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S. MASCI, M. BRUNO, P. FALAGIANI, L. FINIZIO, G. RIVA, D. SIMONETTO

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Efficacy and safety of bis-butyl-carboethylene in the treatment of scabies

S. MASCI [1], M. BRUNO [2], P. FALAGIANI [2], L. FINIZIO [3], G. RIVA [2], D. SIMONETTO [3]

Aim. **Scabies is a skin infestation caused by the mite *Sarcoptes scabiei*. Aim of this study was to investigate the efficacy and safety of a new treatment schedule of a skin lotion for scabies containing bis-butyl-carboethylene.**

Methods. **Eighty-seven patients (42 males and 45 female, with an age ranging from 5 to 76 years; mean age: 36 years) with scabies were evaluated. Treatment lasted 3 days (cycle 1, mandatory) plus, if necessary, other 2 days (cycle 2, optional). For the evaluation of efficacy, disappearance of skin lesions and symptoms like "itch", "nocturnal wake-ups" and "nocturnal itch" was considered.**

Results. **Fourteen patients (16.1%), with a complete remission of the lesions and symptoms at the end of the 1st cycle, were no more treated. The other 73 patients (83.9%) received the 2nd cycle. Disappearance of skin lesions was documented in 70/73 patients (95.9%). On the whole, in 84/87 patients (96.5%), a complete remission of skin lesions was observed at the end of the 1st and/or 2nd cycle. In 85/87 patients (97.7%) improvement of the variable "itch" was observed; 47/61 patients (77%) reported improvement of "nocturnal itch" at the end of cycle 1 and 50/53 (94.3%) at the end of cycle 2. The number of "nocturnal wake-ups" decreased in 59/61 patients (96.7%). Seven patients (8%) reported mild adverse reactions localized in the skin areas where the product was applied.**

Conclusions. **This new therapeutical regimen with bis-butyl-carboethylene resulted effective and safe in the treatment of patients with scabies.**

KEY WORDS: Scabies, drug therapy - Bis-butyl-carboethylene - Scabies, diagnosis.

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Address reprint requests to: Dr. M. Bruno, Divisione Scientifica, Lofarma SpA, Viale Cassala 40, 20143 Milano. E-mail: lofscie@lofarma.it

[1]Department of Dermatology
University of Chieti
"SS. Annunziata Hospital", Chieti
[2]Scientific Division
Lofarma SpA, Milan
[3]Dermatology Unit
"Cà Foncello" Hospital
USSL 9, Treviso

Scabies is an infestation of the skin caused by a mite denominated "*Sarcoptes scabiei*, var. *hominis*", which lives in the horny layer of human skin.[1]

The clinical picture is characterized by the diagnostic presence of "burrows" (which are nevertheless detectable in 7-13% only of the infested subjects) and more frequently by the presence of papules, pimples, nodules and sometimes urticaria. The most characteristic symptom is night-time itch.[1] Once very rare, scabies has recently become more frequent for the presence of diseases, like AIDS, that impair immune system function.[2]

The product tested (PAF® Lotion, Lofarma SpA, Milan, Italy) contains bis-butyl-carboethylene which is the ester of the maleic acid that has a strong acaricidal action, as it attacks the vital centres of the mite, rapidly bringing it to death (in 2-3 min.).[2-4]

The active principle had already been experimented in the past as a repellent to be applied on the fabrics to remove the small bugs like Aedes aegypti. Only later it was possible to demonstrate both the efficacy and the

harmlessness of the product to man. No toxic phenomena, in terms of either local or general reactions, have ever been reported or documented in man so far. In particular, bis-butyl-carboethylene showed to be well tolerated also by infants and children.[2, 5]

Scabies is an important cause of morbidity, as it is a highly contagious infestation which spreads among people who are in close physical contact, particularly among those people who live in communities such as schools, kindergartens, barracks, jails, hospices etc. The poorest classes living in bad hygienic conditions are the ones most at risk. In recent years the spread of ethnically and culturally heterogeneous communities has determined a recrudescence of the infestation.[2, 5, 6]

The objective of this study was to evaluate the efficacy and safety of a new treatment regimen with bis-butyl-carboethylene.

Materials and methods

Design

This was an open, multicentre study conducted on patients suffering from scabies. The trial was not designed on a double-blind basis with a control group since this is an infectious, contagious, notifiable disease in Italy that deserves prompt effective treatment.[2] The study was approved by the Ethical Committee of each Centre.

Patients

Eighty-seven patients (42 males, 45 females, age range: 5-76 years) affected from scabies were enrolled.

Exclusion criteria were: pregnant or nursing women, patients with primary or secondary immunodepression (*e.g.* HIV+), patients who were previously treated (last 7 days) or were under treatment with anti-scabies or, in general, anti-parasitic drugs and patients with poor compliance.

Methods

All patients received the following treatment regimen: 50% of the solution, which was obtained by emulsyfying 5 g of lotion in 150 ml of tap water, was applied over the entire skin surface, with the exception of the face, 2 times/day, for 3 days, with an interval of 12 h between the 2 applications. Five grams of lotion contained: 2.5 g of bis-butyl-carboethylene. The lotion was mixed for a few minutes by a spoon, in order to obtain a homogeneous and milky emulsion.

One week later, a 2nd visit was performed and, if considered necessary by the investigator, a 2nd cycle was administered for other 2 days. A month later, a follow-up visit was performed and a final evaluation for each patient was made.

The choice of this treatment duration was motivated by the high rate of "off-label use" of bis-butyl-carboethylene in current clinical practice. Currently labelled dosage indicated in the product instruction leaflet is 1-day treatment. However, many dermatologists suggest to apply the drug for 3 consecutive days. Furthermore, this 3-day treatment regimen is frequently followed, 1 week later, by additional 2-3 days of treatment, on the basis of clinical judgement by the dermatologist in charge. In order not to rely only on anecdotal reports regarding efficacy and safety of these unlabelled dosages, we decided to carry out a clinical study in order to appropriately investigate both the efficacy and the safety of this new treatment regimen.

Evaluation criteria

The main evaluation criterion for efficacy (primary endpoint) was the "disappearance of clinical manifestations": presence/absence of scabies lesions and itch improvement (assessed by a 5-point scale).

Secondary efficacy endpoints were: improvement of nocturnal itch, decrease in the number of nocturnal wake-ups (both assessed by a 5-point scale) and investigator's judgement on efficacy.

The evaluation of safety was based on adverse events monitoring; an assessment was made about their severity, intensity and relationship of the adverse events to the study medication.

Statistics

Descriptive statistics were calculated by means of mean, standard deviation, minimum, median and maximum values for continuous variables, and absolute and relative frequencies for categorical ones.

The Wilcoxon signed rank test (2-tailed) was used to analyse the evolution of the primary efficacy variable "itch" (measured by a 5 points scale) and of the secondary efficacy variable "nocturnal wake-ups". The evolution (from baseline to last visit before follow-up) of the secondary efficacy variable "nocturnal itch"

(assessed in terms of absence/presence) was estimated by means of the binomial test on the π proportion of success in comparison to the proportion of (unchanged + worsened).

Results

Efficacy

Eighty-seven patients were evaluated for the efficacy according to an intention-to-treat (ITT) analysis. All 87 patients performed the 1st cycle; 14 patients (16.1%) performed only the 1st cycle, while 73 patients (83.9%) performed also the 2nd cycle. As far the variable presence/absence of skin lesions is concerned, a remission was observed in 38/87 patients (43.7%) at the end of the 1st cycle, and in 70/73 patients (95.9%) at the end of the 2nd cycle and at follow-up. Eighty-five patients were finally evaluated at follow-up, 4 weeks after the enrolment visit.

In 85/87 patients (97.7%), a statistically significant improvement ($p = 0.00001$) of the variable "itch" was observed; specifically: from baseline to the end of treatment visit, the symptom "itch" totally disappeared in 64/87 patients (73.6%) and, at the follow-up visit was completely absent in 77/85 patients (90.6%) (Figure 1). Also the variable "night itch" improved from baseline to the last visit: 47/61 patients (77%) with this symptom at baseline did not show it by the end of cycle 1, while 50/53 patients (94.3%) did not show the symptom at the end of cycle 2 ($p=0.00001$). A reduction of night wake ups was observed in 59/61 patients (96.7%) with one of more nocturnal wake-ups at baseline ($p=0.00001$).

According to the investigator's judgement, efficacy was rated as good in 52.9% of cases and excellent in 25.3% of patients at cycle 1, against 53.4% and 42.7%, respectively, at cycle 2.

Safety

No systemic adverse events were recorded. Seven adverse events were recorded in the application site of the product: worsening of itch in 1 patient, burning in 4 and contact dermatitis in 2. Tolerability was judged by investigators as good in 57.5% of patients and excellent in 35.6% at the end of cycle 1, in comparison with 43.8% and 52.1%, respectively, at the end of cycle 2.

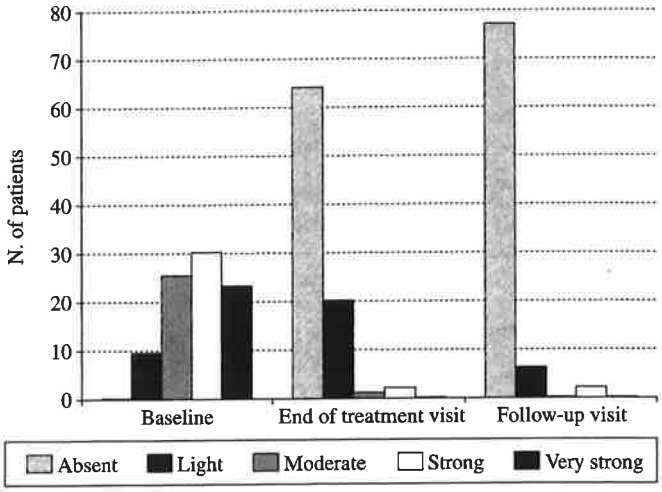

Fig. 1.—Effects of bis-butyl-carboethylene on the symptom "itch".

Discussion and conclusions

This clinical study demonstrated that this new treatment regimen with bis-butyl-carboethylene is effective in the treatment of patients with scabies. A statistically significant improvement of both skin lesions and symptoms was in fact recorded.

Furthermore, this new treatment regimen was well tolerated, in spite of the higher dosage and longer duration of treatment, if compared with the currently labelled one. Only 7 patients (8%) complained of mild skin reactions. The safety of the product was confirmed by the physicians' judgement.

This new treatment regimen (2 applications/day for 3 days followed, 7 days later and if necessary, by a 2nd cycle of 2 applications/day for 2 days), seems to be more effective and with the same tolerability of the regimen previously used.

Riassunto

Efficacia e tollerabilità del bis-butyl-carboethylene nel trattamento della scabbia

Obiettivo. La scabbia è una infestazione della cute causata da un acaro denominato *Sarcoptes scabiei*. Scopo del presente studio è stato quello di verificare l'efficacia e la tollerabilità di un nuovo schema di trattamento di una lozione dermatologica per la scabbia contenente bis-butyl-carboethylene.

Metodi. Sono stati valutati 87 pazienti, (42 maschi e 45

femmine, con età variabile da 5 a 76 anni; età media: 36 anni), affetti da scabbia. La durata del trattamento era di 3 giorni (1° ciclo, obbligatorio), più, se necessario altri 2 giorni (2° ciclo, opzionale). Per la valutazione dell'efficacia, sono state considerate la scomparsa delle lesioni cutanee e i sintomi come il prurito, i risvegli notturni e il prurito notturno.

Risultati. Quattordici pazienti (16,1%), con remissione completa delle lesioni e dei sintomi alla fine del 1° ciclo, hanno sospeso il trattamento. Gli altri 73 (83,9%) hanno ricevuto il 2° ciclo. La scomparsa delle lesioni cutanee è stata documentata in 70 dei 73 pazienti (95,9%). Nel complesso, si è osservata una remissione completa delle lesioni cutanee alla fine del 1° o del 2° ciclo di terapia in 84 degli 87 pazienti (96,5%). In 85 degli 87 pazienti (97,7%), si è osservato un miglioramento del prurito; 47 dei 61 pazienti (77%) hanno riferito un miglioramento del prurito notturno al termine del 1° ciclo e 50 dei 53 pazienti (94,3%) al termine del 2° ciclo. Il numero dei risvegli notturni è diminuito in 59 dei 61 pazienti (96,6%). Sette pazienti (8%) hanno riferito reazioni avverse lievi localizzate all'area cutanea dove era stato applicato il prodotto.

Conclusioni. Questo nuovo regime terapeutico con bis-butyl-carboethylene si è dimostrato efficace e sicuro nel trattamento dei pazienti con scabbia.

PAROLE CHIAVE: Scabbia, terapia farmacologica - Scabbia, diagnosi - Bis-butyl-carboethylene, uso terapeutico.

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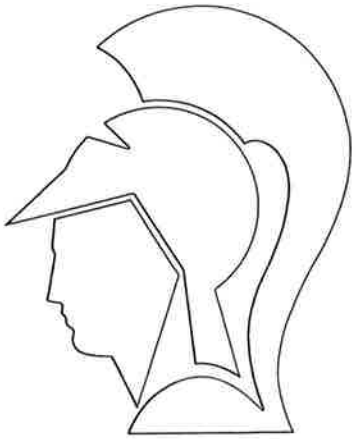

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