

Repellency of Citronella for Head Lice: Double-Blind Randomized Trial of Efficacy and Safety

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Abstract

Background: Head lice move easily from head to head. The lack of safe, effective repellents leads to reinfestation.

Objectives: To test the efficacy of a slow-release citronella formulation as a repellent against the head louse.

Methods: During 4 months in 2003 a randomized, placebo-controlled double-blind clinical study was conducted in four elementary schools; 103 children were treated with the test formulation and 95 with a placebo.

Results: A significant difference was observed during the second examination 2 months later, when 12.0% of the children treated with the test repellent and 50.5% of those treated with placebo were infested with lice. A significant difference was also observed at the third examination 2 months later, when 12.4% of the children treated with the test repellent and 33.7% treated with placebo were infested. Overall, there were significant differences between those treated with the repellent and those treated with the placebo (15.4% and 55.1% respectively, $P < 0.0001$). Side effects were observed in 4.4% of children who disliked the odor of the formulation, and an additional 1.0% who complained of a slight itching and burning sensation.

Conclusions: Use of an effective repellent could significantly lower the incidence of reinfestations, which would lower expenditure on lice control, including pediculicides, combs and products for nit removal, and the time spent on treatment and removal of the nits.

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Head lice are obligate parasites, spending their entire life on the host scalp and feeding exclusively on blood four to five times daily. Normally head lice infest a new host only by close contact between individuals, making social contacts among children and parent-child interactions the more likely routes of infestation than shared combs, brushes, towels, clothing, beds or closets. Head-to-head contact is by far the most common way of lice transmission. Girls are more frequently infested than boys, the differences increasing with age after 4 years of age. Children between 3 and 14 years of age are most frequently infested [1,2].

Head lice move easily from head to head, and the lack of safe, effective repellents leads to reinfestation. Pediculicides have practically no residual activity when applied to the hair and therefore do not protect treated individuals from reinfestation. Essential oils such as lavender, rosemary, piperonal, eucalyptus, D-limonene and citronella as well as their nine components have been

tested for repellency to laboratory colonies of body lice and were found to be effective [3–6]. However, their efficacy has not been tested in clinical trials on human lice and there is no conclusive evidence of their safety and effectiveness. To our knowledge, there are no published clinical trials on louse repellents.

Citronella is a volatile oil obtained from the leaves and stem of the plant *Cymbopogon winteratus* or *Cymbopogon nardus*. The oil contains approximately 30% citronellal and 40% geraniol and, in smaller quantities, citronellic, borneol, citronellol, nerol, citral, camphene, dipentene and limonene. Citronella is a popular ingredient in wax candles as an insect repellent; it is also widely used in perfumes, soaps, skin lotions and deodorants. Citronella oil has therapeutic potential since it includes antiseptic, deodorant, insecticide, parasitic, tonic and stimulant properties. However, it may irritate sensitive skin and cause dermatitis in certain individuals [7].

The aim of this project was to test the *in vivo* efficacy of a slow-release citronella formulation as a repellent against the head louse, *Pediculus humanus capitis*.

Subjects and Methods

Participants

The study was conducted in 2003 in four elementary schools in Jerusalem (designated as DN, ER, NB and YH) with 1,803 pupils. Three of the schools were for girls only. A letter was sent to parents explaining the purpose of the study and asking for permission to examine their children for louse infestation. After receiving the appropriate consent, 660 children (110 boys and 550 girls) aged 6–14 years were examined. Approval for this study was obtained from the ethics committee of the Hadassah University Hospital in Jerusalem and the Israel Ministry of Health.

Examination for lice

The hair of each child was combed first with a regular comb or brush to straighten the hair and then the entire scalp was combed with a louse comb (Innomed, Hogil, Purchase, NY, USA) for about 3–5 minutes or until the first louse was isolated. In cases where the child's hair was too frizzy or curly and did not allow the use of a louse comb, the scalp was examined by hand for 5–7 minutes. At the end of each examination day all examined children received a

letter for their parents explaining that their child was examined and was/was not infested with lice. Parents interested in participating in the study were requested to come with their children to the school. After obtaining written consent from the parents to participate in the trial, they were provided with a bottle of the test formulation free of charge.

Repellent

The test formulation contained a micro-encapsulated citronella (3.7%) solution. The formulation is based on oil droplets coated by a positively charged biopolymer, chitosan. As a placebo, the same formulation without the active ingredient was used. The packaging of the repellent formulation and of the placebo was identical, i.e., a white bottle bearing a code number.

A bottle with 200 ml of the formulation was given to each child participating in the study. Each squeeze of the bottle delivered approximately 0.3 ml of the test solution. Parents were instructed to spray – according to the length of the hair – with 0.3–0.9 ml (one to three squeezes) of the solution in each treatment. The hair was sprayed every morning before school, i.e., 6 days a week. The child's hair could be washed any day of the week, but only after school hours.

Clinical trial

In this placebo-controlled double-blind clinical study the test solution or the placebo was randomly distributed to parents free of charge, together with instructions for use. The distribution of the test solution and the examination of children for lice were conducted by different scientists. Parents were instructed not to use any other remedies such as rosemary oil, or suffocating agents such as olive oil, margarine or hair gels for the duration of the study. A protocol was given to the parents, which was to be filled in daily or at least once a week, indicating the days on which the treatment was carried out. An additional protocol with details of the treatment, side effects, infestation with lice and treatment with pediculicides was also handed to the parents, to be returned to the investigator at the end of the study period.

Every child was examined by a physician for dermatologic abnormalities, e.g., excoriations, insect bites, lymphadenopathy, secondary infections, eczema, severe seborrhea, as well as for conjunctivitis and other eye diseases. Only healthy children who had not been treated with an anti-lice product during the previous 7 days were included in the study. Criteria for exclusion of a child from the study included severe scalp dermatosis, secondary infections, open wounds, tinea of the scalp, conjunctivitis and other eye diseases (other than strabismus).

Children were reexamined 2 months after the beginning of the treatment to determine whether there were any signs of louse infestation. The physician examined the children for side effects on the skin and eyes, and recorded the children's impressions regarding the smell, or any irritation and itching during and after the treatment. The treatment was considered unsuccessful if the child was found to be infested with living lice and eggs. The parents of those children were instructed on how to treat the infestation and were provided with a pediculicide free of charge. A third

examination took place 4 months after the beginning of the treatment. The treatment was again considered unsuccessful if living lice or eggs were detected on the scalp.

During the course of the trial the parents were contacted at least twice by telephone and questioned regarding the treatment, side effects, infestation with lice and treatment with pediculicides. Of 231 children who were either negative for lice or had nits only and were originally included in the study, 198 complied with the instructions for use and were randomly treated with either the test solution or the control product. Five children were absent during the second examination and 17 children were absent during the third examination.

Statistical analysis

Statistical analyses were performed using the SPSS 10.1 software. Fisher's exact test was used to compare possible differences such as the rate and efficacy of treatment between the groups. McNemar's test was used for testing the significance of changes between the first, second and third examinations.

Results

Of 660 children examined, 151 (22.9%) were infested with living lice and eggs, while another 133 (20.1%) were infested with nits only. Girls were infested with lice 7.4 times more than were boys (131/550, 26.7% and 4/110, 3.6%, respectively). Girls were also infested with nits 13.2 times more than were boys (23.8% and 1.8%, respectively) ($P < 0.001$) [Table 1]. The percentage of children examined in each school ranged from 24.5% (NB) to 76.3% (DN) (average 38.8%). There were significant differences in rates of lice or nits-only infestation between the schools ($P < 0.001$). Children from two schools (ER and NB) had the highest infestation rates (68/196, 34.7% and 54/149, 36.2%, respectively) [Table 2]. There were also significant differences in lice and nits-only infestation rates between the grades ($P < 0.001$). Children from the first, second and third grades had the highest infestation rates (35/135, 25.9%; 26/96, 27.1%; and 30/97, 30.9%, respectively) [Table 3]. The test solution was used in 103 children and the placebo in 95. Of 198

Table 1. Percentage and gender distribution of children infested with lice and nits

Gender	n	Positive for lice (%)	Nits only (%)	Negative for lice (%)
Boys	110	4 (3.6)	2 (1.8)	104 (94.6)
Girls	550	147 (26.7)	31 (23.8)	272 (49.5)
Total (%)	660	151 (22.9)	133 (20.1)	376 (57.1)

Table 2. Percentage of infested children with lice and nits in each of the schools

School	n	No. examined (%)	Positive for lice (%)	Nits only (%)	Negative for lice (%)
DN	253	193 (76.3)	14 (7.2)	31 (16.1)	148 (76.7)
ER	534	196 (36.7)	68 (34.7)	57 (29.1)	71 (36.2)
NB	608	149 (24.5)	54 (36.2)	28 (18.8)	67 (45.0)
YH	305	122 (40.0)	15 (12.3)	17 (14.0)	90 (73.8)
Total (%)	1,700	660 (38.8)	151 (22.9)	133 (20.1)	376 (57.1)

Table 3. Percentage of infested children with lice and nits in each grade

Class	n	No. (%) of children with lice	No. (%) of children with nits only
First grade	135	35 (25.9)	27 (20.0)
Second grade	96	26 (27.1)	21 (21.9)
Third grade	97	30 (30.9)	20 (20.6)
Fourth grade	110	24 (21.8)	19 (17.3)
Fifth grade	113	24 (21.2)	27 (23.9)
Sixth grade	64	9 (14.1)	14 (21.9)
Seventh grade	35	1 (2.8)	3 (8.5)
Eighth grade	10	–	2 (20.0)

Table 4. Cross-tabulation between second and third examinations

	Second examination			Total
	Infested	Nits only	Negative	
Third examination				
Infested	25 (59.5)	13 (30.9)	4 (9.5)	42
Nits only	27 (42.2)	36 (56.2)	1 (1.5)	64
Negative	2 (2.8)	23 (32.8)	45 (64.3)	70
Total	54	72	50	176

children included in the study, 146 were infested with nits only, while 52 were negative for lice, eggs and nits at the beginning of the study.

The second examination 2 months later revealed lice infestation in only 11 of 92 children (12.0%) who were treated with the test repellent, compared to 51 of 101 children (50.5%) treated with placebo ($P < 0.0001$). The third examination a further 2 months later revealed lice infestation in only 12.4% (11/89) of the children treated with the test repellent compared to 33.7% (31/92) of children treated with placebo ($P < 0.0001$). There were no significant differences between the various schools and grades.

The chance of being reinfested with lice within the first 2 months of the study was significantly higher in children who were originally infested with nits only, compared to those who were negative for lice, eggs and nits (53/143, 37.1% and 9/50, 18.0% respectively; $P < 0.0001$). The same was true between the second and fourth month of the study (27.3%, 36/132 and 12.2%, 6/49 respectively, $P < 0.0001$). There were significant differences between those treated with the repellent and those treated with the placebo (15.4% and 55.1% respectively, $P < 0.0001$).

Children who were infested with lice at the second examination and who were successfully treated thereafter were also significantly more infested at the third examination, compared to those with nits only or who were negative for lice (59.5%, 10/53; 30.9%, 13/42; and 9.5%, 4/42, respectively, $P < 0.0001$) [Table 4]. Of 31 children previously infested with lice and treated successfully 17 (54.8%) were re-infested between the second and third examinations, compared to 8 of 11 children (72.7%) treated with the placebo ($P < 0.04$). In terms of the side effects, four parents and children (4.4%) disliked the odor of the formulation while one (1.0%) complained of a slight itching and burning sensation.

Discussion

In the present study, after 2 months of application of the repellent formulation only 12.0% of the children were infested with lice compared to 50.5% of children treated with a placebo. After an additional 2 months 12.4% of the children treated with the test repellent and 33.7% treated with placebo were infested with lice, showing that the repellent formulation was 3–4 times more effective than the placebo in protecting against lice infestation.

Studies using a laboratory colony of human body louse (*Pediculus humanus humanus*) found that the absolute or intrinsic repellent activity of concentrated citronella when applied to corduroy patches lasted for 29 days compared to untreated patches. However, the comparative or standard repellent activity of this oil lasted for only 2 days. In that study ammonium bicarbonate was used, which is a known attractant to lice [6,8]. It was suggested that under clinical conditions the duration of the repellent activity would be even shorter due to the effects of host attraction, light exposure, high temperature and humidity, sweat, grooming and shampooing. Sleeves made of cotton and impregnated with citronella were effective in repelling mosquitoes for 5 days, however when applied to the skin this oil was effective for only a few hours [9]. This was the reason why in the present study children were treated daily with the repellent formulation, although it is possible that treatments every second or third day would also have provided protection.

In the present formulation the concentration of citronella was 3.7%, which is considerably lower than those used in the *in vitro* studies. The lower concentration of this oil in a micro-encapsulated formulation significantly lessens the strong odor and decreases the chances of developing a contact dermatitis. Although 3.6% of the parents and children disliked the odor of the formulation and 1.0% complained of a slight itching and burning sensation, this could be improved by adding additional fragrances to the formulation.

The chances of being reinfested with lice are higher in children who had signs of previous infestation, i.e., nits on the scalp, compared to those who were negative at the beginning. Therefore, a repellent should be used particularly by those who are often infested with lice. Although not scientifically proven, our clinical experience shows that there are children who are more readily infested with lice than others. Such cases could also be seen within the same family. Natural attractants or repellents secreted with sweat, the density of hair, hair length, structure and color [10], as well as blood group [11] could play a role, alone or in combination, in the attractiveness of an individual. Reinfestation could also easily occur in families with two or more children if all the infested members are not treated simultaneously, or when the child's close friends or playmates are infested but not treated for lice.

Use of an effective repellent could significantly lower the incidence of reinfestations, which, among other beneficial effects, would lower expenditure on lice control, including pediculicides, combs and products for nit removal, and the time spent on treatment and removal of the nits. No less important would be the psychological and social benefits gained by eliminating the stigma and social isolation associated with louse infestation.

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I live in that solitude which is painful in youth, but delicious in the years of maturity



If we knew what it was we were doing, it would not be called research, would it?

Albert Einstein

Capsule

Vaccinia virus and comet tail

Vaccinia virus moves around infected cells propelled by comet-like actin tails. Newsome and team have uncovered an outside-in signaling mechanism, induced by extracellular vaccinia virus particles, that is ultimately responsible for stimulating actin-based motility of vaccinia virus by locally recruiting and activating Src at the plasma membrane. The highly localized signaling circuit explains why actin tails are only formed at the plasma

membrane and strengthens the hypothesis that actin-based motility of vaccinia mimics receptor kinase signaling at the leading edge of migrating cells. The authors also found a role for Src in regulating a switch from microtubule-based to actin-based motility at the leading edge of cells.

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E. Israeli

Capsule

Controlling flesh-eating bacteria

The "flesh eating bacteria" group A streptococci (GAS, *S. pyogenes*) are responsible for sore throats, for complications of rheumatic fever and glomerulonephritis, and for necrotizing fasciitis. Like most microbial pathogens, the range of host species that can be infected by a particular GAS is highly restricted. Sun et al. found that this host target restriction relies on the highly specific interaction between bacterial streptokinase

and host plasminogen. Mice expressing a human plasminogen transgene showed increased sensitivity and mortality to human GAS pathogens. In these mice, streptokinase activation of human-derived plasminogen facilitated blood clot dissolution and enhanced bacterial spread.

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