randomised, non-comparative study. OTHER REASONS FOR EXCLUSION: Criteria for identification of infection with lice not clear. Not clear regarding prior pediculicide use of combing following treatment. COMPARISON: None - malathion lotion
Armoni 1988	PRIMARY REASON FOR EXCLUSION: Patients enrolled on study with lice and/or eggs. Unclear regarding prior pediculicide application
Bainbridge 1998	PRIMARY REASON FOR EXCLUSION: Nit comb used to remove lice after treatment with pediculicide. OTHER REASONS FOR EXCLUSION: Environmental use of lice spray 'to clean the home' may allow transfer of insecticide to heads of treated participants, especially if bedding, hats and toys have been sprayed. COMPARISON: Pyrethrin plus PBO shampoo vs permethrin cream rinse
Blommers 1978a	PRIMARY REASON FOR EXCLUSION: A non-randomised non-comparative trial. OTHER REASONS FOR EXCLUSION: No clear statement regarding the state of infection of included patients. No clear statement regarding prior use of pediculicide or use of nit comb following treatment. COMPARISON: None - malathion lotion.
Blommers 1978b	PRIMARY REASON FOR EXCLUSION: A non-randomised non-comparative trial. OTHER REASONS FOR EXCLUSION: No clear statement regarding prior use of pediculicide or nit comb use following treatment.

(Continued)

	COMPARISON: None - lindane lotion
Blommers 1978c	PRIMARY REASON FOR EXCLUSION: A non-randomised, non-comparative study. OTHER REASONS FOR EXCLUSION: Criteria for identification of infection with lice not clear. Not clear regarding prior pediculicide use of combing following treatment. COMPARISON: None - malathion shampoo.
Blommers 1978d	PRIMARY REASON FOR EXCLUSION: A non-randomised, non-comparative study. COMPARISON: None - malathion lotion.
Blommers 1978e	PRIMARY REASON FOR EXCLUSION: An in vitro study using field collected lice. COMPARISON:
Bowerman 1987	PRIMARY REASON FOR EXCLUSION: Some participants used another pediculicide only 1 week before enrolment on the study
Brandenburg 1986	PRIMARY REASON FOR EXCLUSION: Patients excluded from study if pediculicide used 1 week or less before start date
Brink-Lindroth 1984	PRIMARY REASON FOR EXCLUSION: An in vitro laboratory study using head louse eggs collected from the field
Budak 1996	PRIMARY REASON FOR EXCLUSION: A non-randomised study. OTHER REASONS FOR EXCLUSION: Criteria for identification of infection with lice not clear. Not clear regarding prior pediculicide use of combing following treatment. COMPARISON: lindane vs. sumithrine (d-phenothrin).
Burgess 1990	PRIMARY REASON FOR EXCLUSION: Not a randomised controlled trial. Laboratory in-vitro study
Burgess 1992	PRIMARY REASON FOR EXCLUSION: Not a randomised controlled trial. Laboratory in vitro study using clothing lice
Burgess 1996	PRIMARY REASON FOR EXCLUSION: Not a randomised controlled trial. An in vitro laboratory study using clothing lice
Busvine 1942	PRIMARY REASON FOR EXCLUSION: Non-randomised. OTHER REASONS FOR EXCLUSION: Methodology not clearly stated. COMPARISON: Lauryl thiocyanate vs. lethane special vs. rotenone
Busvine 1948	PRIMARY REASON FOR EXCLUSION: Not a randomised controlled trial. COMPARISON: DDT vs. gamma-BHC (lindane).
Carson 1988	PRIMARY REASON FOR EXCLUSION: Nit comb used to remove lice following pediculicide use. OTHER REASONS FOR EXCLUSION:
Chosidow 1994	PRIMARY REASON FOR EXCLUSION: Patients enrolled on study with lice and/or eggs. OTHER REASONS FOR EXCLUSION: Unclear regarding prior pediculicide application and nit comb use. COMPARISON:

(Continued)

Clore 1993	PRIMARY REASON FOR EXCLUSION: Patients enrolled on study with lice and/or eggs. OTHER REASONS FOR EXCLUSION: Nit comb used to remove lice and eggs following treatment with pediculicide
Coates 1971	PRIMARY REASON FOR EXCLUSION: A non-randomised, non-comparative study. OTHER REASONS FOR EXCLUSION: Patients included on trial if they were infected with lice or eggs. Not clear regarding prior pediculicide. Nit comb used to remove lice/eggs following treatment
Cordero 1987	PRIMARY REASON FOR EXCLUSION: Patients enrolled on study with viable eggs, no mention of lice. OTHER REASONS FOR EXCLUSION: Unclear regarding the prior use of pediculicide and the use of nit comb
De Boer 1984	PRIMARY REASON FOR EXCLUSION: Method of allocation not stated. OTHER REASONS FOR EXCLUSION: No clear statement regarding prior use of pediculicide. Nit comb used to comb hair thoroughly on day 3, 7 and 14
De Boer 1985	PRIMARY REASON FOR EXCLUSION: Not a randomised controlled trial. OTHER REASONS FOR EXCLUSION: Not a comparative trial. No clear statement regarding prior use of pediculicide. COMPARISON: None - malathion.
De Felice 1989	PRIMARY REASON FOR EXCLUSION: A non-randomised trial. OTHER REASONS FOR EXCLUSION: No clear statement regarding prior use of pediculicide. COMPARISON: Permethrin plus combing vs. permethrin without combing
DiNapoli 1988	PRIMARY REASON FOR EXCLUSION: Pediculicide use 1 week before enrolment on study. OTHER REASONS FOR EXCLUSION:
Donaldson 1986	PRIMARY REASON FOR EXCLUSION: Patients included on trial if they were infected with lice or eggs. OTHER REASONS FOR EXCLUSION: Not clear regarding prior pediculicide and nit comb use. COMPARISON:
Doss 1991	PRIMARY REASON FOR EXCLUSION: Patients enrolled on study with lice and/or eggs. OTHER REASONS FOR EXCLUSION: Unclear regarding prior pediculicide application and nit comb use. COMPARISON:
Dunne 1991	PRIMARY REASON FOR EXCLUSION: Non-randomised. OTHER REASONS FOR EXCLUSION: Patients included on trial if lice or eggs present. Not clear regarding prior pediculicide use of combing following treatment. COMPARISON: Ivermectin vs. placebo?
Fan 1991	PRIMARY REASON FOR EXCLUSION: A non-randomised, non-comparative trial. OTHER REASONS FOR EXCLUSION: Patients enrolled on study with lice and/or eggs. Unclear regarding prior pediculicide application and nit comb use. COMPARISON: None - gamma-BHC (lindane).

(Continued)

Fan 1992	PRIMARY REASON FOR EXCLUSION: A non-randomised study. OTHER REASONS FOR EXCLUSION: Criteria for identification of infection with lice not clear. Not clear regarding prior pediculicide use of combing following treatment. COMPARISON: permethrin creme rinse vs. bioallethrine aerosol vs. malathion shampoo vs. gamma-BHC (lindane)
Goldsmid 1989	PRIMARY REASON FOR EXCLUSION: Patients enrolled on study with lice and/or eggs. OTHER REASONS FOR EXCLUSION: Unclear regarding prior pediculicide application and nit comb use. COMPARISON:
Gomez Urcuyo 1986	PRIMARY REASON FOR EXCLUSION: Criteria for identification of infection with lice not clear. OTHER REASONS FOR EXCLUSION: Not clear regarding prior pediculicide use of combing following treatment. COMPARISON:
Iannantuono 1997	PRIMARY REASON FOR EXCLUSION: Nit comb used to remove lice/eggs following treatment. OTHER REASONS FOR EXCLUSION: Not clear regarding prior pediculicide use. COMPARISON:
Jolley 1991	PRIMARY REASON FOR EXCLUSION: Patients enrolled on trial with lice and/or eggs. OTHER REASONS FOR EXCLUSION: COMPARISON:
Karacic 1982	PRIMARY REASON FOR EXCLUSION: A non-randomised, non-comparative study. OTHER REASONS FOR EXCLUSION: Patients included on trial if they were infected with lice or eggs. Not clear regarding prior pediculicide. Nit comb used to remove lice/eggs following treatment. COMPARISON: crotamiton lotion.
Kyle 1990	PRIMARY REASON FOR EXCLUSION: Patients enrolled on study with lice and/or eggs. OTHER REASONS FOR EXCLUSION: Unclear regarding prior pediculicide application and nit comb use. COMPARISON:
Lange 1980	PRIMARY REASON FOR EXCLUSION: A non-randomised non-comparative trial. OTHER REASONS FOR EXCLUSION: Patients included in study if they had lice and/or eggs. Nit comb used to remove lice following pediculicide treatment. COMPARISON: None - pyrethrin shampoo (synergised with piperonal butoxide)
Lidror 1965	PRIMARY REASON FOR EXCLUSION: Not a randomised controlled trial. OTHER REASONS FOR EXCLUSION: A non-comparative trial using malathion. No clear statement regarding the state of infection of included patients. No clear statement regarding prior use of pediculicide. Nit comb used after application of pediculicide other than to detection comb. COMPARISON: None - malathion.
Maguire 1972	PRIMARY REASON FOR EXCLUSION: A non-randomised non-comparative trial OTHER REASONS FOR EXCLUSION: COMPARISON: None - single treatment with malathion.

(Continued)

Mathias 1984	PRIMARY REASON FOR EXCLUSION: Patients enrolled on study with lice and/or eggs. OTHER REASONS FOR EXCLUSION: COMPARISON:
Maunder 1971a	PRIMARY REASON FOR EXCLUSION: A non-randomised non-comparative trial. OTHER REASONS FOR EXCLUSION: No clear statement regarding the state of infection of included patients. No clear statement regarding prior use of pediculicide or nit comb use. COMPARISON: None - malathion lotion.
Maunder 1971b	PRIMARY REASON FOR EXCLUSION: Non-randomised trial. . OTHER REASONS FOR EXCLUSION: No clear statement regarding prior use of pediculicide or nit comb use. COMPARISON: Malathion vs. carbaryl vs. placebo.
Meinking 1986	PRIMARY REASON FOR EXCLUSION: An in vitro study.
Miller 1988	PRIMARY REASON FOR EXCLUSION: Patients enrolled on trial with lice and/or eggs. OTHER REASONS FOR EXCLUSION: Unclear regarding prior pediculicide application and nit comb use. COMPARISON:
Monheit 1986	PRIMARY REASON FOR EXCLUSION: Patients enrolled with live lice and/or eggs. OTHER REASONS FOR EXCLUSION: Treated with pediculicide to remove all lice and eggs before combing. COMPARISON:
Morsy 1996	PRIMARY REASON FOR EXCLUSION: A non-randomised study. OTHER REASONS FOR EXCLUSION: Criteria used to diagnose infection unclear. Not clear statement regarding prior pediculicide use. Nit comb used to remove lice/eggs following treatment. COMPARISON:
Pai 1992	PRIMARY REASON FOR EXCLUSION: A non-randomised, non-comparative trial. OTHER REASONS FOR EXCLUSION: Participants enrolled with lice and/or eggs. No clear statement regarding prior exposure to pediculicides or nit comb use. COMPARISON:
Pitman 1987	PRIMARY REASON FOR EXCLUSION: Patients excluded if pediculicide used less than two weeks prior to the commencement of the study. OTHER REASONS FOR EXCLUSION: COMPARISON:
Preston 1977	PRIMARY REASON FOR EXCLUSION: Patients enrolled on study with lice and/or viable eggs. OTHER REASONS FOR EXCLUSION: Unclear regarding the prior use of pediculicide and the use of nit comb. COMPARISON:
Preston 1979	PRIMARY REASON FOR EXCLUSION: A non-randomised trial. OTHER REASONS FOR EXCLUSION: Patients enrolled on study with lice and/or viable eggs. Unclear regarding the prior use of pediculicide and the use of nit comb.

(Continued)

	COMPARISON: Carbaryl gel shampoo vs. carbaryl lotion.
Robinson 1980	PRIMARY REASON FOR EXCLUSION: Nit comb used to remove lice and eggs after treatment with pediculicide. OTHER REASONS FOR EXCLUSION: Unclear regarding state of infection before to enrollment on study and prior treatment with pediculicide. COMPARISON:
Rousset 1989	PRIMARY REASON FOR EXCLUSION: A non-randomised non-comparative trial. OTHER REASONS FOR EXCLUSION: Choice of included patients inadequate because patients were enrolled on trial if they had lice or eggs or both. No clear statement regarding prior use of pediculicide. Nit comb used after application of pediculicide other than to detection comb. COMPARISON: None -synergised depallethrin shampoo.
Rupes 1995	PRIMARY REASON FOR EXCLUSION: In vitro study.
Schuld 1996	PRIMARY REASON FOR EXCLUSION: Non-randomised non-comparative trial. OTHER REASONS FOR EXCLUSION: No clear statement regarding the state of infection for included patients. No clear statement regarding prior use of pediculicide or nit comb use. COMPARISON: None - Nemm extract with 4% azadiractin.
Sexton 1991	PRIMARY REASON FOR EXCLUSION: Some patients included on trial with only eggs. OTHER REASONS FOR EXCLUSION: Not clear regarding prior pediculicide use of combing following treatment. COMPARISON:
Shashindran 1978	PRIMARY REASON FOR EXCLUSION: A non-randomised trial. OTHER REASONS FOR EXCLUSION: Criteria for assessing infection not clear. Unclear regarding prior pediculicide application and nit comb use. COMPARISON: Cotrimoxazole vs. trimethoprim vs. sulphamethoxazole
Sinniah 1982	PRIMARY REASON FOR EXCLUSION: Method of allocation into the treatment groups not stated. OTHER REASONS FOR EXCLUSION: A non-comparative trial. COMPARISON: None.
Sinniah 1983a	PRIMARY REASON FOR EXCLUSION: Method of allocation into the treatment groups not defined. OTHER REASONS FOR EXCLUSION: No clear statement regarding prior use of pediculicide or nit comb use. COMPARISON:
Sinniah 1983b	PRIMARY REASON FOR EXCLUSION: A non-randomised study. OTHER REASONS FOR EXCLUSION: Participants included on trial if they were infected with lice or eggs. Not clear regarding prior pediculicide use of combing following treatment. COMPARISON:
Sinniah 1984	PRIMARY REASON FOR EXCLUSION: A non-randomised study. OTHER REASONS FOR EXCLUSION: Method of allocation into the treatment groups not given. No clear statement regarding prior use of pediculicide or nit comb use. COMPARISON:

(Continued)

Sutton 1991	PRIMARY REASON FOR EXCLUSION: A non-randomised trial. OTHER REASONS FOR EXCLUSION: Participants enrolled with either lice and/or eggs. COMPARISON:
Svanasbakken 1982	PRIMARY REASON FOR EXCLUSION:: Non-randomised non-comparative trial. OTHER REASONS FOR EXCLUSION: Choice of included patents inadequate because patients were enrolled on trial if they had lice or eggs or both. No clear statement regarding prior use of pediculicide. Nit comb used after application of pediculicide other than to detection comb. COMPARISON: None - pyrethrum shampoo synergised by PBO.
Vermaak 1996	PRIMARY REASON FOR EXCLUSION: A non-randomised non-comparative trial. COMPARISON: None.
Youssef 1995	PRIMARY REASON FOR EXCLUSION: A non-randomised non-comparative trial. OTHER REASONS FOR EXCLUSION: Criteria for assessing infection not clear. Unclear regarding prior pediculicide application and nit comb use. COMPARISON: None - ivermectin.

DATA AND ANALYSES

Comparison 1. Pediculicide vs placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 primary cure by day 2	1	115	Peto Odds Ratio (Peto, Fixed, 95% CI)	12.63 [2.06, 77.55]
1.1 Permethrin vs. placebo	0	0	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 malathion vs. placebo	1	115	Peto Odds Ratio (Peto, Fixed, 95% CI)	12.63 [2.06, 77.55]
2 free from lice by day 7	2	175	Peto Odds Ratio (Peto, Fixed, 95% CI)	20.82 [10.93, 39.65]
2.1 Permethrin vs. placebo	1	63	Peto Odds Ratio (Peto, Fixed, 95% CI)	36.24 [13.56, 96.85]
2.2 malathion vs. placebo	1	112	Peto Odds Ratio (Peto, Fixed, 95% CI)	13.72 [5.85, 32.19]
3 free from lice by day 14 (cure)	1	63	Peto Odds Ratio (Peto, Fixed, 95% CI)	35.78 [13.37, 95.72]
3.1 Permethrin vs. placebo	1	63	Peto Odds Ratio (Peto, Fixed, 95% CI)	35.78 [13.37, 95.72]
3.2 malathion vs. placebo	0	0	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 ovicidal effect at day 7-14			Other data	No numeric data
4.1 permethrin vs. placebo			Other data	No numeric data
4.2 malathion vs. placebo			Other data	No numeric data

Comparison 2. synergised pyrethrin vs permethrin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 primary cure by day 2	1	47	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 free from lice at day 4	1	32	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.26 [0.00, 24.36]
3 free from lice at day 6	1	22	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.30 [0.00, 18.59]
5 free from lice at day 8	1	7	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 free from lice by day 14 (cure)	0	0	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 ovicidal effect day 7-14			Other data	No numeric data

Comparison 3. Pediculicide vs combing

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 free from lice by day 7	0	0	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 free from lice by day 14 (cure)	1	74	Risk Ratio (M-H, Fixed, 95% CI)	2.10 [1.30, 3.37]
2.1 Malathion vs Bugbusting	1	74	Risk Ratio (M-H, Fixed, 95% CI)	2.10 [1.30, 3.37]

Analysis 1.1. Comparison 1 Pediculicide vs placebo, Outcome 1 primary cure by day 2.

Review: Interventions for treating headlice

Comparison: 1 Pediculicide vs placebo

Outcome: 1 primary cure by day 2

Analysis 1.2. Comparison 1 Pediculicide vs placebo, Outcome 2 free from lice by day 7.

Review: Interventions for treating headlice

Comparison: 1 Pediculicide vs placebo

Outcome: 2 free from lice by day 7

Analysis I.3. Comparison I Pediculicide vs placebo, Outcome 3 free from lice by day 14 (cure).

Review: Interventions for treating headlice

Comparison: I Pediculicide vs placebo

Outcome: 3 free from lice by day 14 (cure)

Analysis I.4. Comparison I Pediculicide vs placebo, Outcome 4 ovidal effect at day 7-14.

ovidal effect at day 7-14

Study	Expt: pre - post HR%	Expt: % motility	Ctrl: pre - post HR%	Ctrl % mortality	
permethrin vs. placebo					
Taplin 1986	92 - 30	62% (day 14)	94 - 86	8% (day 14)	
malathion vs. placebo					
Taplin 1982		54.7% (day 7) 85.8% (day 14)		28.9% (day 7) 47.8% (day 14)	

Analysis 2.1. Comparison 2 synergised pyrethrin vs permethrin, Outcome 1 primary cure by day 2.

Review: Interventions for treating headlice

Comparison: 2 synergised pyrethrin vs permethrin

Outcome: 1 primary cure by day 2

Analysis 2.2. Comparison 2 synergised pyrethrin vs permethrin, Outcome 2 free from lice at day 4.

Review: Interventions for treating headlice

Comparison: 2 synergised pyrethrin vs permethrin

Outcome: 2 free from lice at day 4

Analysis 2.3. Comparison 2 synergised pyrethrin vs permethrin, Outcome 3 free from lice at day 6.

Review: Interventions for treating headlice

Comparison: 2 synergised pyrethrin vs permethrin

Outcome: 3 free from lice at day 6

Analysis 2.5. Comparison 2 synergised pyrethrin vs permethrin, Outcome 5 free from lice at day 8.

Review: Interventions for treating headlice

Comparison: 2 synergised pyrethrin vs permethrin

Outcome: 5 free from lice at day 8

Analysis 2.7. Comparison 2 synergised pyrethrin vs permethrin, Outcome 7 ovicidal effect day 7-14.

ovicidal effect day 7-14

Study	Expt: pre - post HR%	Expt: % mortality	Ctrl: pre - post HR%	Ctrl: % mortality	
Burgess 1994	52 - 17.8	34.2% (day 14)	48.5 - 40.5	8% (day 14)	

Analysis 3.2. Comparison 3 Pediculicide vs combing, Outcome 2 free from lice by day 14 (cure).

Review: Interventions for treating headlice

Comparison: 3 Pediculicide vs combing

Outcome: 2 free from lice by day 14 (cure)

ADDITIONAL TABLES

Table 1. Detailed search strategies

Search set	EMBASE (OVID)*	PubMed*
1	pediculosis.mp	pediculus [MESH]
2	pediculosis capitis.mp	head lice/
3	head lice/	pediculos*/
4	1 or 2 or 3	1 or 2 or 3

Table 1. Detailed search strategies (Continued)

5	pediculid\$/	malathion/
6	malathion.mp	permethrin/
7	permethrin.mp	pyrethrin/
8	pyrethrin.mp	malthion/
9	carbaryl.mp	carbaryl/
10	5 or 6 or 7 or 8 or 9	5 or 6 or 7 or 8 or 9
11	4 and 10	4 and 10
12	treatment .mp	treatment/
13	therapy.mp	therapy/
14	insectid\$/	insectid*
15	shampoo/	shampoo/
16	12 or 13 or 14 or 15	12 or 13 or 14 or 15
17	11 and 16	11 and 16
18	limit 17 to human	limit 17 to human
	*Topic search terms used in combination with the 'Optimal Search Strategy for RCTs' in the Cochrane Reviewers' Handbook (Clarke M, Oxman AD, editors. Cochrane Reviewers' Handbook 4.1.5 [updated April 2002]. In: The Cochrane Library, Issue 2, 2002	

FEEDBACK

CHC 'Bug Buster'

Summary

Community Hygiene Concern (CHC) has many years' experience of working to solve the head louse problem, supporting parents to deal with treatment failures, re-infestation, confusion and frustration. The social stigma associated with head lice still persists and there is growing anxiety about the cost and health implications of repeated treatment applications.

As a public interest charity, we welcomed the announcement that the highly respected Cochrane Collaboration would review interventions for treating head lice. We had high expectations that full examination would be made of the best evidence available on the natural history of *Pediculus capitis*, the epidemiology of pediculosis capitis, the reliability of different detection methods, the validity

of treatment instructions/claims and the sustainability of control strategies. We anticipated the resulting review would be helpful in providing support, an informed choice, and assist in the monitoring of outcomes. CHC has studied the full Cochrane review, as published electronically (Dodd, 1999, 2001a) and an editorial based on its findings published in the BMJ (Dodd 2001b). We have been so disappointed that it is our intention to campaign for a new review. We find this body of work, which concentrates on the UK situation, is shallow, unbalanced, and comes to misleading conclusions.

There is a well-known paucity of randomised controlled trial evidence to support treatment protocols. In the circumstances, we expected that this review would carefully distinguish between speculation, expert opinion and proven fact, but its recommendations are based on a trial rejected as seriously flawed by an earlier systematic review (Vander Stichele et al, 1995). It omits key papers which provide evidence on the appropriate diagnostic techniques for different circumstances, and clinical evaluations of treatments which has led to a false conclusion that no insecticide has been shown to be more effective than another. In the case of the trial by Roberts et al (2000), Roberts himself has protested at the Cochrane misinterpretation of the trial results (bmj.electronic response, 2001). Moreover, Dodd does not call for implementation of the Medicine Control Agency ruling in February 2000 that 'natural' treatments must pass safety and efficacy licensing tests to trade legally.

Contrary to Cochrane principles there has been no consumer participation in this review and the review author declares a serious potential conflict of interest. In our view, it damages the gold standard reputation of the Cochrane reviews in general and should be withdrawn.

We feel that an independent, suitably qualified panel should undertake a new Cochrane review.

Reply

REPLIES TO SPECIFIC COMMENTS

Comment 1

This review accepts, with no adequate explanation, the RCT conducted by Burgess et al. (1994) which was rejected by Vander Stichele et al. (1995) as seriously flawed.

Reply

The review by Vander Stichele et al (1995) was criticised in other publications for choosing inappropriate quality criteria by which to evaluate trials (Burgess 1995, Stallbaumer and Ibarra 1995). Some of the trials included in the Vander Stichele review, upon closer inspection, were found to be seriously flawed in their methodology. The authors agreed that a subsequent Cochrane Review (Vander Stichele and Bogaert 1995) was appropriate.

The trial by Burgess et al (1994) was excluded by Vander Stichele because it failed to meet a number of the quality criteria set for the review, and according to the authors had a high risk of bias. According to Vander Stichele, the trial by Burgess fails on the following criteria; randomization procedure, concealment allocation to patients, definition of exclusion criteria, ethical procedures, appropriateness of conclusions, documentation of prior exposure to pesticides, history of prior head lice treatment, definition of current head lice infection, prevalence of lice in study area, contact tracing, documentation of: pediculicidicity, residual activity and cure rate. In fact the majority of this information is detailed in the paper or was provided by the author when the trial was being assessed for inclusion in the Cochrane Review.

To answer each point in turn: Patients were individually randomised into the test groups, but details of allocation concealment were not given. However as two different pediculicides were used, each of which has a different formulation, with different application procedures, it is impossible to conceal which treatment is being provided to which patient. Patients were allocated to treatment groups in blocks of three, 1 permethrin: 2 pyrethrin. Appropriate exclusion criteria were chosen and reported in the trial. Although prior exposure to pesticides was not documented, the study was carried out in an area where no products were commercially available. Participants were only included in the trial if they exhibited a current infection with lice determined by observing live lice on the head/ scalp. The study was conducted on two sites where the prevalence of lice was 75% and 100%. Contacts were not treated or traced in this study. Participants were followed up at 2,4,6,8,14 days post treatment and assessed for the presence of live lice by detection combing. Overall cure rate was determined at each follow up, but the number of participants assessed at each follow up, except the first, was poor and a direct comparison between the treatment groups could not be made at day 14 as no data was available for one of the groups. Residual activity of the preparations was not considered, although permethrin has been shown to exhibit some residuality. However, most insecticides do not have a residual action, which according to Vander Stichele's inclusion criteria would dismiss the majority of compounds from being considered effective pediculicides. However, in the long term it is not advantageous to use a product with a residual activity, as the residuum slowly diminishes to sub-lethal levels that can lead to the development of resistant strains of lice (Burgess 1995), which now have widespread occurrence.

Despite there being some difficulties with the trial by Burgess et al (1994), the design met with the inclusion criteria chosen for the Cochrane Review and a detailed discussion of the appropriateness of these criteria can be found in the review. The quality criteria by

which Vander Stichele judged the trials are not necessarily relevant to addressing the effectiveness of a product for the curative treatment of head lice. It is clear by the discrepancies between their assessment of the Burgess paper and that made in the Cochrane Review, that their judgement of the trials is doubtful and inconsistent as has been highlighted in previous reports (Burgess 1995, Stallbaumer and Ibarra 1995).

Comment 2

The clinical evaluations by Downs et al.(1998, 1999) made in Bath and Bristol are completely omitted from this review. These show an 87% failure rate for pyrethroids and a 64% failure rate for malathion. The lapse leads Dodd to the false conclusion that no insecticide has been shown to be more effective than another.

Reply

Neither of the papers listed above by Downs et al (1999a,b) are RCTs. Downs et al (1999a) assesses the prevalence of head lice in schoolchildren and looks at resistance in vitro. If treatment was applied to patients directly, the methodology is not detailed. Downs et al (1999b) tests the susceptibility of field collected lice for resistance to different pediculicides, in vitro, by exposing the lice to insecticide impregnated filter papers. In vitro studies were excluded from the Cochrane Review because the methods used and the results obtained are not indicative of the effectiveness of pediculicide when used in the field to treat people infected with head lice. In the Downs et al (1999b) study, a group of children were also treated with one of two commercially available pediculicides. However, one of the preparations was not used according to manufacturers instructions and neither treatment was reapplied 7 days after the initial application to account for the presence of nymphs hatched from eggs that were laid prior to the initial treatment. This is important as neither preparation is 100% ovicidal. Assessment of cure was conducted 24 and 72 hour post treatment and the presence of nymphs post treatment was not taken as treatment failure. This in itself is not incorrect as any first and second stage nymphs found up to one week following treatment are hatched from surviving eggs. Adults and third instar nymphs can only be from reinfection unless there is complete treatment failure, when they should have been found at the first follow up investigation (Burgess 1995). However, even if the product is not reapplied after 7 days, a final assessment at 14 days post treatment should be taken as the definitive evaluation of pediculicidal and ovicidal activity, as eggs that were not killed by treatment can take up to ten days to hatch (Taplin et al 1986).

It is true that in the field, some pediculicides are more effective than others, with treatment success being reflected by local resistance patterns. However, there are currently no RCTs of suitable quality which address these questions and therefore the results cannot be included in a meta-analysis to determine which products are the most effective. In order to provide a meaningful answer to this question, a nation-wide study would have to be conducted, looking at the different local resistance patterns across the country.

The results obtained by Downs et al (1999a,b) could be incorporated into the background section of the review, but the papers do not meet the inclusion criteria to be included in the analysis.

Comment 3

In 1999, the Bug Busting method is inaccurately described and dismissed as “unfeasible” for treatment in advance of the publication of RCT evidence. No consideration is given to its value as a detection method. In 2001, no change has been made inspite of publication in the interim of a review calling for the standardization of detection methods for diagnosis and epidemiological purposes (Figueroa, 2000), a pilot trial which provides evidence on the appropriate diagnostic techniques for different circumstances (Bingham et al, 2000) and an observational study (De Maeseneer et al, 2000).

Reply

In the outcome measures of the review, it is stated that pediculicidal effect should be determined by detection combing, therefore further discussion of detection methods is not relevant for the review.

In answer to the second point, the Bug Busting method of louse control requires the hair to be wet combed with conditioner for at least 30 minutes every 3–4 days using a fine toothed louse detection comb. The use of this method as a control measure was described as unfeasible because “too few people have sufficient motivation or skill” to implement the method effectively and success is most likely “if an infection is found in the earliest stages when few lice are present” (Burgess 1997). Roberts et al (2000) report that Bug Busting requires significant time and effort for it to work as a treatment for head lice. They suggest that when children that had used pediculicide in the 4 weeks before entry on to their trial were excluded from the analysis, the cure rate in the Bug Busting group increased. They propose that an explanation for this could be that children in this subgroup were less likely to report recurrent treatment failure and less socially disadvantaged, and therefore more able to use Bug Busting successfully. They continue by suggesting that the results of their trial indicate that policies advocating the use of Bug Busting as a first line treatment for head lice infection are inappropriate for the general population. The highlighted difficulties with compliance for this treatment method support the notion that Bug Busting is an unfeasible first line treatment method for head lice. That does not mean however, that Bug Busting is unsuitable under all circumstances. It may still be used in cases where all else has failed, or in families who do not wish, for what ever reason, to use insecticides, in which case motivation to comply and persevere with treatment is likely to be high.

It is also worthy of note that the diagnostic methods used in the Bingham study were not those “approved” by CHC, i.e. they first used parting the hair and looking, and then used dry combing alone. However, CHC only approve wet combing in their literature,

and criticised dry combing, because lice move rapidly away from disturbance in dry hair (Stallbaumer and Ibarra 1995), it allows the build up of static electricity and causes pain if sore patches are present (Ibarra 2001).

Comment 4

In 2001, Dodd includes a RCT conducted by Roberts et al. (2000) in North Wales comparing Bug Busting (using the first, more laborious Bug Buster comb) with two applications of malathion a week apart which recorded a 38% and 78% success rate respectively, but inaccurately reports that it found that Bug Busting is ineffective as a curative measure. Roberts himself has protested at the misinterpretation (bmj.electronic response, 2001).

Reply

When choosing a product/method for treating a head lice infection the cure rate is an important outcome measure to consider. The desired outcome of treatment is complete cure of infection, as continuance of infection is possible with only one gravid female or a single male and non-gravid female. It is therefore a matter of interpretation whether one considers a treatment method which has been shown to have a cure rate of 38% to be effective and as described by Roberts et al (2000) “inappropriate for the general population” as a first line treatment against head lice. Downs et al (2001) criticised as “unethical”, Roberts’ use of malathion lotion knowing moderate resistance to be present in the study area. If the use of a proven treatment, achieving a 78% treatment success rate is to be considered unethical, then surely the situation pertaining to the use of an untried and apparently unsuccessful combing method should, by these standards, be totally unethical or at the very least of dubious ethics. Roberts himself, in his BMJ response (2001), lists the Bug Buster Kit to have poor effectiveness against head lice, together with the pyrethroid pediculicides Full Marks and Lynclear, products which are not usually considered effective for treating head lice.

Comment 5a

(5) Correspondence about the trial has been ignored, but these letters raise many important points relevant to the sensible use of resources, including:

(a) that the N Wales study found Bug Busting 2% more effective than malathion was proved in Bath and Bristol (Hill, 2000)

Reply

The results from the Bath/Bristol study (Downs et al 1999b) were based on a trial involving 16 participants (Bristol) and 14 participants (Bath). In order to be able to detect a 20% difference between treatments at 80% power with 95% confidence you need around 60-65 per group using conventional clinical statistical methods. In fact, with the exception of Taplin’s two placebo controlled studies, all RCT’s currently available are underpowered to produce the results required. The results of the Bath/Bristol investigation (Downs et al 1999b) are only pertinent for the locality from which the lice were taken. It is known that resistance patterns vary across the country and even within a locality. If a pediculicide has a cure rate of 36% it should surely be deemed ineffective for the curative treatment of head lice within that locality, as the outcome of treatment should be complete cure of all the individuals treated. In the Taplin et al (1982) trial, the cure rate at day 7 was 44.68% in the control group, in which treatment was with the vehicle alone.

Comment 5b

(b) that skill in managing Bug Busting grows with familiarity, whereas exposure of the louse population to repeatedly applied insecticide increases insect resistance (Ibarra et al, 2000)

Reply

Burgess (in Gross 2001) states that wet combing with conditioner results in foam and slime making it difficult to see the lice and in addition, components such as panthenol and surfactants in conditioners may lead to adverse reactions in some patients. In the same article he commented on wet combing, saying that the problem is not that the method does not work, but that people do not know how to do it. “You need to appreciate what you are doing and why and to continue until you find no more lice,” he said. He recommended that, if necessary, wet combing needs to be continued for up to two hours at a time, depending on the number of lice found and the thickness of the hair, and carried out four times over a period of at least two weeks. This period may need to be extended until all lice have been removed.

The prophylactic use of insecticides should not occur as it will not prevent infection and may promote resistance and increases the risk of toxicity. The use of repellents is not recommended for the same reason (Aston et al 1998). Treatment with a pediculicide should only be undertaken if live lice are found. It is recommended that pediculicides (and combing) should be used in a mosaic strategy. This involves applying a particular insecticide/treatment and repeating application seven days later. If live lice are still found then another insecticide from a different chemical class is used and so on. This method avoids continual repeated use of a single product and is designed to delay the onset of resistance. However, it is inevitable that insects will eventually develop some degree of resistance to insecticides.

However, some of the currently unlicensed products that appear to work contain nothing more than conditioning agents found in conventional hair conditioners e.g. Nice n’ Clear. This product appears to kill lice just by surfactant activity over a relatively extended application time, in some cases not much exceeding that used for Bug busting (Burgess pers comms 2002). It is possible that quite a lot of the “activity” observed by CHC when Bug Busting was introduced, was due to the killing effects of conditioner as much as

the effects of combing, but over time, however, strains of lice more tolerant of the conditioning agents have been selected and so Bug Busting is likely to be less effective now as a result (Burgess pers comms 2002). We can see this in the use of Nix/Lyclear. Taplin's placebo controlled study found a reduction of cases in the placebo group at the first assessment even using only 10 minutes application. However, these days the lice are more tolerant of both the permethrin and the vehicle so these effects are no longer experienced (Burgess pers comms 2002).

Comment 5c

(c) that the N Wales trial, in common with all others cited in the review, lacks information on long-term outcome (Richards, 2000) which Dodd does not remark upon; this is vital when families face multiple episodes of infestation

Reply

It is believed that time spent curing an individual is wasted unless infectious contacts are also treated and traced (Dodd 2001). By doing this, the risk of reinfection to the patient is reduced, as will be the degree of transmission of lice on a wider scale. As most infections have existed for weeks rather than days before they are detected, contacts over the last month should be traced (Dodd 2001). Contact tracing is essential to prevent reinfection. All proven cases should be treated at the same time with the same insecticide (Aston et al 1998). Prevention is best achieved by regular detection combing and early intervention, although in practical terms the solution lies as much in education as in treatment. With regard to the long-term implications of resistance management, see the comments above. In cases of consistent treatment failure and/or multiple episodes of infestation, Bug Busting is not necessarily the 'cure-all' that it claims to be, some families are using it almost constantly and not achieving any effect (Burgess pers comms 2002). We should not forget that resistance operates at two levels, lice and humans!

Comment 5d

(d) the judgement that it is unethical to sell products for use on children where widespread insect resistance has been demonstrated (Downs et al, 2000b) on which Dodd gives no opinion.

Reply

See previous comments.

Comment 6

Review of key materials that influence parental choice has been omitted. This divorces the review from reality. There is no acknowledgement that pharmaceutical companies advertise and market to the general public their pyrethroid preparations, claiming instant success - 10 minutes for permethrin (Warner Lambert, 2000) and 30 minutes for phenothrin (SSL International, 2000) - and all their products, with the exception of shampoo formulations, state that a single application kills not only lice but their eggs.

Reply

This is fair comment, but the review was not designed to be a critical appraisal of the marketing strategies of pharmaceutical companies, rather an objective and impartial review of the best evidence relating to the effectiveness of the available treatments. The review states: "The way in which these insecticides are formulated into the marketed products may have a pronounced effect on their efficacy and acceptability. In some cases the vehicle for the pediculicide may also have some degree of pediculicidal effect which will enhance the performance of the insecticide. This must be taken into account when comparing products, which may have the same active ingredient (insecticide), but different formulation. Formulation can also affect the acceptability of the pediculicide to the public. The products which become the most popular and hence used most frequently, are those which in general tend to be the easiest to use, with the shortest application time and the most pleasing cosmetic attributes (such as smell). This can lead to single product domination of the market which in turn may mean an increased rate of resistance development."

The review also recommends "a mosaic model in which the same product is used for a course of treatment (2 applications spaced 7 days apart) and then a different insecticide from another resistance group is used for a course of treatment if the first insecticide fails." It should be noted that until a year or so ago advertising directly to the public was not permitted and therefore would not have had a direct influence on public choice. It is true that what they might be seeing currently is potentially biased, but the actual wording of the claims is relatively vague and usually implies that the products "help" to get rid of lice (Burgess pers comms 2002).

Comment 7

Dodd fails to offer guidance to the licensing authorities to prevent history from repeating itself. It was clear when resistance was demonstrated to the first generation of modern insecticides, DDT and lindane, (Maunder, 1971) that provision should be made in the licences of new compounds for the inevitable development of resistance. The point was not taken up when malathion, carbaryl or the pyrethroids were launched and we are suffering the consequences now.

Reply

This is outside the scope of the review.

Comment 8

This review ignores work on a likely new insecticide for head lice, imidocloprid, (Downs et al, 2000a) belonging to the neonicotinoid group. These compounds are predicted to have only 5 years useful life (Hill, 2001).

Reply

The imidacloprid study (Downs et al 2000) is not a RCT and therefore is not suitable for inclusion in the review. It is not the intention of the review to speculate about the development of new compounds for use as pediculicides, only to review the evidence for the effectiveness of currently available treatments.

Comment 9

Dodd does not call for implementation of the Medicine Control Agency ruling in February 2000 that 'natural' treatments must pass safety and efficacy licensing tests to trade legally.

Reply

This is outside the scope of the review.

Comment 10

Contrary to Cochrane principles there has been no consumer participation in this review. If CHC had been consulted, we would have suggested that a main objective should be determination of licensing regulations that protect a vulnerable public from expensive, ineffective and possibly unsafe products.

Reply

We plan to add a second reviewer for future versions, and this could be a consumer representative.

Comment 11

Serious potential conflict of interests In the review Dodd declares a potential conflict of interest because she has been a research assistant at the Medical Entomology Centre involved in clinical trials of treatments for head lice run by Burgess (results unpublished to date). A second serious potential conflict of interest is declared in the BMJ editorial, which is the author's receipt of a grant from Warner Lambert, the pharmaceutical company which manufactures the permethrin product with a third share of the UK market.

Reply

The only conflict of interest that may be relevant to the review is the one stated within it. The research grant from Warner Lambert was paid to the Medical Entomology Centre for a series of literature reviews evaluating potential active ingredients that could be used in pediculicides. As I have no knowledge of the outcome of the company's decision, or influence over it, then I do not think that this affects my impartiality in any way. None of the work done for Warner Lambert had any relation to their existing products. My involvement in follow-up investigations for clinical trials whilst working at the Medical Entomology Centre does not affect my impartiality as I had, and still have, no involvement in the outcome of the trials and no knowledge of the treatments that the individual participants received. I have no contact with any pharmaceutical company and now work in a completely different area and therefore I will not be involved in any trials etc. in the future.

References

- Aston R, Duggal H et al 1998. Head Lice: Report for Consultants in communicable Disease Control (CCDCs). The Public Health Medicine Environmental Group Executive Committee.
- Burgess, IF; CM Brown and NA Burgess. 1994. Synergised pyrethrin mousse, a new approach to head lice eradication: efficacy in field and laboratory studies. *Clinical Therapeutics*, 16(1): 57-64.
- Burgess, IF. 1995. Clinical efficacy of treatment for head lice: Authors differ on assessment of flaws in trials. *British Medical Journal*, 311(7016): 1369-1370.
- Burgess, IF. 1997. The management of head lice infections. *Surgery OTC Review*, 4(5): 15-17.
- Downs, AMR; KA Stafford and GC Coles. 1999. Head Lice: Prevalence in schoolchildren and insecticide resistance. *Parasitology Today*, 15(1): 1-4.
- Downs, AMR; KA Stafford and GC Coles. 1999. Evidence for double resistance to permethrin and malathion in head lice. *British Journal of Dermatology*, 141: 508-511.
- Downs, AMR; KA Stafford and GC Coles. 2000. Susceptibility of British head lice, *Pediculus capitis*, to imidacloprid and fipronil. *Medical and veterinary Entomology*, 14:15-17.
- Gross, Z. 2001. Pharmacy-based head lice management. *The Pharmaceutical Journal*, 267(7164): 317.
- Richards SM. 2000. Treatment of head lice. *The Lancet*, 356: 2007.
- Roberts, RJ; D Casey; DA Morgan and M Petrovich. 2000. Comparison of wet combing with malathion for treatment of head lice in the UK: a pragmatic randomised controlled trial. *The Lancet*, 356: 540-544.
- Stallbaumer, M and J Ibarra. 1995. Clinical efficacy of treatment for head lice. Counting lice by visual inspection flaws trials' results. *British Medical Journal*, 311(7016): 1369.
- Taplin, D; PM Castillero; J Spiegel; S Mercer; AA Rivara and L Schachner. 1982. Malathion for treatment of *Pediculus humanus var capitis* infestation. *Journal of the American Medical Association*, 247(22): 3103-3105.
- Vander Stichele, RH and MG Bogaert. 1995. Authors reply. *British Medical Journal*, 311(7016): 1369-1370.

Vander Stichele, RH; EM Dezeure and MG Bogaert. 1995. Systematic review of clinical efficacy of topical treatments for head lice. British Medical Journal, 311(7005): 604-608.

Contributors

Community Hygiene Concern (CHC)
Distributors of 'Bug Busting' products
January 2002

WHAT'S NEW

Date	Event	Description
9 November 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 3, 1998

Review first published: Issue 2, 1999

Date	Event	Description
20 August 2006	Amended	Review withdrawn as of Issue 4, 2006
30 November 2004	Amended	Date new studies found but not yet included/excluded
22 April 2002	Amended	Response to comment/criticism added
26 January 2002	Amended	Comment/criticism added
28 February 2001	New citation required and conclusions have changed	Substantive amendment

DECLARATIONS OF INTEREST

The reviewer used to work at the Medical Entomology Centre and had involvement in follow-up investigations as part of clinical trials for the treatment of head lice. Therefore a proportion of salary was covered by participation in these trials.

SOURCES OF SUPPORT

Internal sources

- Medical Entomology Centre, UK.

External sources

- Department for International Development, UK.
- European Commission (Directorate General XII), Belgium.
- Liverpool School of Tropical Medicine, UK.
- National Health Service R&D Programme, UK.

NOTES

The Editor withdrew this review as of Issue 4, 2006. This review will be reinstated following a substantive update.

INDEX TERMS

Medical Subject Headings (MeSH)

*Pediculus; Antiparasitic Agents [therapeutic use]; Carbaryl [therapeutic use]; Health Education; Hygiene; Lice Infestations [prevention & control; *therapy]; Malathion [therapeutic use]; Permethrin; Phytotherapy; Pyrethrins [therapeutic use]; Randomized Controlled Trials as Topic; Scalp Dermatoses [prevention & control; *therapy]

MeSH check words

Adult; Animals; Humans