The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 1, 2012 VOL. 367 NO. 18

Topical 0.5% Ivermectin Lotion for Treatment of Head Lice

David M. Pariser, M.D., Terri Lynn Meinking, Ph.D., Margie Bell, M.S., and William G. Ryan, B.V.Sc.

ABSTRACT

BACKGROUND

The emergence of resistance to treatment complicates the public health problem of head-louse infestations and drives the need for continuing development of new treatments. There are limited data on the activity of ivermectin as a topical lousicide.

METHODS

In two multisite, randomized, double-blind studies, we compared a single application of 0.5% ivermectin lotion with vehicle control for the elimination of infestations without nit combing in patients 6 months of age or older. A tube of topical ivermectin or vehicle control was dispensed on day 1, to be applied to dry hair, left for 10 minutes, then rinsed with water. The primary end point was the percentage of index patients (youngest household member with ≥3 live lice) in the intention-to-treat population who were louse-free 1 day after treatment (day 2) and remained so through days 8 and 15.

RESULTS

A total of 765 patients completed the studies. In the intention-to-treat population, significantly more patients receiving ivermectin than patients receiving vehicle control were louse-free on day 2 (94.9% vs. 31.3%), day 8 (85.2% vs. 20.8%), and day 15 (73.8% vs. 17.6%) ($P<0.001$ for each comparison). The frequency and severity of adverse events were similar in the two groups.

CONCLUSIONS

A single, 10-minute, at-home application of ivermectin was more effective than vehicle control in eliminating head-louse infestations at 1, 7, and 14 days after treatment. (Funded by Topaz Pharmaceuticals [now Sanofi Pasteur]; ClinicalTrials.gov numbers, NCT01066585 and NCT01068158.)

From the Department of Dermatology, Eastern Virginia Medical School, Norfolk (D.M.P.); Global Health Association of Miami, Coral Gables, FL (T.L.M.); Clin-Data Services, Fort Collins, CO (M.B.); and Ryan Mitchell Associates, Westfield, NJ (W.G.R.). Address reprint requests to Dr. Ryan at 16 Stoneleigh Park, Westfield, NJ 07090-3306, or at wgryan@yahoo.com.

N Engl J Med 2012;367:1687-93.
DOI: 10.1056/NEJMoa1200107

Infestations of head lice (*Pediculus humanus capitis*) lead to social disruption by stigmatizing infested children and causing parental anxiety, loss of income because of the need to care for the child at home, and absenteeism from school or day care.[1,2] The first-line pediculosis treatments, permethrin and pyrethrins, belong to a chemical class to which there is now increasing resistance.[3] The established second-line treatments, lindane and malathion, have limitations related to safety and concerns about flammability and unpleasant odor.[4] Investigations of benzyl alcohol and spinosad, both recently approved by the Food and Drug Administration (FDA) for the treatment of head lice, indicate that up to two treatments with either agent are effective in eliminating infestations.[4,5] However, the short generation time of head lice and the exposure of all life-cycle stages to any applied treatment are predisposing factors to the emergence of resistance; therefore, new therapies are needed.[6]

Ivermectin is used extensively as an oral treatment for nematode infections.[7-9] There are also reports of its oral use to treat scabies and louse infestations when conventional treatments have failed.[8,10,11] The drug may have efficacy in these situations because it has a different target site on parasites than that of traditional insecticidal treatments; it acts primarily at glutamate-gated chloride ion channels and secondarily at γ-aminobutyric acid–gated chloride ion channels.[12] In one study, ivermectin was effective against permethrin-resistant head lice in vitro,[13] and an in vivo study showed that two oral doses (each 400 μg per kilogram of body weight) 1 week apart eliminated head lice that were at least partially refractory to malathion.[10] The development of ivermectin as a pediculosis treatment would expand options for delaying the emergence of resistance or for managing resistance when it has already developed.[10,13]

A topical ivermectin formulation could avoid systemic medication administration. Two reports suggested that a single topical application might have potential for treating infestations, but final assessments were inadequate to determine the degree of efficacy or the possibility of reinfestations from the hatching of louse eggs present at the time of application.[14,15] We report on two parallel trials investigating the efficacy and safety of a single application of a new 0.5% ivermectin lotion formulation (Sklice, Sanofi Pasteur) as compared with vehicle control, an identical formulation without ivermectin, in patients with head-louse infestation.

Methods

Study Design

The two studies were multicenter, randomized, double-blinded, vehicle-controlled, two-group parallel trials. The studies were funded by Topaz Pharmaceuticals (now Sanofi Pasteur). The protocols, which were identical for the two studies, were designed by means of an iterative process among the authors, with guidance from the FDA. The final protocols, available with the full text of this article at NEJM.org, were reviewed by an investigational review board, and the studies were conducted in compliance with the Declaration of Helsinki and current International Conference on Harmonization and Good Clinical Practice guidelines. The data were gathered by a contract research organization and analyzed by the third author. All the authors made the decision to submit the manuscript for publication, and all vouch for the completeness and accuracy of the data and analysis and for the fidelity of the studies to the protocols. Sanofi Pasteur provided funding for editorial support of the manuscript. All authors had full access to the data and provided substantial input to the manuscript, which was written primarily by the last author. Word Consulting Group provided copy editing support, assistance with charts, and verification of accuracy. No confidentiality arrangements limit the first and second authors from disclosing study data; the third and fourth authors were retained by the sponsor under consulting confidentiality agreements.

Written informed consent or assent for each patient was obtained after the nature of the study had been fully explained and before the performance of any study-related activity. Children of a specified age were administered an assent form that met Department of Health and Human Services regulations. The studies were conducted from March through July 2010 at eight separate sites per study: study A sites were in Arizona, California, Florida (two sites), Mississippi, Ohio, Tennessee, and Virginia, and study B sites were in Arkansas (two sites), Florida (two sites), New Mexico, North Carolina, Tennessee, and Texas.

STUDY PATIENTS

Eligible patients were healthy persons 6 months of age or older with head-louse infestation who agreed not to use any other louse treatment, comb out nits, or cut or chemically treat hair during the study. A list of all inclusion and exclusion criteria is provided in the Supplementary Appendix, available at NEJM.org. All household members were asked to undergo head-louse assessment at the enrollment visit. To ensure that enrollment was based on established infestations, the criterion for active infestation was the finding of three or more live lice on the scalp or hair. This criterion has been used in recent clinical pediculicide investigations[4,5,10,16] and is considered to be more reliable than the diagnostic standard of a single live head louse, which could represent a transient or waning infestation. The household index patient was the youngest member meeting our criterion for infestation. Once the index patient was identified, additional household members with one or more live lice on the scalp or hair were also enrolled in the study and were given the same study drug as the index patient. No household member was included unless he or she was found to be infested with at least one live louse.

ASSESSMENTS AND STUDY DRUGS

On day 1, index patients were randomly assigned to a study drug. Each enrolled patient received a single 4-oz tube containing either ivermectin or vehicle control, the same for all enrolled members in any household, to be applied at home on day 1 by the patient or a caregiver. Patients received written instructions to thoroughly coat dry hair and scalp with the lotion and leave it on for 10 minutes before rinsing the hair with water. Written instructions regarding environmental hygiene measures to reduce the risk of reinfestation were also supplied. The final visit was to occur on day 15 (14 days after use of the study drug) or up to 2 days later. If any live lice were present at this visit, the study treatment was considered to have failed and the patient received rescue treatment with either a commercially available formulation of 1% permethrin or professional lice and nit combing undertaken at the study site. (For full details, see the study protocols.)

Adverse events were assessed at each site by the attending physician, who graded the severity of each event as mild, moderate, severe, or serious (life-threatening or requiring hospitalization) and gauged the likelihood that it was related to the study drug. Assessments of skin or scalp irritation, including pruritus, erythema, excoriation, and pyoderma, were made on days 1 (baseline), 2, 8, and 15; if present, irritation was scored as 1 (mild), 2 (moderate), or 3 (severe). The presence or absence of ocular irritation was assessed on days 1 and 2. A trained evaluator at each study site assessed efficacy (presence or absence of live lice) and safety on days 2, 8, and 15. Louse examination was conducted for 15 minutes or longer, unless any live lice were detected in less time. Whenever possible, the same evaluator performed each patient's examination at each visit. All evaluators were trained before the study in the technique for lice assessment (which included combing and detecting head lice in infested patients).

END POINTS

The primary efficacy end point was the number of index patients who were louse-free by day 2 and remained louse-free through days 8 and 15. The primary analysis examined the percentage of index patients (intention-to-treat population) who met this end point. The secondary efficacy analysis was the same assessment applied to the index patients plus all enrolled household members (extended intention-to-treat population). Safety was assessed on the basis of reported adverse events and evaluations for skin, scalp, and ocular irritation in all patients.

STATISTICAL ANALYSIS

The target sample in each study (132 index patients, with 66 in each study group) was planned to provide more than 90% power (at a two-sided alpha level of 0.05) to detect a difference of 45 percentage points between ivermectin and vehicle control in the proportion of patients with louse-free status on days 2, 8, and 15. This sample was also sufficient to achieve a lower limit of the 95% confidence interval of more than 30 percentage points, with an anticipated treatment effect of 45 percentage points.

For the primary end-point comparison, the Cochran–Mantel–Haenszel test with adjustment for study site was used, with use of the last-observation-carried-forward method of imputation for missing data; treatment-failure imputation for missing data was used as a sensitivity analysis. The chi-square test was also applied to the primary and secondary end points, and 95% con-

Table 1. Demographic and Clinical Characteristics of the Patients in the Intention-to-Treat Population, Study A and Study B Combined.*

Characteristic	Ivermectin (N=141)	Vehicle Control (N=148)	P Value†
Sex — no. (%)			0.26
Female	117 (83.0)	115 (77.7)	
Male	24 (17.0)	33 (22.3)	
Age			0.41
Mean — yr	7.8±6.5	8.5±8.2	
Median — yr	6.0	7.0	
Range — yr	0.8–46.0	1.0–51.0	
6 mo to 2 yr — no. (%)	18 (12.8)	19 (12.8)	
>2 yr to <4 yr — no. (%)	16 (11.3)	9 (6.1)	
4 yr to <12 yr — no. (%)	80 (56.7)	99 (66.9)	
12 yr to 16 yr — no. (%)	17 (12.1)	15 (10.1)	
>16 yr — no. (%)	10 (7.1)	6 (4.1)	
Hispanic or Latino ethnic group — no. (%)‡	57 (40.4)	57 (38.5)	0.74
White race — no. (%)‡	135 (95.7)	142 (95.9)	
Weight — kg			0.95
Mean	31.8±20.4	31.6±19.2	
Range	8.2–120.5	10.0–110.4	

* Plus–minus values are means ±SD.
† The P values for categorical variables were derived with the use of the chi-square test; P values for continuous variables were derived by means of analysis of variance with study treatment as a factor.
‡ Race and ethnic group were self-reported.

fidence intervals for the difference between the success rates in the study groups were calculated.

Logistic-regression modeling was used to assess possible study-site effects and interactions between study drug and study site. The model used success versus failure as the dependent variable; fixed terms for treatment, study site, and treatment-by-study-site interaction were the independent variables. The model was reduced in a stepwise manner until only statistically significant ($P \leq 0.05$) terms or treatment remained.

Safety results, including adverse events and data on skin, scalp, and ocular irritation, were described for all patients and summarized according to study group. Individual changes from day 1 to each subsequent visit were calculated. Descriptive statistics (i.e., number of patients, mean, standard deviation, median, and minimum and maximum values) were presented according to study-drug group. Differences between groups were assessed by means of an analysis of variance with study treatment as a factor.

RESULTS

ENROLLMENT AND FOLLOW-UP

Enrollments for the intention-to-treat populations were 145 patients in study A (extended intention-to-treat population, 410 patients) and 144 in study B (extended intention-to-treat population, 371 patients). Of the 781 patients in the extended intention-to-treat population, 780 were included in the safety population — 1 patient assigned to ivermectin was excluded from the safety population owing to a protocol violation (she did not use the study drug). Another 15 patients did not complete all scheduled visits: 7 in the ivermectin group (4 from one household) were lost to follow-up; 6 (1 in the ivermectin group and 5 in the vehicle-control group) withdrew consent; and 2 — a child and caregiver, both in the vehicle-control group — did not return for the day 2 visit because the child was vomiting (reported as an adverse event). Of the patients in the intention-to-treat population who were lost to follow-up, 3 patients in the ivermectin group and 1 in the vehicle-control group did not return after their initial visit; in all 4 patients, the study treatment was considered to have failed. In both studies, the demographic characteristics of the extended intention-to-treat population were similar to those of the intention-to-treat population (Table 1), and there were no significant baseline differences between groups. In the intention-to-treat populations, viable nits were observed at baseline in all patients in study A and in more than 97% of patients in study B.

EFFICACY

In the intention-to-treat population in each study and in the two studies combined, significantly more patients in the ivermectin group than in the vehicle-control group were free of live lice at the first post-application observation on day 2 (1 day after use of the study drug) and at the subsequent observations through day 15 ($P<0.001$ for each comparison) (Fig. 1). There were no significant treatment-by-study-site interactions. The combined intention-to-treat analysis showed that significantly more patients in the ivermectin group than in the vehicle-control group were louse-free on day 2 (131 of 138 [94.9%] vs. 46 of 147 [31.3%]) and day 8 (115 of 135 [85.2%] vs. 30 of 144 [20.8%]) and remained louse-free through day 15 (104 of 141 [73.8%] vs. 26 of 148 [17.6%]) ($P<0.001$ for each day). In both studies, the results were con-

sistent when treatment-failure imputation was used for missing data and when data in the extended intention-to-treat populations were analyzed (Fig. 2) (P<0.001 for all comparisons), with no treatment-by-study-site interactions.

SAFETY

Pruritus, excoriation, and erythema were the most common adverse events, occurring at a rate of more than 1% in the vehicle-control group and less than 1% in the ivermectin group (Table 2). There was one severe adverse event (pain in an extremity with vehicle control) and no serious adverse events. All other adverse events were mild to moderate. The frequency and severity of adverse events were similar in the two study groups and across age groups (a full listing of adverse events is available in the Supplementary Appendix). No events were considered to be definitely related to the study drug. Two were considered to be probably related to the study drug (eye irritation and skin-burning sensation). Ocular irritation was noted in 7 patients (2 of 379 patients in the ivermectin group [0.5%] and 5 of 401 in the vehicle-control group [1.2%]) on day 2; 4 of the 7 patients also had ocular irritation at baseline. All adverse events in patients 6 months to 4 years of age were considered to be unrelated to the study drug, with no age-related trends.

Pruritus was a baseline finding in 533 of 781 patients (68.2%) in the extended intention-to-treat population. In both studies combined, the ivermectin group had a significantly greater mean reduction in the pruritus score from baseline to day 2 (P<0.001) (Fig. 3). In the combined intention-to-treat populations, on day 1, 77.3% of the patients in the ivermectin group and 76.4% of those in the vehicle-control group had pruritus. On day 2, pruritus was reduced in both groups, with significantly more patients in the ivermectin group than in the vehicle-control group free of pruritus (66.7% and 42.6%, respectively; P<0.001). The ratings of skin or scalp irritation in both studies were similar across age groups, with no age-related trends observed.

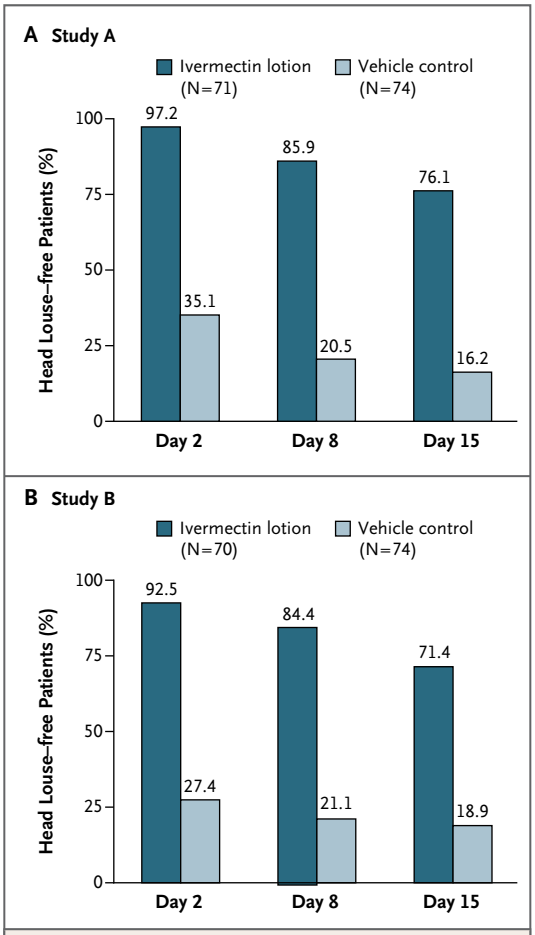

Figure 1. Percentage of Head Louse–free Patients in the Intention-to-Treat Population in Study A and Study B.

Study drugs were applied on day 1. In study A (Panel A), the between-group difference in the proportion of patients who were louse-free on day 15 was 59.8 percentage points (95% confidence interval [CI], 45.5 to 74.2). In study B (Panel B), the between-group difference on day 15 was 52.5 percentage points (95% CI, 37.3 to 67.7). P<0.001 for the between-group difference at each time point in each study.

DISCUSSION

The most frequent sign of pediculosis is pruritus; other common manifestations include excoriations, cervical adenopathy, and conjunctivitis.[17,18] Beyond physical manifestations, there are negative social effects and potential economic effects on households. We found that 94.9% of ivermectin-treated patients were louse-free 1 day after application, a finding that parallels the report of 92.4% efficacy 1 day after administration of oral ivermectin (at a dose of 400 μg per kilogram).[10] In that study, 82.4% of malathion-treated patients were free of lice the day after application.

Pruritus in pediculosis is attributed to sensitization to louse saliva injected at the time of feeding.[17,18] In our study, the significant reduction in pruritus between day 1 and day 2 in the ivermectin

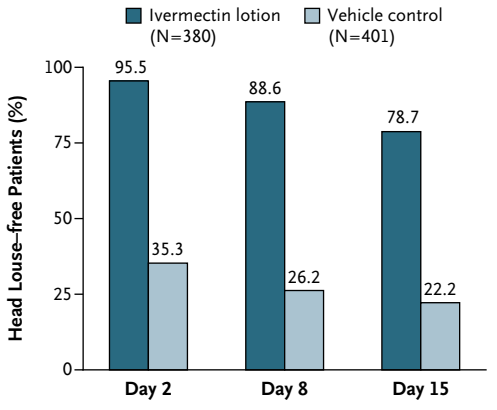

Figure 2. Percentage of Head Louse–free Patients in the Extended Intention-to-Treat Population, Study A and Study B Combined.

The extended intention-to-treat population comprised the intention-to-treat population plus all enrolled household members. Study drugs were applied on day 1. The between-group difference on day 15 was 56.2 percentage points (95% CI, 50.1 to 62.2). P<0.001 for the between-group difference at all three time points.

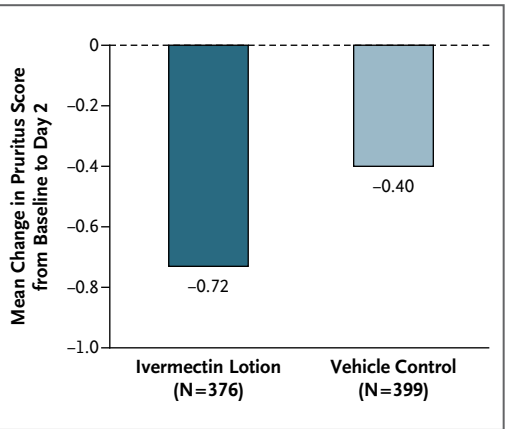

Figure 3. Mean Change in Pruritus Score from Baseline to Day 2 in the Extended Intention-to-Treat Population, Study A and Study B Combined.

A score of 0 indicates no pruritus, 1 mild pruritus, 2 moderate pruritus, and 3 severe pruritus. The mean (±SD) score at baseline was 1.30±0.92 in the ivermectin group and 1.22±0.88 in the vehicle-control group. P values were derived by means of analysis of variance with study treatment as a factor, with values ranked before analysis of variance.

Table 2. Adverse Events with an Incidence of More Than 1% in Either Group (Safety Population of Combined Studies).

Event	Ivermectin (N=379)	Vehicle Control (N=401)
	number of patients (percent)	
Pruritus	3 (0.8)	6 (1.5)
Excoriation	1 (0.3)	5 (1.2)
Erythema	2 (0.5)	5 (1.2)

group, as compared with the vehicle-control group, may have been due to the antipruritic effect of louse eradication. However, the rapid response in both groups with regard to the severity of pruritus and the number of patients having an absence of pruritus was unexpected, particularly in patients receiving the vehicle control. This finding may reflect an emollient effect of the formulation, which warrants further investigation.

The proportion of head louse–free patients in the ivermectin group was 85.2% on day 8 and 73.8% on day 15. These outcomes are similar to those achieved 2 weeks after the second of two applications of benzyl alcohol lotion or after one or two applications of spinosad suspension.[4,5] The increasing proportion of louse-infested patients with increasing time from the point of application is consistent with other assessments of pediculicide activity and may be attributed to a number of factors.[4,5] These include improper product application; inadequate exposure of ivermectin to louse eggs, which subsequently hatch and produce viable nymphs; and reinfestations as patients continue to be exposed to head lice within or outside their households.

The continued efficacy of treatment with topical ivermectin through the final assessment 2 weeks after a single treatment suggests that this formulation has activity against louse eggs, although systemic ivermectin appears to have no such activity. The activity of topical treatment is probably due to the direct exposure of eggs to ivermectin that occurs with topical application. A recent report described laboratory studies in which ivermectin was applied to head louse ova; although the ova subsequently hatched, all the released nymphs quickly died. The nymphal mortality was attributed to ivermectin-induced mouthpart paralysis, which severely limited or completely prevented feeding.[19]

Ivermectin primarily targets glutamate-gated

chloride ion channels, whereas the easily available permethrin and pyrethrins act by binding to voltage-gated sodium channels. Widespread resistance to permethrin has been reported, and even with adjunctive nit combing, it has failed to achieve an efficacy of 50%.[5,16] In contrast, ivermectin has been shown under laboratory conditions to be active against permethrin-resistant head lice.[13] The results of the two studies reported here indicate that ivermectin is a treatment option when permethrin or pyrethrins have failed or when there is a desire to reduce the need for nit combing and increase the probability of success with a single application.

In our two studies, the minimum age of the patients was 0.8 years and 1.0 years, and the minimum weight was 8 kg and 10 kg, respectively. We identified no safety or adverse event concerns, and there were no age-related trends in ratings of skin or scalp irritation, findings that are consistent with the results of an earlier study in which ivermectin was applied to 30 children with head-louse infestation who were 6 months to 3 years of age.[20]

In conclusion, ivermectin has a well-established safety profile, on the basis of extensive oral use, and a novel mode of action. Topical ivermectin showed high efficacy within 24 hours, with most treated patients remaining louse-free through the final assessment 2 weeks after a single treatment, without the need for nit combing.

Supported by Topaz Pharmaceuticals, which provided the study medications.

Ms. Bell reports receiving consulting fees from Topaz Pharmaceuticals and Sanofi Pasteur. Dr. Ryan reports being a former employee of Topaz Pharmaceuticals, receiving consulting fees and stock or stock options from Topaz Pharmaceuticals, and receiving consulting fees and payment for manuscript preparation from Sanofi Pasteur. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

REFERENCES

1. Frankowski BL, Weiner LB. Head lice. Pediatrics 2002;110:638-43.
2. Gordon SC. Shared vulnerability: a theory of caring for children with persistent head lice. J Sch Nurs 2007;23:283-92.
3. Yoon KS, Gao JR, Lee SH, Clark JM, Brown L, Taplin D. Permethrin-resistant human head lice, Pediculus capitis, and their treatment. Arch Dermatol 2003;139:994-1000.
4. Meinking TL, Villar ME, Vicaria M, et al. The clinical trials supporting benzyl alcohol lotion 5% (Ulesfia): a safe and effective topical treatment for head lice (Pediculosis humanus capitis). Pediatr Dermatol 2010;27:19-24.
5. Stough D, Shellabarger S, Quiring J, Gabrielsen AA Jr. Efficacy and safety of spinosad and permethrin crème rinses for Pediculosis capitis (head lice). Pediatrics 2009;124(3):e389-e395.
6. Yoon KS, Strycharz JP, Baek JH, et al. Brief exposures of human body lice to sublethal amounts of ivermectin over-transcribes detoxification genes involved in tolerance. Insect Mol Biol 2011;20:687-99.
7. Colatrella B. The Mectizan Donation Program: 20 years of successful collaboration — a retrospective. Ann Trop Med Parasitol 2008;102:Suppl 1:7-11.
8. Meinking TL, Taplin D, Hermida JL, Pardo R, Kerdel FA. The treatment of scabies with ivermectin. N Engl J Med 1995;333:26-30.
9. Moreno Y, Nabhan JF, Solomon J, Mackenzie CD, Geary TG. Ivermectin disrupts the function of the excretory-secretory apparatus in microfilariae of Brugia malayi. Proc Natl Acad Sci U S A 2010;107:20120-5.
10. Chosidow O, Giraudeau B, Cottrell J, et al. Oral ivermectin versus malathion lotion for difficult-to-treat head lice. N Engl J Med 2010;362:896-905. [Erratum, N Engl J Med 2010;362:1647.]
11. Foucault C, Ranque S, Badiaga S, Rovery C, Raoult D, Brouqui P. Oral ivermectin in the treatment of body lice. J Infect Dis 2006;193:474-6.
12. Cully DF, Paress PS, Liu KK, Schaeffer JM, Arena JP. Identification of a Drosophila melanogaster glutamate-gated chloride channel sensitive to the antiparasitic agent avermectin. J Biol Chem 1996;271:20187-91.
13. Strycharz JP, Yoon KS, Clark JM. A new ivermectin formulation topically kills permethrin-resistant human head lice (Anoplura: Pediculidae). J Med Entomol 2008;45:75-81.
14. Halpert OE. Comparative study of ivermectin and gamma benzene hexachloride in shampoo for the treatment of pediculosis capitis. Presented at the 8th International Congress of Pediatric Dermatology, Paris, May 17–20, 1998. abstract.
15. Youssef MY, Sadaka HA, Eissa MM, El-Ariny AF. Topical application of ivermectin for human ectoparasites. Am J Trop Med Hyg 1995;53:652-3.
16. Meinking TL, Vicaria M, Eyerdam DH, Villar ME, Reyna S, Suarez G. A randomized, investigator-blinded study of the comparative efficacy of 0.5% malathion gel versus Ovide Lotion (0.5% malathion) or Nix Crème Rinse (1% permethrin) used as labeled for the treatment of head lice. Ped Dermatol 2007;24:405-11.
17. Ko CJ, Elston DM. Pediculosis. J Am Acad Dermatol 2004;50:1-12.
18. Meinking T, Taplin D, Vicaria M. Infestations. In: Schachner LA, Hansen RC, eds. Pediatric dermatology. 4th ed. St. Louis: Mosby Elsevier, 2011:1535-83.
19. Strycharz JP, Berge NM, Alves A, Clark JM. Ivermectin acts as a posteclosion nymphicide by reducing blood feeding of human head lice (Anoplura: Pediculidae) that hatched from treated eggs. J Med Entomol 2011;48:1174-82.
20. Hazan L, Corrado M. Pharmacokinetics, safety and effectiveness of a 0.5% ivermectin lotion cream in head lice infested children. Presented at the 36th annual meeting of the Society for Pediatric Dermatology, Portland, OR, July 15, 2010. abstract.