Reprint

173644

Comparison of wet combing with malathion for treatment of head lice in the UK: a pragmatic randomised controlled trial

R J Roberts, D Casey, D A Morgan, M Petrovic

Summary

Background Concern about the effectiveness and toxicity of insecticide lotions has led to promotion of mechanical methods to remove head lice. We compared the effectiveness of "bug-busting" (wet combing with a fine-toothed comb) and malathion lotion.

Methods We screened 4037 schoolchildren in two counties in Wales, UK (intermediate resistance to malathion). Of 167 found to have head lice, 81 (aged 3–14 years) were eligible to participate in a randomised controlled trial that compared mechanical removal of lice by a commercial kit every 3–4 days for 2 weeks with two applications of 0·5% malathion lotion 7 days apart; parents carried out both treatments. The outcome measure was the presence of live lice 7 days after the end of treatment. Analyses were by intention to treat.

Findings 74 children completed the study and 72 were included in the analysis. The cure rate was 38% (12 of 32) for bug-busting and 78% (31 of 40) for malathion. Children assigned bug-busting were 2·8 (95% CI 1·5–5·2) times more likely than those assigned malathion to have lice at the end of treatment (p=0·0006).

Interpretation Malathion lotion was twice as effective as bug-busting, even in an area with intermediate resistance. Policies advocating bug-busting as first-line treatment for head lice in the general population are inappropriate. Assessment of the outcome of treatment 1–2 weeks after completion is essential for successful management. Only about 50% of participants complied fully with treatment, so future trials should be pragmatic in design, avoid false incentives, and study representative samples of children.

Lancet 2000; **356:** 540–44
See Commentary page 523

Department of Public Health, North Wales Health Authority, Mold CH7 1PZ, UK (R J Roberts MFPHM, D Casey RGN, D A Morgan MCPP, M Petrovic DFPHM)

Correspondence to: Dr R J Roberts
(e-mail: richard.roberts@nwales-ha.wales.nhs.uk)

Introduction

Mechanical removal of head lice by combing to control or eradicate infestation is not new, but during the past few years in the UK the "bug-busting" (Community Hygiene Concern, London, UK) wet-combing method has been promoted as a treatment for head lice in response to concerns about the effectiveness and potential toxicity of insecticide lotions.[1] Bug-busting involves combing of wet hair with a fine-toothed comb every 3–4 days for 2 weeks (slightly longer than the maximum incubation period of lice eggs) to remove all lice as they hatch, ensuring that none reach maturity and lay the next generation of eggs. Public concern over the use of insecticides on children, an increase in resistance to the popular pyrethroid preparations, and a large rise in prescribing costs are additional pressures that contribute towards the increased use of mechanical methods of treatment.[2–7] The UK Department of Health has supported the use of the method, publishing a leaflet to demonstrate its use. Despite this support and the availability of a bug-buster kit, there have been no published trials of the method.[8,9]

A recent Cochrane review of interventions for treatment of head lice called for trials of the bug-busting method.[9] The reviewer also requested that trials of insecticide lotions be done in western populations infected with lice that may not be fully susceptible to the relevant insecticide so that the effectiveness of existing products can be accurately assessed. The only studies that met the rigorous inclusion criteria for that review had been carried out in populations in which insecticide lotions had never previously been used.[10–12]

We undertook a pragmatic trial, analysed by intention to treat, comparing the effectiveness of a commercial bug-busting kit with that of commercial 0·5% malathion lotion in a representative sample of children from an area with established intermediate resistance to malathion. This design provides an estimate of the effectiveness of each method in normal use by the general public.[13]

Methods

Participants

We selected a random sample of 24 primary schools (children aged 5–11 years) from the counties of Flintshire and Denbighshire in North Wales, where previous local studies of head lice, by standard laboratory methods, had identified intermediate resistance to malathion (lethal time 50% [LT50] by the method of Burgess 160 min).[14,15] Small rural schools (fewer than 40 pupils) in remote areas were excluded for logistical reasons. School nurses, following a standard protocol and using detection combs, screened all pupils present in the schools and identified children with live moving lice.

Each child was given a letter to take home, and a member of the research team visited the home on the same day. The letter asked parents, if the team were unable to contact them that evening, to treat the child for head lice. A member of the research team or a nurse

carried out home visits following a standard protocol. Families contacted were invited to take part in the study. Inclusion criteria were: live (moving) lice present, no treatment with insecticide lotion in the previous 2 weeks, and no broken skin on the scalp. All other children in the household were examined for lice. If head lice were found and the child was aged 3–14 years, he or she was invited to enter the study and was individually assigned randomised treatment. All children with lice were offered treatment in any case. Adults in the household were offered examination and treatment, a comb to allow examination by a partner, or lotion for treatment without examination, if inspection was refused. Treatment without evidence of infestation was not encouraged, so that unnecessary exposure to insecticide lotion was kept to a minimum.[5] We did not offer any payment for participation.

Ethical approval was granted by the Central North Wales and North East Wales Local Research Ethics Committees of the North Wales Health Authority.

Design

At the initial visit, we recorded baseline data on age, sex, the presence of asthma, scalp disorders, and presence of head lice. Data were collected on all household members (including adults who accepted examination) on the observed presence of lice, and which treatment was allocated. The participants were examined for the presence of lice on day 7 and then 7 days after the end of treatment (day 15 for most individuals in the malathion group, variable for bug-busting because the parent determined the duration of treatment) by use of detection combs and direct observation on dry hair. Outcome assessments were carried out without knowledge of treatment allocation. Parents kept a treatment diary for each child; they recorded when treatments were given and how much time was spent combing or how much lotion was used. Parents were asked to stick any live lice found on bug-busting or normal combing (malathion) on an adhesive strip on the diary. After publication of the Cochrane review, we carried out a retrospective questionnaire survey of participants to ascertain concurrent use of antibiotics and pediculocides during the 4 weeks before trial entry.

A series of study numbers were assigned to bug-busting or malathion by random numbers. An envelope was marked with the study number, and the name of the allocated treatment was placed inside. Each researcher was allocated a supply of envelopes. Once the parent had given written informed consent for the study, eligibility had been confirmed, and baseline data collected, the participating child was asked to choose an envelope, and his or her name was written on it before the treatment was revealed by opening the envelope.

At the first visit, parents received a standard oral explanation of how to use the treatment, closely based on the manufacturers' instructions. Instructions were repeated until the parent was satisfied that he or she understood the method. The study diary did not indicate when the treatments should be applied.

Participants in the bug-busting group were given an individually boxed bug-buster kit containing instructions, two nit (fine-toothed) combs, one normal comb, a plastic cape, and stickers. Parents were instructed to follow the instructions in the box: to wash the hair, apply lots of conditioner, comb the hair straight, then use the detector comb to comb out the lice until none were found. They were asked to repeat this treatment every 3–4 days for 2 weeks, but if an adult louse was found after the first session, to extend the course of treatment by three further sessions.

Participants in the malathion group were given one or more (depending on amount required according to the thickness and length of the hair) individual boxes containing a 50 mL bottle of Suleo M (SSL International plc, Oldham, UK) and instructions, or if asthmatic (alcoholic lotion contraindicated) a similar presentation of Derbac M (SSL International). Parents were instructed to keep wet hair away from flames and lighted objects and not to use a hair-dryer, and to follow the instructions on the box: to use lotion to wet hair thoroughly down to the roots, and allow to dry, to leave the lotion on the hair for 8–10 h, and not to use a nit comb. They were asked to repeat the application 7 days later.

Other household members with head lice were given malathion lotion for simultaneous treatment. Other pupils in the same school found to have lice were either treated simultaneously as part of the study or were advised about treatment. The findings of the inspection on day 7, and any other inspections, were not disclosed to the parents until the end of the study. Children who still had lice at the end of the study were prescribed appropriate treatment and followed up until clear.

Statistical analysis

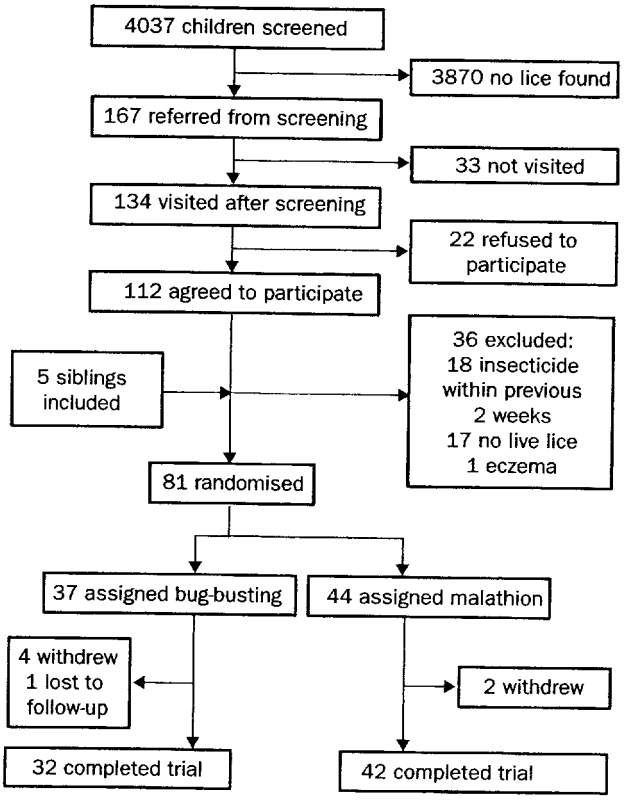
The study was designed as a pragmatic randomised controlled trial.[13] We calculated that a sample size of 70 would be sufficient for a significant difference between the treatments to be detected with confidence of 5% and power of 80%, on the assumption of 80% effectiveness in one group and 45% effectiveness in the other.

Analysis was carried out by intention to treat with Epi Info (version 6). All participants who provided outcome data were included in the analysis, except two who had used both treatment methods simultaneously. Cure rates in the two treatment groups were calculated and compared by use of the χ^2 test or Fisher's exact test when expected cell values were less than five. The relative risk of treatment failure was calculated, with 95% CI. Participants were included in the analysis whether or not they complied with the allocated treatment. Participants who withdrew from the study and did not provide outcome data were excluded. We used extreme case analysis to estimate the effect of missing responses on outcome.[16]

Results

4037 children were screened in schools and 167 were referred (crude prevalence 4·1%). 134 were visited in the time available. 112 agreed to take part in the study (response rate 83·6%, figure). 36 children did not meet the inclusion criteria. Five siblings were included. 81 children started the study and were randomly assigned bug-busting (37) or malathion lotion (44).

74 children (91%) completed the study and received outcome visits. Six withdrew from the study (four from bug-busting and two from malathion, Fisher's exact test p=0·40) and one was lost to follow-up (bug-busting). Reasons for withdrawal were given by three participants assigned bug-busting (two had a house fire and one wanted to use lotion) and one participant assigned



Trial profile

malathion (wanted to use bug-busting). Two children assigned malathion were excluded from analysis (treatment was successful in both cases) because the parent had simultaneously carried out bug-busting, being used by a sibling, leaving 72 children for outcome analysis.

Of the 72 children in the analyses, 32 (44%) used bug-busting and 40 (56%) malathion, of whom 27 used Suleo M and 13 Derbac M. The mean age was 7·7 years (range 3–14), with no significant difference by treatment group (7·5 *vs* 8·0 years, p=0·39). There were 51 (71%) girls and 21 (29%) boys, with the sexes distributed equally between the two treatment groups (male 28% *vs* 30%, p=0·86). 36 (50%) recorded good compliance with treatment on the diary, with no significant difference by treatment group (good compliance 47% *vs* 53%, p=0·64). Most of the children who did not comply fully (31 of 36 [86%]) deviated in minor ways, such as extending or shortening recommended treatment intervals by 1 or 2 days. No participant was taking antibiotics. The parent of one child assigned Suleo M complained of the strong smell, so the assignment was changed to Derbac M for the second application. No other participant reported adverse effects. Among the bug-busting group, the duration of treatment was 7–13 days in five cases, 14–20 days in 14 cases, 21–27 days in ten cases, longer than 27 days in two cases, and not known in one case (mean duration 17·7 days, n=31).

Analysis	Bug-busting		Malathion		p
	Total	Cured	Total	Cured	
All participants*	32	12 (38%)	40	31 (78%)	0·0006
Exclusions					
Four malathion group who used a nit comb	32	12 (38%)	36	27 (75%)	0·0019
Four with outcome assessment delayed >7 days	30	10 (33%)	38	30 (79%)	0·0002
Eight who used nit comb or had delayed outcome assessment	30	10 (33%)	34	26 (77%)	0·0006
All participants with outcome data	32	12 (38%)	42	33 (79%)	0·0004

*Except two who used both methods simultaneously.

Main findings and subgroup analyses

The overall cure rate was 38% (12 of 32) for bug-busting and 78% (31 of 40) for malathion lotion (table). The bug-busting group were 2·8 times (95% CI 1·5–5·2) more likely to have lice at the end of treatment than those who used malathion lotion (p=0·0006). Extreme case analysis of the effect of missing outcome data (on the assumption that all five missing individuals assigned bug-busting were cured and all four missing or excluded individuals assigned malathion were not cured) did not change the finding that malathion was significantly more effective than bug-busting (bug-busting 46% [17/37], malathion 71% [31/44], p=0·026).

42 participants retrospectively reported that they had not used pediculocides in the 4 weeks before trial entry (19 assigned bug-busting and 23 malathion). The cure rate was 58% (11 of 19) for bug-busting and 78% (18 of 23) for malathion lotion. Participants assigned bug-busting were 1·9 times (0·8–5·0) more likely to have lice at the end of treatment than those assigned malathion lotion. In this subgroup, the difference in the effectiveness of treatments did not reach significance (p=0·16).

Discussion

We found that malathion was twice as effective as bug-busting in eradication of head lice.

This study was pragmatic and designed to give an estimate of the effect of different treatment policies rather than of potential benefit in children who received treatment exactly as planned. The participants were a random sample of the local population of children at primary schools and their siblings who were found to have head lice. The random sample recruitment and the high response rate suggest that our study sample closely represented the general population of children infected with head lice. Unlike some other studies, we did not pay participants and therefore avoided any false incentive to comply with treatment.[17] Reinfestation was kept to a minimum by simultaneous screening and treatment of all household members and all other pupils in the same school.

More girls than boys took part in the study, reflecting the higher prevalence of head lice in girls.[4] There were no significant differences between the treatment groups in mean age, sex distribution, or compliance with treatment, indicating successful randomisation. Participants were given oral instructions on the use of the product and advised to follow the manufacturer's written instructions, reflecting the type and amount of advice that they would receive during clinical contact with a health professional. Outcome data were collected without knowledge of treatment assignment to control researcher-related bias. Although intention-to-treat analysis can only be applied fully when complete outcome data are available for all randomised individuals, we had outcome data on 91% of our participants. Because this was a pragmatic trial, participants were included in the analysis whether or not they complied with treatment. Various imputation methods can be used to estimate the effect of missing responses, but even extreme case analysis did not change our finding that malathion lotion was significantly more effective than bug-busting.[16]

There are four sources of bias that may have caused us to overestimate the effectiveness of the treatments under study: if the children who withdrew from the study still had head lice; if visits by researchers and completion of the treatment diary encouraged parents to comply with treatment; if there was a significant residual effect from pediculocide used more than 2 weeks previously; and because our outcome assessment was done after 7 days, when some of the lice present would have been small stage one and two instar nymphs, we may have missed some infestations. However, one trial included in the Cochrane review also assessed final outcome at 7 days, and in another only seven of 52 participants were available for outcome assessment after 1 week.[10–12] Although the design limited the opportunity for reinfestation, if this occurred it would have caused us to underestimate the effectiveness of treatment. All these factors would have affected both treatment groups equally and would therefore not influence the comparison of the two methods.

The three trials judged sufficiently robust to be included in the Cochrane review and eight other reviewed trials that used the presence of live lice to indicate infestation, were all trials of efficacy.[10–12,17–24] In all those studies, a researcher applied the pediculocide, following the manufacturers' instructions exactly. Ours was a pragmatic trial. The parents applied the treatment themselves, following instructions similar to those that would be received during a normal clinical encounter.

The three trials included in the Cochrane review were carried out in developing countries in populations who had never previously used pediculocides, and therefore the lice treated were fully susceptible.[10–12] Application of their findings directly to the UK may therefore be misleading. Our participants came from areas where field studies in primary schools, by standard methods, had shown intermediate resistance to malathion (and complete resistance to pyrethroids). Because resistance to malathion is already common in the UK, and resistance to pyrethroids is even more widespread, our randomly selected study population is similar to the wider UK population in this respect.[9,25] We did not have sufficiently detailed data on resistance by locality to allow us to compare the outcome of treatment with malathion in areas with different rates of resistance.

Other trials have recruited participants from clinics, schools, or localities without aiming to obtain representative samples of the population with head lice. The participants in our study were a representative sample of children with head lice locally. This feature is especially important in assessing effectiveness of a treatment in the hands of an average parent who may not follow the manufacturers' instructions.

Our study complies with two of the three inclusion criteria for the Cochrane review and ten of 11 methodological quality criteria used within it.[9] The Cochrane inclusion criteria were: diagnosis based on the presence of live lice, no pediculocide used in the previous month, and no adjunctive use of nit combs with lotion. Most of the Cochrane criteria were unequivocal improvements in methodological rigor, which do not potentially introduce selection bias into a pragmatic study of resistant lice or the bug-busting method. However, we excluded children who had used pediculocide in the previous 2 weeks, not 4 weeks as required by the Cochrane reviewer. The reviewer did not refer to any experimental evidence to support the choice of 4 weeks, and any residual effect would affect both treatment groups equally. We argue that 2 weeks after treatment any residual pediculocidal effect, or priming of louse detoxification systems, is clinically insignificant, and the use of a 4-week cut-off could introduce bias into recruitment in studies of the bug-busting method, which could compromise the generalisability of the findings. This suggestion is supported by the finding that exclusion of children who had used pediculocide in the 4 weeks before trial entry did not significantly change the cure rate in the malathion group. However, cure rate in the bug-busting group increased when children who had used pediculocide in the month before entry were excluded. A plausible explanation for this finding is that the 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; this treatment requires a significant investment of time and effort for it to work. For malathion lotion, which is easier to use, such differences would be less important.

Until now, experts have held unassailable but conflicting opinions on the effectiveness of bug-busting and the usefulness of pediculocides in a partly resistant UK population.[1–5] This trial of the bug-busting method suggests that policies advocating bug-busting as a first-line treatment for head lice infestation are inappropriate for the general population. Malathion was twice as effective as bug-busting, even in a population of children in whom intermediate resistance to malathion has been shown. However, treatment failure with malathion was frequent enough to make the assessment of the outcome of treatment 1–2 weeks after completion an important part of management. Half of our participants did not comply fully with treatment, therefore future trials should be pragmatic in design, avoid false incentives, and study representative samples of infested children.

Contributors

R J Roberts initiated the research and led the analysis of the data. R J Roberts and D A Morgan led the design of the study. All the investigators contributed to all aspects of the study, participated in fieldwork, and contributed to writing of the report.

Acknowledgments

We thank Ian Burgess and Robert Aston for advice on the study design, Sue Williams and Sue Davies for help with organising the fieldwork and data entry, and the school nurses of the North East Wales NHS Trust and Conway and Denbighshire NHS Trust for carrying out school inspections.

This trial was supported by a grant from the Wales Office for Research and Development.

References

1 Ibarra J, Hall DM. Head lice in schoolchildren. *Arch Dis Child* 1996; **75**: 471–73.
2 Anon. Head lice. *Commun Dis Rep CDR Weekly* 1997; **7**: 365.
3 Burgess I. Management guidelines for lice and scabies. *Prescriber* 1996; **7**: 87–99.
4 Downs AM, Harvey I, Kennedy CT. The epidemiology of head lice and scabies in the UK. *Epidemiol Infect* 1999; **122**: 471-77.
5 Burgess I. Head lice–developing a practical approach. *Practitioner* 1998; **242**: 126-29.
6 Pollack RJ, Kiszewski A, Armstrong P, et al. Differential permethrin susceptibility of head lice sampled in the United States and Borneo. *Arch Pediatr Adolesc Med* 1999; **153**: 969–73.
7 Mumcuoglu KY, Hemingway J, Miller J, et al. Permethrin resistance in the head louse *Pediculus capitis* from Israel. *Med Vet Entomol* 1995; **9**: 427–32.
8 Department of Health. The prevention and treatment of head lice. London: Department of Health, 1996.
9 Dodd CS. Interventions for treating head lice. In: Cochrane Library, Issue 2, 1999. Oxford: Update Software.

10 Taplin D, Castillero PM, Spiegel J, Mercer S, Rivera AA, Schachner L. Malathion for treatment of *Pediculus humanus var capitis infestation*. *JAMA* 1982; **247:** 3103–05.

11 Taplin D, Meinking TL, Castillero PM, Sanchez R. Permethrin 1% crème rinse for the treatment of *Pediculus humanus var capitis* infestation. *Pediatr Dermatol* 1986; **3:** 344–48.

12 Burgess IF, Brown CM, Burgess NA. Synergized pyrethrin mousse, a new approach to head lice eradication: efficacy in field and laboratory studies. *Clin Ther* 1994; **16:** 57–64.

13 Hollis S, Campbell F. What is meant by intention to treat analysis? Survey of published randomised controlled trials. *BMJ* 1999; **319:** 670–74.

14 Linnane E, Roberts RJ, Casey D. The use of field testing to produce rational treatment protocols for the eradication of *Pediculus humanus capitis*. In: Bartlett C, McEvoy M, Reacher M, Stuart J, Fitch V, eds. Proceedings of the Conference on the Epidemiology and Control of Communicable Diseases and Environmental Hazards; 1999 Nov 1-3. London: PHLS, 1999: 24–25.

15 Burgess IF, Brown CM. Measuring insecticide resistance in human head lice, *Pediculus capitis* (*anoplura pediculidae*). In: Robinson WH, Rettich F, Rambo GW, eds. Proceedings of the third international conference on urban pests; 1999 July. Prague: Conference Organising Committee, 1999: 634.

16 Sackett DL, Richardson WS, Rosenberg W, Haynes RB. Evidence-based medicine. Edinburgh: Churchill Livingstone, 1997.

17 Carson DS, Tribble PW, Weart CW. Pyrethrins combined with piperonyl butoxide (RID) vs 1% permethrin (NIX) in the treatment of head lice. *Am J Dis Children* 1988; **142:** 768–69.

18 Robinson DH, Shepherd DA. Control of head lice in school children. *Curr Ther Res* 1980; **27:** 1–6.

19 Brandenburg K, Deinard AS, DiNapoli J, et al. 1% permethrin cream rinse vs 1% lindane shampoo in treating pediculosis capitis. *Am J Dis Children* 1986; **140:** 894–96.

20 Bowerman JG, Gomez MP, Austin RD, Wold DE. Comparative study of permethrin 1% crème rinse and lindane shampoo for the treatment of head lice. *Pediatr Infect Dis J* 1987; **6:** 252–55.

21 Pitman NK, Hernandez A, Hernandez E. Comparison of pediculocidal and ovicidal effects of two pyrethrin-piperonyl-butoxide agents. *Clin Ther* 1987; **9:** 368–72.

22 DiNapoli JB, Austin RD, Englender SJ, et al. Eradication of head lice with a single treatment. *Am J Public Health* 1988; **78:** 978–80.

23 Bainbridge CV, Klein GL, Neibart SI, et al. Comparative study of the clinical effectiveness of a pyrethrin-based pediculocide with combing versus a permethrin-based pediculocide with combing. *Clin Pediatr* 1998; **37:** 17–22.

24 Iannantuono RF, Devoto F, Saitta MF, et al. Pediculocidal activity of an antidandruff shampoo in a 1% copper-oleate formulation. *Adv Ther* 1997; **14:** 134–39.

25 Burgess IF, Brown CM, Peock S, Kaufman J. Head lice resistant to pyrethroid insecticides in Britain. *BMJ* 1995; **311:** 752.