Title: The Clinical Effectiveness of Treatment Options for Pediculus Capitis (Head Lice)

Date: September 25, 2007

Context and Policy Issues:

Pediculus capitis, also known as the human head louse, is a six-legged, wingless, blood-sucking insect. Head lice spend their entire life on a host scalp sucking exclusively on blood four to five times a day. Head lice rarely results in a serious health condition, but may lead to secondary infections if untreated. Conversely, repeated treatment of an individual can be harmful and result in resistance.

The three primary methods for treating head lice include chemical shampoos (pediculicides), specialized louse combs and “home remedies” that range from bug spray to mayonnaise to kerosene. Essential oils (lavender, rosemary, piperonal, eucalyptus, D-lomin, and citronella) and hot air are considered alternative methods to treating health lice. Treatments for head lice available in Canada include selected medicated shampoos such as permethrin, pyrethrin and lindane, acetic acid, citronella oil, camphor, sodium lauryl ether sulphate formulation and wetcombing.

The prevalence of head lice infestations has increased worldwide since the mid-1960s, reaching hundreds of millions yearly. In the United States alone, six to twelve million cases are reported annually. One reason attributed to the rise in prevalence is the increased resistance to pediculicides. Children between three and fourteen years of age are most frequently infested, regardless of race, socioeconomic status, family background or personal hygiene habits. Transmission of head lice typically occurs from direct head-to-head contact and eggs are attached to the hair close to the scalp, where they normally hatch within 7-10 days.
To diagnose infestation, a living louse must be detected.\textsuperscript{11} According to the Canadian Paediatric Society’s clinical practice guidelines for head lice, nits or eggs close to the scalp suggest a potential case of head lice. On average, children with head lice will have no more than ten to twenty live lice.\textsuperscript{11} The entire scalp must be combed with a louse comb, and the teeth of the comb should be examined for the presence of living lice. Another method of diagnosis involves the parting of the hair at 2 cm intervals for moving lice and eggs near the scalp. Special attention should be paid around the ears and nape of the neck. It is recommended that the examiner spend at least 5 minutes for the entire examination.\textsuperscript{12}

**Research Questions:**

What are the clinical effectiveness and safety of head lice treatments?

**Methods:**

A literature search was conducted on key health technology assessment resources, including PubMed, CINAHL (OVID), The Cochrane Library (Issue 2, 2007), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI’s HTAIS, EuroScan, international HTA agencies, and a focused Internet search. Results include English language publications from 2002 to date.

**Summary of Findings:**

1) **Systematic Reviews**

In 2007, Burgess conducted a systematic review on the effects of treatments for head lice.\textsuperscript{13} Details, such as selection criteria, timeframe of literature searches and number of studies included were not specified in the review. Malathion and permethrin were found to be the most beneficial treatments for the eradication of head lice and the effectiveness of combinations of insecticides, dimeticone, herbal and essential oils, lindane, mechanical removal of lice or viable eggs by combing, phenothrin, and pyrethrum remained unknown.\textsuperscript{13} Oral co-trimoxazole (trimethoprim plus sulfamethoxazole) was effective in the eradication of head lice. However, it was associated with potentially serious but rare harmful effects.\textsuperscript{13}

The Cochrane Collaboration published a systematic review in 2007.\textsuperscript{14} However, the study was withdrawn, but the reason for doing so was not specified.

2) **Clinical Trials**

Appendix A provides details on the clinical trials found on treatments for head lice in a table format. Trials were included in this review if they measured the clinical effectiveness and/or harm of head lice treatments.

Head lice treatments examined include 1\% permethrin cream rinse, 4.0\% dimeticone, 0.5\% phenothrin liquid, 0.5\% mamathion, 0.4\% d-phenothrin shampoo, trimethoprim or sulfamethoxazole, hot air, bug buster kit, essential oils (e.g. citronella), and albendazole.
The patient population in all studies ranged from two year olds to adults. All studies in the report measured the effectiveness of treatment to eliminate lice and/or eggs. Nine studies also assessed the safety of such treatments.

a) Physical removal of nits
One clinical trial compared a pediculicide with the physical removal of nits with a pediculicide without the physical removal of nits. There were no statistically significant differences in the clinical outcomes in the two treatment arms. Meinking et al. assessed the effectiveness of 1% permethrin cream rinse lice treatment (PLT) with combing and 1% PLT without combing. There were no statistically significant differences between the two treatment groups (p>0.05). Adverse events were reported among three patients in the non-combing group, but all recovered.

b) Malathion
One randomized observer-blinded study compared a 20-minute treatment of malathion with the standard 10-minute residual reducing treatment of permethrin. Visual inspections occurred on days 1, 2, 8, 9, and 15, and shampooing/straining on days 2, 9 and 15. The results at the end of the 15-day study indicate that malathion was more effective that permethrin in live head lice removal from the scalp (p<0.0001).

c) Permethrin
A clinical trial compared 1% permethrin with 0.4% phenothrin shampoo. Overall, subjects treated with 1% permethrin experienced a statistically significant higher success rate compared with subjects treated with 0.4% phenothrin shampoo (p<0.01).

d) Dimeticone
Authors Burgess et al. compared the success rate of head lice removal and evidence of reinfestation after successful head lice removal between 4.0% dimeticone and 0.5% phenothrin. There were no statistically significant differences in the success rates between the two treatments regardless of intensity of infestation (i.e. high, medium or low).

e) Citronella
In 2003, a study was conducted to test for the effectiveness of citronella, oil that contains approximately 30% citronellal and 40% geraniol, as a repellent against head lice compared with the placebo. Both at the 2-month and 4-month follow-up, subjects in the intervention group demonstrated a lower rate of lice infestation compared with the control group (p<0.0001).

f) Natural remedy (Chick Chack)
An open clinical trial was conducted that compared “Chick-Chack”, a spray containing natural products such as coconut, anise and ylang ylang oils with a formulation made of 0.5% permethrin, 0.25% malathion, 2% piperonyl butoxide, 47.25% isododecane, and 50% propellant gas for the treatment head lice. There were no significant differences in efficacy between treatments; the level of significance was not reported (i.e. p-value). Clinical detectable side effects were not found in any of the study subjects.

g) Water-free neem seed extract shampoos
Authors Abdel-Ghaffer and Semmler conducted three sets of clinical trials to test for the presence of live lice or nits with the treatment of water-free neem seed extract shampoo.
The overall results of all trials indicate that water-free neem seed extract shampoo is highly effective in the treatment of head lice irrespective of intensity level and treatment exposure time.\(^9\)

**h) Hair dryer**

One clinical trial study tested six different treatment methods that delivered hot air to the scalp in different ways. The findings suggest one 30-minute application of hot air has the potential to eradicate head lice infestations, and hot air is a safe and an effective treatment to which lice will unlikely develop a resistance.\(^5\)

**i) Combination therapies**

Authors Akisu et al. measured the effectiveness of albendazole alone as an oral medication, 1% permethrin aline and combination of albenzadole and 1% permethrin at various doses. The results indicated no statistically significant differences among the cohorts (p>0.05), and no adverse events were reported.\(^8\)

A second clinical trial measured the success rate of head lice eradication of home use of proprietary pediculicide (0.5% malathion or aqueous permethrin) and “Bug Buster Kit”, a fine tooth comb. The “Bug Buster Kit” group had a statistically significantly higher success rate compared with pediculicides groups.\(^3\)

**Conclusions and Implications for Decision or Policy Making:**

Our search found two systematic reviews and eleven clinical trials on head lice treatments. The studies have shown that some head lice treatments are more effective, such as permethrin cream rinse lice treatment with combing, citronella, malathion, and Bug Buser Kit compared with their alternatives in the trials; however, we do not know their efficacies across all interventions. Some trials reported more adverse events with citronella and PLT without combing, but none were serious. Results must be interpreted with caution due to study limitations highlighted in Appendix A. Such limitations include study design (e.g. lack of randomization, blinding, unequal sample sizes of groups), lack of monitoring of treatment application, and questionable re-treatment, follow-up durations and examination procedures.

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### Appendix A: Clinical Effectiveness and Safety of Head Lice Treatments

<table>
<thead>
<tr>
<th>Study (Author, Year, Country)</th>
<th>Study Design</th>
<th>Participants</th>
<th>Intervention versus Comparator</th>
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<td>Pearlman, 2004, United Kingdom</td>
<td>2 open clinical trials 3-weeks with a follow-up visit after 6 months</td>
<td>Trial 1: n=93 (27M and 66F) Trial 2: n=40 (12M and 28F) Subjects with positive wet combing test results (i.e. presence of lice)</td>
<td>Trial 1: non-toxic dry-on, suffocation-based pediculicide lotion, minimal household measures and physical removal of nits Trial 2: same as Trial 1 except there was no physical removal of nits A control group was not specified</td>
<td>1) Presence of lice: Successful test result=no lice are present Failure test result=lice are present 2) If subjects no longer complained of increased scalp itching or exhibited increased head scratching and no new nits or crawling lice</td>
<td>No statistically significant differences in the cure rate (i.e. negative test result) were reported between the 2 trials (97% vs. 95%) or a after a 6-month follow-up visit (94% vs. 95%) (p=0.001) No adverse events were reported</td>
<td>Lacking of blinding and randomization Inclusion of a control or therapeutic comparative group Uneven numbers between two study groups</td>
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<td>Meinking et al., 2004, USA</td>
<td>Randomized observer-blinded study 8 follow-up evaluation with same treatment with the identical methodology as on day 1 Final follow-up visit at day 15</td>
<td>66 subjects with at least 3 live lice and 10 viable eggs upon initial visual examination and between 6-70 years of age were enrolled. 63 subjects completed the safety and efficacy analyses Intervention group: mean age=10.1 years; M=1 and F=21 Group 1 (n=22): reduced, nonresidual 20-minute treatment of malathion (Ovide) Group 2 (n=44): standard 10-minute residual reducing treatment of 1% permethrin (Nix)</td>
<td>Presence of lice on day 8 and 15: Successful test result=no lice are present Failure test result=lice are present All subjects with live lice on day 8 received the second treatment with the same product and treatment time that they received on day 1</td>
<td>The presence of live lice found on the subjects as follows: Day 8: 19.5% (Group 1) vs. 40.9% (Group 2) (p=0.08) Day 15: 88% (Group 1) vs. 33% (Group 2) who required a second treatment on day 8 were lice-free on day 15 (p=0.05) At the end of the study: 98% (Group 1) vs. 55% (Group 2) were lice-free</td>
<td>Unequal sample sizes between study groups</td>
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<td>Meinking et al., 2002, USA</td>
<td>Randomized observer-blinded study 15 days</td>
<td>95 infested adults and children (19M vs. 76F; Median age=8.0; Range=2-45 years) 93 subjects were included in all analyses</td>
<td>Control group: mean age=12.7 years; M=3 and F=41</td>
<td>Group 1 (n=34): 1% Permethrin Cream Rinse Lice Treatment (PLT) with combing Group 2 (n=61): 1% Permethrin Cream Rinse Lice Treatment (PLT) without combing</td>
<td>1) Presence of lice on day 2, 8, 9, and 15: Successful test result=no lice are present Failure test result=lice are present 2) Efficacy of nit removal combing as an adjunctive measure to PLT</td>
<td>(p&lt;0.0001) No serious adverse events were found</td>
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<td>Tanyuksel et al. 2003, Turkey</td>
<td>Single blind, randomized, parallel-group comparative study</td>
<td>566 children infested with pediculosis humanus capitis and/or more than 5 creamy white or white nits closer than 1.5 cm to the scalp</td>
<td>Group 1 (n=382): Subjects were treated with 1% permethrin cream rinse (Zalvor®) Group 2: (n=184): Subjects were treated with 0.4%-phenothrin shampoo (Antibit®)</td>
<td>Presence of live adult lice, nymphs or nits. Successful test result=no lice are present Failure test result=lice are present</td>
<td>The success rates are as follows: 93.7% (Group 1) vs. 75.5% (Group 2) had no evidence of viable eggs and/or adults at the 2-week follow-up. The results were statistically significant between both groups (p&lt;0.01) Day 15: No live lice or eggs were present on the children's scalp</td>
<td>No mention of adverse events Unequal sample sizes between study groups</td>
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<td>Burgess et al. 2005, United Kingdom</td>
<td>Randomized controlled equivalence trial</td>
<td>214 young people aged 4 to 18 years and 39 adults with active head louse infestation Groups were similar in age, sex, intensity of infestation, and hair length, thickness, degree of curl, and dryness or greasiness.</td>
<td>2 applications 7 days apart of either: Group 1 (n=127): 4.0% dimeticone lotion, applied for 8 hours or overnight Group 2 (n=125): 0.5% phenothrin liquid, applied for 12 hours or overnight</td>
<td>1. Presence of lice: Successful test result=no lice are present Failure test result=lice are present 2. Evidence of reinfestation after positive test result</td>
<td>Successful treatment rate was reported as follows: 83 participants in group 1 compared with 87 participants in group 2. Reinfestation after cure was present in 6 participants in dimeticone group compared with 7 in the phenothrin group No difference in success rate was</td>
<td>Authors were unable to undertake random sampling of the population by screening in schools Authors had difficulty in ensuring that the hair scalp had been thoroughly covered in some cases.</td>
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| Mumcuoglu et al. 2004, Israel ² | Randomized, placebo-controlled double-blind clinical 4-month study | 198 children infested with head lice | Group 1 (n=103): Subjects were treated with a test formulation that contained a micro-encapsulated citronella (3.7%) solution  
Group 2 (n=95): Subjects were treated with a placebo (the same formulation without the citronella as the active ingredient)  
Treatments were performed every morning before school (i.e. 6 days a week) | After 2 and 4 months of the beginning of the treatment, subjects were examined for louse infestation. | After 2 months of the initial treatment, 12% of children in the intervention group had lice infestation compared with 50.5% of in the control group (p<0.0001).  
After 4 months of the initial treatment, 12.4% of children in the intervention group had lice infestation compared with 33.7% of children in the placebo group.  
Four parents and children (4.4%) disliked the odour of the formulation while 1 (1.0%) complained | Treatments were conducted by the parents, rendering it difficult for the investigator to monitor the procedure  
Follow-up length (2 and 4 months) may be long since treatment could have been successful, but there could have been a new infestation. |
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<td>Mumcuoglu et al. 2002, Israel</td>
<td>4-month open randomized clinical study</td>
<td>143 children from 6 different schools infested with living lice and eggs were included in the study and 129 compiled with the instructions for use</td>
<td>Intervention group (n=65): Natural remedy (Chick-Chack, a spray containing natural products-coconut, anise and ylang ylang) Control group (n=64): pediculicide with the following formulation: 0.5% permethrin, 0.25% malathion, 2% pipronly butoxide, 47.25% isododecane and 50% propellant gas Infested subjects were treated twice for 10 min with a 10 day interval between treatments</td>
<td>Presence of live lice or nits. Successful test result=no lice are present Failure test result=lice are present</td>
<td>92.3% were successfully treated with the natural remedy compared with 92.2% in the control group. No serious adverse events were reported among the subjects.</td>
<td>Treatments were conducted at home rendering it difficult for research investigator to monitor procedure</td>
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<td>Abdel-Ghaffar and Semmler, 2007, Egypt</td>
<td>3 sets of clinical trials Each set of trials lasts for 3 successive weeks</td>
<td>60 naturally-infected subjects between 4-15 years of both sexes suffering from heavy infestations were included in the study</td>
<td>20-30ml of water-free neem seed extract shampoo remained mixed in the hair for four different exposure times: 5, 10, 15, and 30 min At the end of each exposure time, the shampoo was washed out thoroughly and hair was combed.</td>
<td>Presence of live lice or nits. Successful test result=no lice are present Failure test result=lice are present</td>
<td>Trial 1-Week 1: 86% (n=7) were free of head lice Trial 1-Week 2: (n=10) same results as in week 1 Trial 1-Week 3: 88% (n=15) were of any infestation same results as in week 1</td>
<td>Study was a little difficult to follow.</td>
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<td>No adverse events were reported during this first trial period</td>
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<td>Trial 2 (n=25): identical results were obtained as in the first trial; percentage of head lice-free children after a single application of the shampoo reached to 97% as confirmed by reexamination 1 week after initial treatment</td>
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<td>3% were re-treated once and stayed free of head-lice</td>
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<td>Trial 3: 18 girls with long, heavily-infested hair were divided into 3 groups of equal size and were subjected to different exposures to the shampoo treatment. No obvious differences were observed between an exposure time of 10 and 15 min (group 2 and 3). An average of 12% (3 out of 25)</td>
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<td>Goates et al., 2006 (USA)</td>
<td>Clinical trial study</td>
<td>169 individuals with infestations varying in size from a few lice to hundreds of lice; F = 94.1% and median age = 10 years</td>
<td>Group 1 (n=54): Bonnet-Style Hair Dryer Group 2 (n=26): Handheld blow-dryer: diffuse heating Group 3 (n=27): Handheld blow-dryer: directed heating Group 4 (n=15): Wall-mounted dryer Group 5 (n=18): LouseBuster with sections (LouseBuster is a custom built, high volume, hot-air blower) Group 6 (n=18): LouseBuster with hand piece A control group was not specified.</td>
<td>Comparison of percentage of viable lice and eggs removed from the pretreatment and posttreatment sides of the scalp</td>
<td>Group 1: Control-egg-hatch rate was 30.4% and treated-egg hatch rate was 11.2%, a significant absolute difference of 19.2% (95%CI: 15% to 24%) Group 2: Control-egg-hatch rate was 48.7% and treated-egg hatch rate was 3.3%, a significant absolute difference of 45.4% (95%CI: 42% to 49%) Group 3: Control-egg-hatch rate was 44.3% and treated-egg hatch rate was 2.1%, a significant absolute difference of 42.2% (95%CI: 39% to 45%) Group 4: Control-egg-hatch rate was 51.0% and treated-egg hatch rate was 3.5%, a significant absolute difference of 47.5% (95%CI: 40% to 55%)</td>
<td>Treatments were conducted at home rendering it difficult for research investigator to monitor procedure Unequal sizes among study cohorts</td>
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<td>Akisu et al., 2006, Turkey</td>
<td>RCT</td>
<td>150 children with head lice. Subjects were randomly divided in 5 groups of 30 each. Subjects with enterobius vermicularis infestation that</td>
<td>Group 1: 400mg of albendazole daily for 3 days and a repeated 400 mg dose after 1 week Group 2: 400 mg of albendazole daily for 3 days and a repeated 400 mg single dose 1 week after the initial treatment</td>
<td>Presence of live adult lice, nymphs or nits close to the scalp as seen by the naked eye Successful test result=no lice are present Failure test result=lice are present</td>
<td>The success rate of treatment at the 2 weeks follow-up for all groups was 65.1%, 66.6%, 80.0%, 84.6%, and 82.1%, respectively. No statistically significant difference was found between the groups (p&gt;0.05)</td>
<td>Unclear whether subjects were blinded Small study groups (n=30) Length of clinical trial was not mentioned Lice were checked with the naked eye only and not with a fine tooth</td>
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<td>Hill et al. 2005 (United Kingdom)</td>
<td>Single-blind, randomized, comparative clinical study</td>
<td>133 young people aged 2-15 years with head louse infestation</td>
<td>Group 1: Home use of proprietary pediculicides (either 0.5% aqueous malathion (n=30) or aqueous permethrin (n=40)) Group 2 (n=56): Bug Buster Kit (a fine tooth comb)</td>
<td>Presence, number and stage of live lice. Successful test result=no lice are present Failure test result=lice are present</td>
<td>Success rates for malathion and permethrin were 17% (5/30) and 10% (4/40). Success rate for group 2 was significantly greater than that for the pediculicides (57% vs. 13%, RR=4.4, 95% CI = 2.3 to 8.5, p&lt;0.0001)</td>
<td>Effectiveness of pediculicides was much lower in this trial is lower than in the Welsh trial. Discrepancies may be accounted for in differences in the study methodology. As a result, it is difficult to make a direct comparison of results between the 2 studies. No mention of adverse events</td>
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References:


