Current treatments for pediculosis capitis

Ian F. Burgess

Medical Entomology Centre, Insect Research and Development Limited, Cambridge, UK

Correspondence to Ian F. Burgess, Director, Medical Entomology Centre, Insect Research and Development Limited, 6 Quy Court, Colliers Lane, Stow-cum-Quy, Cambridge CB25 9AU, UK
Tel: +44 1223 810070;
e-mail: ian@insectresearch.com

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Purpose of review

Following the increase in prevalence of head lice during the 1990s, research interest in human louse infestation is now greater than at any time since World War I. Problems with treatment, resulting from the selection of populations of lice resistant to insecticides by overuse of some types of product, have triggered an interest in the development of novel therapeutic agents.

Recent findings

This review first discusses the background to treatment options, basic diagnostic criteria for deciding whether treatment is required and the efficiency of different techniques. Following recent evidence for resistance to insecticides, alternative therapies are examined, including plant-derived essential and fixed oils that are seen by consumers as safer alternatives to pesticides, physically acting preparations and combing options.

Summary

I have found that most diagnostic methods lack evidence of efficacy or effectiveness and the evidence for efficacy of several 'popular' options for alternatives to insecticides in treatment is either scant or missing. Claims related to the activity of some products need to be examined more deeply to determine whether they are of real value.

Keywords

diagnostic methods, essential oils, head lice, insecticides, resistance, silicones

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Introduction

For the past 40 years, treatment of head louse infestation has largely been by use of neurotoxic insecticides. Over that time, public health authorities have supplied, used, and encouraged their use in a variety of dosage forms with little consideration for the potential impacts on child health, environment, or the possibility that lice could develop resistance. Since the beginning of the 1990s, two factors have emerged that influence therapy. First, there has been an increased awareness of the possibility that medicinal insecticides might be harmful. Second, lice in most territories have acquired some degree of resistance to insecticides.

Background

Pediculosis capitis is infestation of the human hair and scalp by the head louse, *Pediculus capitis*. The exact definition of an infestation is that living lice of any or all stages of development are present together with their eggs, which they cement to hairs close enough to the scalp that the warmth from the skin acts as an incubator for the developing embryos. However, controversially, some people, including public authorities, have preferred, and in some cases still do prefer, to define infestation as any identifiable sign of infestation past or present that can be found on the hair or scalp. As the empty eggshells of lice remain fixed to the hairs for months after hatching, and these and killed eggs persist after a successful treatment, there have also been controversies about how to accurately diagnose, who needs to be treated and what actually requires treatment.

Throughout the world, treatments for pediculosis capitis fall into three main categories: medicinal products, medical devices, and traditional remedies. The exact definition of each of these varies with the jurisdiction and the culture, but overall, they are similar to the degree that the majority of medicinal products contain some form of pharmacologically active compound that kills lice by physiological activity at the cellular level. In practice, and historically, the majority of registered medicinal products contain neurotoxic insecticides as the active ingredients. However, recent trends for product development have changed this pattern so that in some countries medicinal products now contain active substances that act by physical means.

The category that includes medical devices, which in some cases may be known as cosmeceuticals [a category not recognized by the US Food and Drug Administration (FDA) and other regulatory agencies] because they are

composed of cosmetic ingredients, generally requires a lower level of regulatory oversight and also permits a lower level of claim for the activity of the product. Most of the most recently developed physically acting preparations are regulated under this category in the majority of countries. This category of product also includes combs designed to physically remove lice or to pull louse eggs and nits (hatched eggshells) from the hair.

Traditional remedies have, until recently, been fringe treatments, either being limited to use by small numbers of people attending registered herbalists and similar professionals in developed countries or else restricted to particular ethnic groups using local herbal extracts within their own communities. However, with the increased use of internet marketing, numerous preparations based on herbal extracts of undefined provenance can now be obtained throughout the world.

Diagnosis

Correct diagnosis of pediculosis capitis is fundamental to making a treatment decision and for determining whether treatment has been effective. In theory, diagnosis of head lice is straightforward, either lice are present on the head or there are none, yet finding them is not as simple an exercise as might be thought. Traditionally, visual inspection while parting the hair was the method used. In some cultures, combs are used to assist this process, and recently visual aids, such as illuminated magnifiers, have been used by some. Nevertheless, some methods for diagnosis are relatively inefficient, and many people have difficulty identifying what is found amongst the hairs [1].

Different methods of diagnosis, by finding lice, have little evidence or clear consensus in support of one method in comparison with another [2]. Possibilities include wet combing with conditioner [2,3•,4,5••,6••], self diagnosis [4], washing with shampoo and straining the rinse water [7••], dry detection combing [2,8••,9•,10••], and collection of hair clippings from hairdressers [11•]. Previous evidence for the sensitivity of these methods showed that visual inspection was of similar sensitivity to wet combing [12], but about 25% as effective as combing dry hair with one type of metal comb [2].

Studies investigating the effectiveness of diagnostic methods have now shown that in one Brazilian community, self-diagnosis was 80.5% as sensitive as wet combing with conditioner compared with only 35.1% sensitivity for visual inspection for finding live lice [4]. Similarly, dry combing with a specially designed plastic comb was 3.84 times more effective for finding lice than visual inspection (31.3% sensitivity) in screening schoolchildren in Turkey [10••], and examination of hair samples from hairdressers found visual inspection to be twice as sensitive a method for finding any evidence (i.e. lice or nits) [11•]. Evidence so far suggests that dry and wet combing are similar in sensitivity but dry combing has the advantage in that it does not require more than just a comb, although this must be of a suitable design, and can be performed quickly without the need for additional equipment to shampoo and condition hair. This is particularly important for epidemiological screening studies, in which disruption of school routine is minimized, and for clinical trials, in which additional interventions that might lead to bias are undesirable.

Treatment

Worldwide, treatments using neurotoxic insecticides have suffered considerable loss of activity due to the selection of resistant populations of lice. Most prominent is resistance to synthetic pyrethroids because permethrin is probably the most widely used insecticide for louse control. Resistance to pyrethroids caused by the recessive *kdr* ('knockdown' resistance) para-orthologous sodium channel mutation has been found in head lice from various countries since first isolated in Israel [13]. Presence of this form of resistance was confirmed in Bobigny, France, where only 3.3% of 3345 children were found infested but, of the 90 lice screened, 33 were homozygous for the mutation T929I and 37 were heterozygous, a frequency of 57%. The high incidence of this mutation was attributed to intense local selection pressure from permethrin use [14•].

Researchers in the USA have shown, using a quantitative sequencing screen for three similar mutations (M815I, T917I, and L920F), that the predicted frequencies of the allele using either pooled DNA from individual lice or DNA from a pool of specimens agreed well with the frequencies obtained from individual lice. The protocol was found to be reliable for predicting resistance gene frequencies above 7.4% and showed considerable variation between different geographic isolates of lice [15••]. Inserting the same mutations from head lice into house fly, voltage-sensitive sodium channel alpha-subunit genes expressed in *Xenopus* oocytes showed that combinations of the mutation produced different shifts in the voltage dependence of both activation and inactivation curves. Of the three, M827I and L932F reduced permethrin sensitivity but T921I, an almost identical codon to that found in the French study [14•], eliminated sensitivity and was identified as the primary cause of permethrin resistance [16••].

Alternative treatments: insecticides

Overcoming resistance to therapy poses various problems. First, there are few physiologically acting synthetic chemicals that are likely to avoid current resistance

patterns to pyrethroids and malathion, and second, many that could act in this way are either toxicologically unacceptable or commercially unavailable. One that has been investigated *in vitro* is ivermectin, which was shown to be more than three times faster acting when formulated than when applied as a technical substance in solution [17], reinforcing evidence that formulation is the key to a successful treatment, perhaps more than the named active. This feature was identified for other insecticides nearly 20 years ago [18] but, because most manufacturers of pediculicides are not specialists in either formulation (most contract out to cosmetic formulation houses) or insecticides, the preparations are frequently not optimal delivery systems for the insecticides.

Traditionally, many preparations were simple solutions of insecticides in a volatile solvent such as alcohol. To this could be added various materials such as monoterpenoids derived from essential oils, which enhance the activity of insecticide or are effective alone. One of the most successful preparations of this type is a 0.5% malathion product variously known as Prioderm (SSL International, Manchester, UK; Meda Pharma, Paris, France) and Ovide (Taro Pharmaceuticals USA Inc., Hawthorne, New York, USA) that contains around 16% terpenoids. Formulating the mixture in a hydroxypropyl cellulose gel, and applying for just 30 min proved nearly as efficacious (98%) as the alcoholic solution (100%) applied for 8 h, and significantly more than 1% permethrin (50% effective), which was probably influenced by resistance [7••].

Alternative treatments: essential oils

There is considerable difference in activity between monoterpenoids, with (+) and (−)terpenin-4-ol, pulegone, and thymol most active against lice, whereas nerolidol, thymol, geraniol, and carveol are more active against louse eggs [19]. Resistance to insecticides has now stimulated renewed interest in the activity both of essential oil components and other potentially active chemicals of plant origin that may be effective to kill lice and their eggs. Four essential oils (lavender, peppermint, or eucalyptus) at 5% concentration showed activity against permethrin-resistant lice in alcoholic solution, and not surprisingly, a 1 : 1 combination of peppermint and eucalyptus (total 10%) in ethanol was more active, but only after addition of 10% 1-dodecanol was the essential oil mix as effective as a marketed insecticide product, also containing 10% 1-dodencanol [20].

Curiously, a great deal of interest has been generated in use of cineole, whether alone or as part of an essential oil, for control of lice [20–24]. Presumably, this is because it is a widely used and familiar material available from a variety of sources. However, despite the fact that cineole has been shown to have an acetylcholine esterase inhibiting effect able to rapidly intoxicate lice [23,25], the evidence for its activity clinically is poor, even when used at 10% solution in alcohol, because although the outcome was 83% success per protocol there was a high dropout rate from the study that rendered the results unclear overall [24].

One possible reason cineole may not be as active as expected is that resistance to acetylcholine-inhibiting insecticides such as malathion is now fairly widespread. Also, essential oil mixtures have been popular as components of consumer products for several years so that either the malathion resistance may be sufficiently nonspecific to also inhibit the action of terpenoid compounds or else consumer use of products containing essential oils and monoterpenoids at low concentrations may have selected for specific resistance to these materials.

Irrespective of whether consumer products containing essential oils might have an effect to kill lice, it has been shown that they have potentially undesirable pharmacological activity on humans. Two of the most popular oils used in toiletries, as well as in products to treat head lice, are lavender oil and tea tree oil. Both oils have been implicated in triggering cases of prepubertal gynecomastia in boys with normal serum concentrations of endogenous steroids. In each case, the condition resolved soon after they stopped using the products containing the essential oils and the authors of the study cautioned repeat exposure to products containing these oils [26•].

Alternative treatments: fixed oils

Alternative plant-derived materials such as fixed oils have been proposed as potentially active against lice. For example, extracts of fruits, seeds, leaves, or bark from the neem tree, *Azadirachta indica*, have been used to treat skin conditions in traditional herbal medicine for centuries, but there is little convincing evidence in support of their use against lice. One investigation of the in-vitro effects of fruit oil and fruit extract from the chinaberry tree, *Melia azedarach*, which contains tetranortriterpenoids related to some found in the neem tree such as azadirachtin, showed a high level of activity for an emulsion of the two against both lice and louse eggs, but the results may have been confounded by a high control mortality [27]. A neem seed extract shampoo was also reported to have a high level of efficacy to cure in a trial conducted in Egypt [28]. The effects reported in the studies are mainly attributed to azadirachtin or similar compounds in the extract, which have been identified as antifeedant and growth regulatory compounds that have been used to control plant pests. However, their use against head lice is counter intuitive because neem compounds are slow acting, with insects requiring chronic exposures that limit their numbers and reproductive rates in plant protection. Nothing about neem suggests potential activity of the kind reported other than that it

has an extremely heavy and sticky fixed oil that readily coats louse cuticles and in combination with surfactants may have an impact on louse viability through damage to cuticular lipids. Other fixed oil derivatives include modified coconut oils, for example, cocamide diethanolamide, a detergent stripping agent used in shampoos that may remove louse cuticular lipid, resulting in more rapid dehydration of the insects. This appears to be the effect obtained by a coconut-derived emulsion shampoo that showed a 56% efficacy (intention to treat analysis) when used as a course of treatment [29].

Alternative treatments: synthetic physically acting compounds

Since 2005, the most important developments in louse control have come from specifically developed physically acting treatments. At the forefront of such developments are treatments based on silicones [5••,8••,9•,30•,31,32•].

Clinically, preparations of this type demonstrated a high level of per-protocol efficacy in comparison with neurotoxic insecticides (Table 1), and were not affected by acquired resistance to currently used insecticides because of the physical rather than physiological mode of action [5••,8••,9•,30•]. However, the results of some of the studies were unclear because the methodology employed did not have a clear-cut distinction between the treatment regimen and the assessments of outcome; for example, in two studies of isopropyl myristate solution, participants received a second treatment 1 week after the first only if lice were present. However, if no lice were found on the seventh day after first treatment but were found on the fourteenth day, the second application of treatment was applied then [30•]. This approach makes nonsense of any specification for a regimen of treatment because there are no fixed parameters for comparison with other types of treatment. Similarly, the study of low-molecular-weight dimeticones [5••] made a final assessment only 24 h after the second application of product (day 9). Although this was for logistical reasons, it renders the results incomparable with other studies in which final assessment was at least 7 days after the final application of treatment. This single assessment at such a short interval could not identify latent treatment failure from louse eggs not killed by the treatment.

Lice treated with silicone-based fluids are rendered immobile almost immediately, similar to the effect of immersing lice in water, but, whereas they recover soon after removal from water, they fail to recover activity when soaked with silicone. It appears that this is mainly because silicone coats the louse surface and enters the respiratory tract, blocking spiracles and tracheae. One study [32•] has suggested that mixtures based on low viscosity, low surface tension silicones are capable of flooding the tracheal system, asphyxiating the lice. However, claims for suffocation are controversial, and not confirmed by other experiments (Burgess I.F., unpublished data), because normal application even of low-viscosity fluids is unlikely to expel all air from the insect respiratory system and, as silicones are highly permeable to oxygen, anoxia may not be achieved even if the tracheae are filled. The actual mode of action therefore remains to be elucidated.

The human element in control

Irrespective of what therapy is used or its inherent activity, unless the carer uses it correctly, and understands the biology of lice, efforts to eliminate infestation may be ineffective. This was highlighted in a survey of parental knowledge in two regions of Australia that found only 7.1% of carers could correctly answer 10 questions about lice and although they wanted responsibility for managing infestations, appeared unsuccessful because up to 30.3% of children missed schooling because of head lice [33••]. Up to 67% of parents also tried preventive methods, including repellents, but these materials showed little true repellent effect in a laboratory study [34]. Although some essential oils such as tea tree and lavender showed activity, this was incomplete and would soon diminish due to evaporation of the terpenoid components, which possibly explains why in communities using them prevalence of lice may be as high as 40% in some schools, although practical issues of treatment methods, time involved, difficulties of diagnosis, and social factors all contribute to increased problems with head lice [33••,35]. Some of these issues may be addressed by engaging all members of a community (school) in louse control, for example, a review of 'Bug Busting' combing projects considered the approach able to empower families to control lice sustainably provided

Table 1 Comparison of products and treatment outcomes from clinical trials of physically acting pediculicides

Treatment	Solvent/excipients	Cure rate (%)	Comparator	Cure rate (%)	Duration of study (days)	Reference
4% dimeticone	Cyclomethicone	76.9	0.5% malathion	34.5	14	[8••]
4% dimeticone	Cyclomethicone	97.1	–	–	14	Kurt O, Burgess IF, unpublished
92% dimeticone	Triglycerides, jojoba wax	97.2	1% permethrin	67.6	9	[5••]
50% isopropyl myristate	Cyclomethicone	96.6	–	–	21	[30•]
50% isopropyl myristate	Cyclomethicone	63.0	0.33% pyrethrum, 4% piperonyl butoxide	22.2	21	[30•]
50% isopropyl myristate	Cyclomethicone	82.0	1% permethrin	19.3	14	[9•]

they are supplied with adequate education and materials [3•]. This may ultimately allow communities to become louse free by process of attrition but does not satisfy the need for rapid and immediate relief from infestation that most carers seek in using the various chemical therapeutic agents. Consequently, mechanical removal of lice or their eggs is unlikely to become the treatment of choice for most families dealing with head lice.

Conclusion

Head lice have acquired resistance to the most widely used insecticides, which has a profound impact on therapeutic outcome. There is now considerable interest in finding alternative treatments. Several classes of material have been investigated but the most promising options to date are silicone mixtures that have a physical activity by blocking the louse respiratory tract. However, successful therapy requires reliable diagnosis. Somewhat belatedly, there is now much more interest in identifying effective diagnostic tools, although so far there is little consensus on what is an appropriate and effective diagnostic method.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 199–201).

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