REFERENCES

1. Sloan JB, Soltani K. Iontophoresis in dermatology. J Am Acad Dermatol 1986; 15: 671–684.
2. Hölzle E, Pauli M, Braun-Falco O. Leitungswasser-Iontophorese zur Behandlung von Hyperhidrosis manuum et pedum. Hautarzt 1984; 35: 142–147.
3. Boumann HD, Lentzer EMG. The treatment of hyperhidrosis of hands and feet with constant current. Am J Phys Med 1952; 31: 158–169.
4. Hölzle E, Alberti N. Long-term efficacy and side effects of tap water iontophoresis of palmoplantar hyperhidrosis—the usefulness of home therapy. Dermatologica 1987; 175: 126–135.
5. Stolman LP. Treatment of excess sweating of the palms by iontophoresis. Arch Dermatol 1987; 123: 893–896.
6. Zankel HT. Effect of physical modalities upon Ra I^{131} iontophoresis. Arch Phys Med Rehabil 1963; 44: 93–97.
7. Levit F. Treatment of hyperhidrosis by tap water iontophoresis. Cutis 1980; 26: 192–194.
8. Shrivastava SN, Singh G. Tap water iontophoresis in palmo-plantar hyperhidrosis. Br J Dermatol 1977; 96: 189–195.
9. Quatrale RP, Stoner KL, Felger CB. A method for the study of emotional sweating. J Soc Cosmet Chem 1977; 28: 91–101.
10. Rahe AJ. Tables of critical values for the Pratt matched pair signed rank statistic. J Am Stat Assoc 1974; 69: 368–373.
11. Zlotogorski A, Shafran A. Iontophoresis in dermatology. J Am Acad Dermatol 1987; 17: 690.
12. Dahl JC. Iontoforesebehandling af emotional hyperhidrose. Månedsskrift for praktisk lægegerning (in press).
13. Akins DL, Meisenheimer JL, Dobson RL. Efficacy of the Drionic unit in the treatment of hyperhidrosis. J Am Acad Dermatol 1987; 16: 828–832.
14. Hölzle E, Ruzicka T. Treatment of hyperhidrosis by a battery-operated iontophoretic device. Dermatologica 1986; 172: 41–47.
15. Jensen O, Karlsmark T. Palmoplantar hyperhidrosis. Treatment with alcoholic solution of aluminium chloride hexahydrate: a simple method of transpiration measurement. Dermatologica 1980; 161: 133–135.

Treatment of Scabies with Permethrin Versus Lindane and Benzyl Benzoate

UWE-FRITHJOF HAUSTEIN and BARBARA HLAWA

Department of Dermatology, School of Medicine, Karl Marx University, Leipzig, GDR

This open clinical study was designed to evaluate and compare the efficacy and side effects of lindane (1% and 0.3%), benzyl benzoate (20% and 10%) and permethrin (5% and 2.5%) after two, three, and one application at bedtime, in the treatment of scabies in 114 adults and 80 children aged between 0 and 5 years. Treatment failures were registered after lindane in 3 adults and 2 children, whereas benzyl benzoate and permethrin cured all patients as assessed after a 3-week follow-up. The number of irritations and post-scabious eczematous reactions was increased after benzyl benzoate treatment. Permethrin proved to be very reliable and exhibited few side effects when applied once at bedtime. Because of the percutaneous absorption and neurotoxicity of lindane, the application of permethrin can be recommended as a useful alternative in premature infants and small children, patients with seizures and neurological complications, in cases of therapeutic failure with lindane the treatment needs to be repeated, in scabies crustosa, as well as in children, pregnant women and nursing mothers.

(Accepted January 31, 1989.)

Acta Derm Venereol (Stockh) 1989; 69: 348–351.

U.-F. Haustein, Department of Dermatology, School of Medicine, Karl Marx University, Liebigstr. 21, Leipzig, GDR-7010.

For 30 to 40 years the insectizide lindane (γ-hexachlorcyclohexane) has been known to be effective and reliable in the treatment of scabies (1), even in children, pregnant women and nursing mothers (2). It is neither a mutagen nor a teratogen. Lindane has a LD_{50} of 90 mg/kg in mice and exerts neurotoxic effects, especially upon the central nervous system, due to its lipophilic properties (3). In recent years, side-effects of lindane such as irritability, nervousness, apprehension, insomnia, seizures, apathy, coma, respiratory arrest and death (4) were reported repeatedly in isolated cases of small children (5, 6) and patients with neurological disorders. In most cases this was attributed to abuse, overuse or treatment failure, or even to accidental ingestion. On the other hand small amounts of epicutaneously applied lindane (in particular on wet, inflamed or excoriated skin in small

children) are known to be absorbed percutaneously, lead to an increased blood concentration with the peak after 6 h, and are excreted in the urine (4, 7, 8).

Usually, adults were treated with lindane on the dry skin at bedtime on 2 consecutive days. In small children we have modified our regular treatment schedule. Lindane (HCH ointment) is applied only once and its concentration has been reduced from 1% to 0.3%, or else the upper and lower parts of the body surface are treated alternately on 2 consecutive days (split application).

The purpose of this study was to look for alternatives to lindane therapy and to test them in an open clinical trial. Less effective scabicides such as crotamiton (10%) and precipitated sulfur (6%) are not discussed here. Benzyl benzoate, an ingredient of balsam of Peru, also exerts a scabicide effect (9) and has been recommended in various countries, partly in combination with disulfiram (10). It is a thick, sticky liquid with strong odour and it stings and burns on the excoriated skin and should be applied on 3 consecutive nights (11). In addition, it has certain antibacterial, fungicidal and local anaesthetic effects.

Permethrin (3-phenoxybenzyl(±)-*cis-trans*-3(2.2-dichlorvinyl)-2.2-dimethyl-cyclopropane-carboxylate) occurs as a natural ingredient in various kinds of chrysanthemum and has been synthesized (12). This thermostable and photostable highly effective insecticide is inherently less toxic (LD_{50} 3000 mg/kg in mice) than lindane, by a factor of approximately 36 (13) and is practically not absorbed through the skin (<2%). It is metabolized rapidly by esterases of the skin and excreted very quickly via the urine. It has no odour and does not stain clothes. It is acceptable from the cosmetic point of view and reliable in its scabicidic activity, even after a single application in the *cis–trans* ratio 25:75 (12, 13).

In the following, we report on our results in the treatment of 194 scabies patients with lindane, benzyl benzoate and permethrin in a comparative study.

MATERIAL AND METHODS

Adults and children up to the age of 5 years were allocated to different groups ($n = 21$ to 40). Children were always treated with lower concentrations. Lindane and benzyl benzoate were applied over the whole body surface at bed-time for 2 and 3 consecutive nights, respect.; but permethrin only once.

The formulations were as follows:

Lindane (HCH ointment, L/W emulsion): Lindane, 1.0; Parabens, 0.2; Ung. emulsificans aquosum ad, 100.0; (for children, 0.3%).

Benzyl benzoate: Benzyl benzoate, 20.0; Sorbimacrogol ol. 80, 2.0; Aqua ad, 100.0; (for children 10%).

Permethrin (L/W emulsion): Permethrin, 5.0; Linimentum aquosum ad, 100.0; (for children 2.5%).

Permethrin was purchased from Welcome, England, in a mixture of 25% *cis*- to 75% *trans*-isomers.

In the majority of cases (85%) the diagnosis had been confirmed microscopically by the detection of mites. The treatment was performed by trained staff, mainly in in-patients (97 adults, 75 children). Out-patients (17 adults, 5 children) were only included in cases of good compliance and after an intensive education. We performed head-to-toe treatment, on the dry skin, paying particular attention to crevices, including the post-auricular folds, intergluteal cleft, and toe webs, and of course the axillar, mamillar, genital as well as peri- and subungual areas. The perioral and periorbital regions were omitted and the sucking of fingers was discouraged. All family members were also included. Therapy was stopped consequently after 2, 3 and 1 day(s), respect., at which time the patients bathed with soap and water. The post-scabious pruritus was treated with steroid-, tar- and/or hydroxychinoline sulfate-containing creams and antihistamines. Patients with significant impetiginization were excluded from this study. The clinical examination of patients was performed after the completion of the treatment as well as after 1 and 3 weeks to assess the tolerance and the efficacy of the drugs. All bed linen, pyjamas, underclothing, and towels were washed in a hot cycle; non-washables were dry cleaned or just not worn for up to 1 week, because the mite cannot survive away the host for longer than 4 days. The statistical evaluation was performed by χ^2-test.

RESULTS

194 patients in the age range 0–72 years were involved, 114 adults and 80 children up to the age of 5 years. Their average age was 26, 24 and 21 years in the various adult groups, and 1.7, 1.7 and 1.6 years in children. The sex ratio was 81 males to 113 females (42%:58%). The extent of skin involvement was mild (<50 lesion such as burrows, papules, vesicles, scales) and moderate (50–100 lesions) in about 20% each and severe (>100 lesions) in about 60%. The data indicate that groups were mutually comparable.

As shown in Table I, there were some treatment failures, due to lindane in 5 cases proved by mites (3 adults and 2 children, not after split application) equal to 8% ($p<0.05$), while all other patients could be assessed as cured after 3 weeks, e.g. there were no treatment failures due to benzyl benzoate and permethrin. There was a remarkably high proportion (33%) of post-scabious eczematous reactions, especially after the application of 20% benzyl benzoate ($p<0.05$). Concerning side-effects, burning and redness as well as exsiccation had to be registered after

Table I. *Results of treatment (patients with impetiginization were excluded)*

Treatment	Total of patients *n*	Day 8 Postscab. eczema *n*	Day 22 Cured *n*	Side-effects Burning *n*	Redness *n*	Others *n*
Lindane 1%	40	12	*37*	1	3	–
Lindane 0.5%	21	6	*19*	–	2	–
Benzyl benzoate 20%	31	*16*	31	3	3	–
Benzyl benzoate 10%	31	10	31	*6*	*6*	2[a]
Permethrin 5%	43	10	43	1	(1)	1[b]
Permethrin 2.5%	28	7	28	–	1	–

[a] Exsiccation.
[b] Follicular irritation.

benzyl benzoate in 14 patients (22% of the cases), which occurred more rarely after application of lindane and permethrin ($p<0.05$).

DISCUSSION

This study has shown that the three scabicides studied gave good therapeutic results, i.e. cure rates of 92% (lindane) and 100% (benzyl benzoate and permethrin), probably due to the careful selection of patients and their treatment in the hospital in most cases. Lindane has hitherto been the preferred drug. During the last 28 years we have seen insomnia, irritability and nervousness in 2 infants (not included in this study). These features might be interpreted as signs of CNS toxicity and call for caution in the application of lindane in small infants. The 5 treatment failures with lindane are also remarkable, recalling the possibility of resistance of occasional mite strains (14), at least.

Benzyl benzoate proved to be effective and reliable (9, 11), though it is less recommendable because of its strong odour and the irritation induced. By the way, Sampaio (15) could cure only 57% of his patients with benzyl benzoate, probably due to resistance of mites and failures in the self-applications by the patients.

On the other hand, permethrin exerted a reliable effect even after single application. It has the lowest toxicity and is applicable as an emulsion in a cosmetically elegant and acceptable way. Therefore we recommend the gradual introduction of permethrin as a scabicide into clinical practice. Because of its highly pediculicidal and ovicidal action, it has already been applied successfully in the treatment of pediculosis capitis (12)—also in our country.

The weaker concentration of scabicides in the group of children is based on the differences in their penetration through the thinner horny layer in younger children as compared to the adults in order to avoid side-effects by percutaneous absorption (7).

As an absolute indication for permethrin, we see premature infants and small children, patients with seizures and neurological complications, treatment failures with lindane (if repeated treatment is necessary) and resistance of mite strains to lindane, as well as scabies crustosa. As relative indications, children, pregnant women and nursing mothers should be included. In the future, the daily practice will show whether the well tolerated, highly effective and cosmetically acceptable permethrin will be an acceptable replacement for lindane completely.

REFERENCES

1. Cannon AB, McCreae ME. Treatment of scabies; report of one hundred patients treated with hexachlorocyclohexane in vanishing creme basis. J Am Med Acad 1948; 138: 557.
2. Rasmussen JE. Lindane. A prudent approach. Arch Dermatol 1987; 123: 1 008–1 010.
3. Solomon LM, Fahrner L, West DP. Gamma benzene hexachloride toxicity. Arch Dermatol 1977; 113: 353–357.
4. Feldman RJ, Maibach HI. Percutaneous penetration of some pesticides and herbicides in man. Toxicol Appl Pharmacol 1974; 28: 126–132.
5. Ginsburg CM, Lowry W, Reisch JS. Absorption of lindane (γ-benzene hexachloride) in infants and children. J Pediatr 1977; 91: 998–1 000.
6. Pramanik AK, Hansen RC. Transcutaneous gamma benzene hexachloride absorption and toxicity in infants and children. Arch Dermatol 1979; 115:1 224–1 225.

7. Lange M. Aspekte zur Sicherheit lokaler Lindan-Anwendung. Orientierende Daten zur perkutanen Resorption bei unterschiedlicher Hautbeschaffenheit und nach verschiedenartigen Abwaschmodalitäten. Inaugural-Diss. Berlin (West) 1986.
8. Zesch A, Nitzsche K, Lange M. Demonstration of the percutaneous resorption of a lipophilic pesticide and its possible storage in the human body. Arch Dermatol Res 1982; 273: 43–49.
9. Levkov AA. On experimental substantion of scabies and pediculosis treatment with benzyl benzoate. Vestn Dermatol Venerol 1980; 12: 28–31.
10. Landegren J, Borglund E, Storgards K. Treatment of scabies with disulfiram and benzyl benzoate emulsion: a controlled study. Acta Derm Venereol (Stockh) 1979; 59: 274–276.
11. Pönitzsch I, Haustein UF. Zur Benzylbenzoattherapie der Skabies. Dermatol Monatsschr 1981; 167: 722.
12. Taplin D, Meinking TL, Castillero PM, Sanchez R. Permethrin 1% creme rinse for the treatment of *Pediculus humanus* var capitis infestation. Pediatr Dermatol 1986; 3: 344–348.
13. Taplin D, Meinking TL, Percelain SL, Castillero PM, Chen JA. Permethrin 5% dermal creme: a new treatment for scabies. J Am Acad Dermatol 1986; 15: 995–1001.
14. Hernandez-Preez E. Resistance to antiscabietic drugs. J Am Acad Dermatol 1983; 8: 121–122.
15. Sampaio NV. Estudo comparativo entre o monosulfiram e o benzoata de benzilla no tratamento da escabiose. Ann Brasil Dermatol 1984; 59: 213–214.

Short-contact Therapy for Psoriasis with 3.9% Butantrone (10-Butyryl Dithranol)

ANITA REMITZ

Department of Dermatology, Helsinki University Central Hospital, Helsinki, Finland

Previous studies have shown that when butantrone and dithranol were used in equimolar gradually increasing concentrations in short-contact therapy for psoriasis the efficacy of butantrone was somewhat lower compared to dithranol. To see whether the efficacy of butantrone in short-contact therapy could be increased by starting with a single high-concentration directly, 20 psoriatic patients were treated with dithranol (0.1,–0.5,–1.0,–2.0%) and butantrone (3.9%) short-contact therapy as a right-left comparison. With these treatment modalities the antipsoriatic effects of dithranol and butantrone were similar. Although the efficacy of 3.9% butantrone was better than the previously used butantrone therapy with gradually increasing doses, there was a parallel increase in side-effects. In general, the side-effects (erythema and staining) remained weaker on the butantrone-treated side than on the dithranol-treated side. No systemic adverse-effects were observed in any of the treated patients. *Key word: Anthralin.*

(Accepted January 19, 1989)

Acta Derm Venereol (Stockh) 1989; 69: 351–354.

A. Remitz (Göransson), Department of Dermatology, Helsinki University Central Hospital, Snellmanninkatu 14, SF-00170 Helsinki, Finland.

The introduction of dithranol (anthralin) short-contact therapy for psoriasis (1) has made it also possible to use dithranol in the treatment of out-patients, and even home-patients. The major problems with dithranol therapy, even when short-contact therapy has been used, have been irritation of the surrounding healthy-looking skin, and to a lesser extent the staining of skin, clothes, bathtubs and shower basins. Mustakallio tried to reduce the side-effects by designing derivatives of dithranol with similar antipsoriatic properties as dithranol but which produced less irritation and staining. In experimental studies 10-butyryl dithranol (butantrone) seemed to meet these criteria best (2, 3).

When butantrone (0.66, 1.3, 2.0 and 3.9%) was used in the treatment of psoriasis patients as a right-left comparison with dithranol (0.1–0.5, 1.0 and 2.0%) in short-contact therapy for 30 min, butantrone was almost as effective as dithranol in the treatment of psoriasis but less irritation was observed (4). The present study was designed to see if 3.9% butantrone could be used directly in short-contact therapy without increasing the side-effects. The effect of 3.9% butantrone was compared with regular dithranol treatment in short-contact therapy.