

A randomised, double-blind, comparative efficacy trial of three head lice treatment options: malathion, pyrethrins with piperonyl butoxide and *MOOV Head Lice Solution*

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Abstract

Head lice are a growing source of parental and social concern. The introduction of pesticide based head lice treatments several decades ago saw the infestation rate fall dramatically; today, due to growing pesticide resistance, the head louse is staging a come back. New, effective, clinically proven head lice treatments are urgently needed to control the growing head lice problem. *MOOV Head Lice Solution* is the first herbal based head lice treatment to be registered by the TGA and has been clinically tested to ICH-GCP standards. A randomised, double blind, comparative efficacy trial of *MOOV Head Lice Solution* against malathion and pyrethrins with piperonyl butoxide was conducted using Queensland primary school children who had active head lice infestations. *MOOV Head Lice Solution* achieved a cure rate of 33/40 (82.5%), versus malathion 11/37 (29.7%, $p < 0.0001$) and pyrethrins with piperonyl butoxide 13/36 (36.1%, $p < 0.0001$) The 82.5% cure rate for *MOOV Head Lice Solution* was achieved without the use of supportive combing, thus representing a significant reduction in time cost to caregivers. All three treatment products were well tolerated by the subjects. *MOOV Head Lice Solution* is the first TGA registered herbal based head lice treatment and is more than twice as effective as pesticide based head lice treatments.

Introduction

Head lice has been a community concern since the earliest civilisations, with evidence of head lice infestations found on 5,000-year-old Egyptian mummies.¹ Today the head louse is making a come back after a number of relatively quiet decades.^{2,3} In Australian schools head lice infestation rates of up to 35.1% have been published,^{4,5} with head lice the third most commonly reported outbreak in day care centres after diarrhoea and conjunctivitis.⁶

Although largely a condition of childhood and most commonly affecting children aged 3-11 years,² a head louse infestation can be passed from child to parent, student to teacher, sibling to sibling, or from any prolonged head to head contact.⁷ Head lice do not discriminate on the basis of age, gender, race or social class.⁸ Head lice are not concerned with hair type, colour or hygiene status.

Lice are most often found behind the ears or at the back of the neck, and they attach their eggs to the hair shaft close to the scalp.⁷ A head louse must feed on the host's blood every three to six hours or it will dehydrate and die.⁷

Although distressing to parents and children alike, head lice are harmless and there is no evidence to support cleaning bedding, clothing or furniture; lice found on chairs, pillows and hats are dead, sick or elderly.⁷

Although an itchy scalp is often considered a good indicator of a head lice infestation, one study found that 36.1% of children with an infestation and 20.6% of children without an infestation reported having an itchy scalp.⁹ The majority of head lice infestations are asymptomatic.⁷ It is therefore important that every member of the household be checked – adults⁷ and children – if a family member has head lice.

The head lice cycle

A louse egg that has been laid on a hair shaft is called a 'nit'. The nits are firmly attached with proteaceous biological glue.⁸ There are currently no commercial products available that will dissolve this glue.⁸ The nit will hatch six to 10 days after deposition. The louse will then go through three growth stages, each marked by an exoskeleton moult. The first moult occurs two to three days after hatching with subsequent moults around five and 10 days after hatching. Once the lice have moulted for the third time they are adults and able to mate and reproduce. The female will begin to lay eggs one to two days after mating, and will continue to lay three to eight eggs a day for the next 16 days. A louse will die around 32-35 days after hatching.¹⁰

One female louse can produce up to 128 lice in one generation, and over 8,000 in just two. A head lice infestation will consist of lice and eggs at all developmental stages.

Unlike many conditions of childhood such as chicken pox, a past head lice infestation offers no protection from the next infestation. It is common for a cycle of cure and reinfestation to be seen, i.e. the infestation is cured during school holidays, and reinfestation occurs within days of school starting again.

Treatments for head lice

On the market today are a host of products that claim to cure a head lice infestation. An international review of head lice treatments from the Cochrane Collaboration¹¹ concluded that although permethrin, synergised pyrethrin and malathion were once effective, the emergence of drug resistant lice means that there is no direct contemporary evidence for the effectiveness of these compounds. While malathion, permethrins and piperonyl butoxide/pyrethrins have been the mainstay of the battle against head lice, their residual nature and misapplication has led to a dramatic increase in resistance in head lice populations.¹² This resistance has been found in Australia¹³ and across the world.¹⁴⁻¹⁹

The increasingly poor performance of traditional head lice products has led to a surge in the commercialisation of herbal or natural based head lice treatments. While herbal based head lice treatments are appealing, a 2003 review²⁰ by the Therapeutic Goods Administration of Australia (TGA) found no published clinical trials supporting the efficacy or safety of the herbal head lice products on the Australian market. This was supported by the Cochrane review which concluded that there was no evidence for herbal treatments.¹¹ This has been recognised in the wider scientific community.⁷

The poor efficacy of traditional products and the unproven nature of herbal products is resulting in

parental frustration so great that drastic alternatives such as kerosene and veterinary flea products²¹ are being used on children in a desperate attempt to cure recalcitrant head lice infestations. The lack of reliable treatment products is becoming a health and safety risk for children.

Health departments in Australia have been recommending wet combing as a method for treating head lice infestation.²²⁻²⁴ This method involves saturating the hair with conditioner and combing it with a nit comb until no more head lice are found. This procedure is repeated every two days until no head lice are found for 10 consecutive days of combing.^{22,23} This method is laborious, time consuming and does not produce satisfying cure rates as a treatment on its own²⁵ or improve cure rates when used in conjunction with traditional treatments.¹⁴ A family with several children can spend many hours each night wet combing in an attempt to cure an infestation. When conducted by trained nurses in a clinical, controlled setting with a standardised protocol, wet combing has a reported cure rate of 50-60%.^{18,26} A home based trial using parents to perform the wet combing achieved a cure rate of only 38% and concluded that wet combing as the first line treatment for head lice is inappropriate.²⁵ This conclusion is supported by the Cochrane review that concluded physical methods such as wet combing were ineffective in treating head lice.¹¹

There is a clear need for an effective, natural and quick head lice treatment that can deliver the results parents need without a significant lifestyle impact. *MOOV Head Lice Solution* AUST R 128237, is a natural-based head lice treatment that utilises eucalyptus oil in an optimised base, and is the first herbal based head lice treatment to be registered with the TGA.

In order to demonstrate the clinical efficacy of *MOOV Head Lice Solution* a double blind, randomised, comparative clinical trial was conducted. This trial was conducted according to the International Conference on Harmonisation Good Clinical Practice (ICH-GCP) guidelines, and addressed the protocol criticisms outlined in the TGA Head Lice Review²⁰ and the Cochrane Review.¹¹

Method

This phase four clinical trial was a multi-centred, randomised, three-parallel group, comparative, double blind study designed according to ICH-GCP guidelines. The protocol was registered (NCT00381082) and approved by the Human Research Ethics Committee of the University of Queensland (Clearance no. 2003000184). The parents of the children involved provided written informed consent. The children gave

verbal consent to participate in the trial at the start of each treatment day. The trial was conducted in 2004 and involved Queensland primary school children from seven different schools.

The three products tested were registered with the TGA for the treatment of head lice: *Banlice Mousse* AUST R 46708 containing 16.5mg/g piperonyl butoxide and 1.65mg/g pyrethrins; *KP24 Medicated Foam* AUST R 18867 containing 1.0% malathion (maldison); and *MOOV Head Lice Solution* AUST R 128237 containing 11.0% eucalyptus oil.

Banlice Mousse and *KP24 Medicated Foam* were purchased from a pharmacy wholesaler, while *MOOV Head Lice Solution* was supplied by Ego Pharmaceuticals.

Although *Banlice* and *KP24* claimed that only one treatment was required to effect a cure, both were applied twice using the manufacturers' directions, with a week between applications, i.e. at day 0 and day 7. The use of two applications for *Banlice* and *KP24* was in accordance with the recommendations of the TGA Head Lice Review.²⁰

MOOV Head Lice Solution was applied three times with a week between applications as per the manufacturer's directions, i.e. at day 0, day 7 and day 14. As head lice eggs can take up to 10 days to hatch, the use of three applications was designed to ensure that any lice hatching from eggs laid immediately before the first application would be killed by the third application.

Subjects were screened for head lice using visual inspection and dry combing. Those children meeting the entry criteria were randomised to receive one of the three treatments.

The entry criteria were: primary school children; presence of live head lice, not just eggs; available for trial duration; parent or guardian willing to abstain from using any other head lice product, including head louse combs, on their child for the duration of the trial; parent or guardian gave written informed consent.

The exclusion criteria were: history of allergies or adverse reactions to head lice products or the specific components being tested; treatment for head lice in the four weeks before day 0; presence of scalp disease; more than one fixed place of residence. In addition, if a subject had primary school aged siblings, those siblings had to be screened, and enrolled if they had head lice.

During the trial, subjects were free to wash their hair with ordinary shampoo and conditioner and to comb with standard combs. Head louse combs, other head lice products, hair dyes or bleaches were not permitted during the trial. Subjects were free to withdraw from

the trial at any time, and adverse events were monitored and recorded.

Per protocol assessment

To be considered per protocol, the subject must have received two treatments of *Banlice* or *KP24*, each seven days apart, or three treatments with *MOOV*, each seven days apart. In addition, all primary school aged siblings of the subject who were found to be infested must have received at least one treatment with either *Banlice* or *KP24*, or two treatments with *MOOV* in the context of the trial.

Efficacy assessment

A 'cure' was defined as the absence of live lice as diagnosed by wet combing of the hair. The primary efficacy endpoint was the cure rate seven days after the last application, i.e. day 14 for *Banlice* and *KP24*, and day 21 for *MOOV*. Wet combing is considered the best technique for diagnosing a head louse infestation.^{27,28} For this study the wet comb technique was standardised and carried out by trained technicians.

Despite the difference in appearance of the three treatments, double blinding was maintained. The treatments were randomly assigned to the subjects. One group of personnel applied the treatments, while a second group carried out the efficacy assessments. Although it was not possible to blind the treatment personnel, the subjects were unaware that three different treatments were involved. The efficacy assessors were physically removed from the treatment areas, and were unaware of which treatment the subjects had received.

Safety assessment

Safety was assessed by comparing the adverse events reported by the three treatment groups.

Results

Efficacy

During the study period, September to November 2004, 822 subjects were examined, of which 237 had live head lice. Of these 237 subjects, 152 met the inclusion and exclusion criteria and were enrolled; 113 were assessed as per protocol for the purposes of safety and efficacy analysis. Of the 113, 36 were treated with *Banlice*, 37 were treated with *KP24* and 40 with *MOOV*. Reasons for a subject being deemed not per protocol were: an infested primary school aged sibling not treated with the minimal application of *Banlice*, *KP24* or *MOOV* (20); use of alternative head lice treatments during the trial (12); subject did not undergo the entire treatment/assessment, i.e. due to non-attendance at school (7).

The cure rates were determined one week after the final product application: day 14 for *KP24* and *Banlice*, day 21 for *MOOV*. *KP24* had a cure rate of 29.7%, *Banlice* had a cure rate of 36.1% and *MOOV* had a cure rate of 82.5% (See Table 1).

TABLE 1: Cure rates for the primary efficacy endpoint

Treatment product	Subjects cured	Cure rate
<i>MOOV Head Lice Solution</i>	33/40	82.5% [†]
<i>Banlice Mousse</i>	13/36	36.1%
<i>KP24 Medicated Foam</i>	11/37	29.7%

[†] Significantly better than either comparator ($p < 0.0001$)

Using chi-squared tests with a Bonferroni adjustment to allow for multiple comparisons, it was found that *MOOV* was significantly more effective in curing head lice infestations than either *Banlice* ($p < 0.0001$), or *KP24* ($p < 0.0001$).

Safety

Of the 152 subjects enrolled, 23 adverse events were reported: 18 for *MOOV*, three for *Banlice*, two for *KP24*. The adverse events related to scalp sensations experienced by the subjects during product application, i.e. itching, a hot sensation, stinging and burning. All the adverse events resolved completely within five minutes of the products being washed from the hair.

Discussion

Head lice are a community concern that is not being sufficiently addressed by current treatments, be they traditional, herbal or combing. The World Health Organisation has recognised that without new compounds it will be difficult to maintain effective control of head lice,²⁹ and with head lice infestations causing increasing parental frustration, and fear and anxiety in children,^{2,7} effective treatments are needed.

MOOV Head Lice Solution is an herbal-based head lice treatment that has been clinically proven to be more effective than both malathion and piperonyl butoxide/pyrethrin products.

This present study addressed all the concerns raised in the Cochrane Review¹¹ and the TGA Review²⁰ and included strict definitions of head lice infestation, i.e. live head lice had to be found, eggs alone were not enough. Further to this, subjects that had been treated with a head lice product in the previous four weeks were excluded to avoid complications from any residual product, combing procedures were defined and standardised, trained operators performed the

combing, efficacy was determined one week after the final application, subjects were randomised, the study was double-blinded and adequately powered to allow statistical analysis. In addition, the siblings of the enrolled subjects were examined for head lice.

MOOV Head Lice Solution achieved an 82.5% cure rate, while *Banlice* and *KP24* achieved cure rates of 36.1% and 29.7% respectively. *MOOV Head Lice Solution* is not only significantly more effective than *Banlice* ($p < 0.0001$) and *KP24* ($p < 0.0001$), it is twice as effective as either product.

Banlice and *KP24* have promoted their ability to kill head lice and eggs in one application. In accordance with the recent recommendations from the TGA²⁰ *Banlice* and *KP24* were applied twice in this study, with seven days between each application.

MOOV Head Lice Solution was applied three times, each application being seven days apart. Head lice eggs can take up to 10 days to hatch, so by including a third application in the treatment regimen, any lice that hatch from an egg laid immediately before the first application will be killed by the third application. This reduces the likelihood of the primary head lice infestation continuing. While *MOOV Head Lice Solution* kills eggs and lice, the survival of only a few out of thousands of eggs is sufficient for the infestation to continue. By incorporating a third application into the regimen, it ensures that the infestation is eradicated.

Transient, mild to moderate adverse events were reported for all three treatments and were largely described as itching, stinging or burning. The sensations dissipated when the treatments were washed out after the prescribed application periods. Overall the three treatments were well tolerated by the subjects.

Treatment failure versus reinfestation

While *MOOV Head Lice Solution* is significantly better than the comparator products, it did not achieve a 100% cure rate. As preliminary clinical data submitted to the TGA demonstrated that *MOOV Head Lice Solution* killed all live lice on the scalp in one application, and the three treatment protocol ensures that eggs and all hatching lice are killed, the 17.5% failure rate can be attributed to reinfestation. The final efficacy checkpoint was seven days after the last product application, giving seven days for reinfestation to occur. As it was not possible to treat all the children in a given class or school due to lack of parental consent, it is likely that children cured after the last application may have become reinfested before the final efficacy endpoint, and thus be counted as treatment failure. Unlike many other childhood diseases, having head lice once does not

prevent repeat infestation. A highly efficacious treatment in combination with constant vigilance is the best defence against reinfestation.

Resistance

The relatively low cure rates for *Banlice* and *KP24* may be explained by resistance within the louse population, or by the stringent definition of a cure as measured one week after the last treatment application. It has clearly been demonstrated that head lice around the globe is becoming increasingly resistant to traditional head lice treatments such as malathion and permethrin.¹⁴¹⁹ The residual nature of these materials results in low levels remaining in the hair for many days after product application. These persistent low levels, allow for the selection and dominance of resistant lice. Although once very effective, due to their residual nature, these treatments have now become ineffective.

MOOV Head Lice Solution has a volatile active combination that will enable the high cure rates observed in this trial to be maintained into the future. Once the product is washed from the hair, any residual eucalyptus oil will rapidly volatilise from the hair. This should prevent the emergence of resistance, thus helping to maintain the efficacy of *MOOV Head Lice Solution*.

Wet combing

The best technique for detecting a head lice infestation is the wet-combing technique.^{27,28} The conditioner that is combed from the hair provides a contrast to the black-grey lice that are combed from the hair. An infestation is confirmed by finding live lice.⁷ Nits on their own do not represent an active infestation and should not be treated as one.⁷ Once a head lice infestation is confirmed by finding live lice, treatment should begin immediately to prevent the infestation getting worse or transmitting to others. Prophylactic or 'just in case' treatment should be discouraged.²

It is common for head lice products to recommend that product application be followed with the wet combing procedure. If a head lice product is effective, the use of wet combing is unnecessary and significantly increases the time burden of treatment. If a head lice product needs wet combing as a supportive procedure the product efficacy must be questioned and an alternative product should be sought. With wet combing shown to be ineffective as a treatment or a supportive practice, it is redundant in the treatment of head lice.^{11,14,18,25,26} This trial was conducted without wet combing and clearly demonstrated that *MOOV Head Lice Solution* is highly effective and does not need wet combing as a supportive procedure. This significantly reduces the time burden associated with treating head lice to a total of three 10 minute applications. For a family with several

children, this represents a significant improvement in the lifestyle impact of a head lice infestation.

Reinfestation is an ongoing concern for diligent parents. Although currently no product can prevent reinfestation, the availability of an effective head lice product will always make the treatment of a head lice infestation easier.

Conclusion

MOOV Head Lice Solution has been shown in a randomised, double-blind clinical trial in a relevant population to be twice as effective in curing head lice infestations as two popular treatments, piperonyl butoxide with pyrethrins, and malathion.

MOOV Head Lice Solution is the first herbal-based head lice treatment registered by the Australian TGA. In addition it does not need to be combined with combing to effect a cure; this represents a significant time saving for parents and an improvement in the lifestyle impact a head lice infestation will have.

MOOV Head Lice Solution is an effective head lice treatment using natural active ingredients that provides a quick treatment protocol that is twice as effective as traditional treatments and does not require supportive combing.

Declarations of interest

Kerryn Greive and Jane Oppenheim are employed full time by Ego Pharmaceuticals, the sponsor of the clinical trial and manufacturer of *MOOV Head Lice Solution*. James Rowe, Phillip Altman and John Staton are consultants employed by Ego Pharmaceuticals.

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