

Dimethindene maleate (Fenistil® Gel) in the control of itching due to insect bites and sunburns

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Abstract

In a double-blind, randomized, comparative study, 101 patients subjected to natural events like insect bites or solar erythemas were treated locally with either dimethindene (DIM) gel ($n=49$) or placebo (PLA) gel ($n=52$). Mosquito bites were the most frequent incidents. Efficacy assessment was based on the speed of disappearance of itching. When only the first event is taken into account, 43 out of 49 patients (88%) treated with DIM were relieved from itching within 30 min of the gel application. The corresponding figures for PLA were 33/52 (64%) ($p < 0.01$). For all events ($n=226$), the results gave 85/101 (84%) cases relieved for DIM and 82/125 (66%) for PLA ($p < 0.01$). Only minor and transient side-effects were notified in either group. In these everyday life conditions, DIM gel was shown to relieve pruritus more quickly than PLA, especially in mosquito-bitten patients.

Introduction

Dimethindene maleate is an H₁-antagonist [1], whose antiallergic and antipruritic properties have been extensively confirmed for the systemic forms, i.e. oral [2, 3] and intravenous [4, 5]. The gel form is designed to specifically act at the local level [6, 7]. Insect bites and sunburn are common lesions that affect a large number of people, causing itch and sometimes unrest. Although seeking relief from pruritus, these patients do not generally consult their doctor for such disorders, and have recourse to all kinds of self-medications. The main goal of this study was to assess, in double-blind and placebo-controlled conditions, the antipruritic activity of dimethindene maleate gel 0.1% (Fenistil® Gel; Zyma SA, Nyon, Switzerland) in everyday use.

Methods and materials

The study was a double-blind, randomized comparison of dimethindene gel (DIM) vs placebo gel

(PLA) in two parallel groups. The study protocol was approved by an independent ethics committee and written informed consent was obtained from subjects prior to any clinical procedure. Given the unpredictable nature of itch-producing summer events (insect bites, solar erythema, contact allergy to plants), a special design was chosen. Volunteers of either sex and above 16 years old were recruited. They were not eligible if suffering from a dermatological disease, if receiving H₁-antagonists or corticosteroids, or if allergic to the test drug. Pregnant and breast-feeding women were excluded. Persons with a history of bee or wasp sting allergy were instructed to resort to an emergency treatment in case of such events.

Before summer, 180 volunteers who had met all inclusion criteria were randomly given neutral-looking 40 g tubes of gel containing either DIM ($n=87$) or PLA ($n=93$). The subjects were instructed to apply the test gel on the affected site as soon as possible after the occurrence of the itch

sensations. Repeated applications were allowed up to 4 times daily for the same incident. When treated, patients had to immediately record in a diary the type of event and speed of relief, as well as possible further applications of the gel or scratching attacks. The use of another medication in case of insufficient efficacy of the test gel was permitted. Space was provided for free comments and adverse drug event reports (ADEs) in the case record form. The volunteers were instructed to treat as many incidents as possible. In order to avoid statistical bias due to a "learning process", statistical evaluation focussed on the first application of the gel made necessary by the first incident occurring in the trial. Absence of relief within 30 min or a new application during this period of time were both to be considered as a treatment failure.

Results

Out of 180 volunteers, 101 subjects (49 DIM and 52 PLA) became patients in experiencing during summer one or several of the set events. DIM and PLA groups were comparable. There was no difference between groups (DIM versus PLA) either for the sex ratio: 24 male/25 female versus 25 male/27 female, nor for age (mean \pm SEM): 42.8 ± 1.6 versus 38.2 ± 1.8 years. The type of events: single insect bite and multiple insect bites (30 versus 37), sunburn (10 versus 11) and miscellaneous (9 versus 6), including e.g. contact allergy to plants, were also evenly distributed in both treatment groups. The time elapsed (mean \pm SEM) between the incident and the gel application on the skin was not statistically different: 4.4 ± 1.3 h for DIM and 3.6 ± 0.8 h for PLA recipients ($p=0.605/t$ -test).

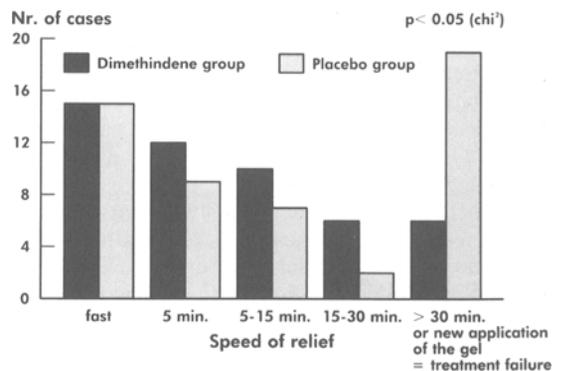
The figure shows the breakdown pattern for the speed of relief as reported by the patients. The statistical analysis showed this distribution to be significantly different between DIM and PLA ($p < 0.05/\text{chi square}$). The respective proportions of patients successfully relieved within 30 min were 43/49 (88%) for DIM and 33/52 (64%) for PLA ($p < 0.01/\text{chi square}$). For all the events, 101 in DIM and 125 in PLA group, there was a clear confirmation that, after the first application of the gel, DIM provided a quicker relief ($p=0.0047/\text{chi square}$). Interestingly, the use of a rescue medication (topical) was felt necessary twice in the DIM group versus fourteen times in the PLA group. The subjective sensation of a pleasant transient "cooling effect" was often expressed in both groups. This was

however felt as distinct from pruritic relief in many cases.

With far more than two hundred applications in each group, untoward effects were reported 7 times (4 in DIM and 3 in PLA group). All were minor and their kinds (prickling, smarting, heat sensation) were similar. No skin alteration occurred, whether irritating or phototoxic. One patient on PLA stopped the treatment.

Discussion

Proper clinical investigation of an everyday management of mosquito bites or sunburn comes up against numerous practical and methodological difficulties [8, 9]. Whatever the quality of the study design, much depends on the quirks of fate, because of the unpredictable nature of the targeted events. The fact that 55% of the volunteers finally reported itching lesions indicates that not everyone was bound to become a "patient". Mosquitos provoked the greatest proportion (71%) of all events. However, an even breakdown of all types in the two treatment groups permitted a valid comparison, which showed a clear superiority of DIM over PLA. The high rate of PLA "fast" responders is, at first site, a rather surprising finding. However, the pleasant feeling of coolness produced by the gel form may positively influence the itching sensations of milder skin reactions whilst more severe ones can only be significantly relieved by the active sub-



Speed of relief after the first application of the gel following the first incident (DIM=49 patients, PLA=52 patients). The bars represent the number of patients relieved from itching within the consecutive time limits as actually defined in the patient's diary. These numbers are non-cumulative.

stance. In this respect, the local anaesthetic activity of dimethindene maleate might have played an essential role in this study whereas another placebo controlled trial [10] had shown DIM to reduce exanthema provoked by mosquitos, thus suggesting an antihistaminic action. After a discriminative analysis on age, sex, cause of event, and time elapsed, no other parameter than the treatment was found to have significantly influenced the results. It should be stressed that, unlike most experimental designs aimed at assessing antihistaminic efficacy of topical agents, the test medications were applied after the triggering event and not before.

ADEs were quite scarce and their kinds were not different in the two groups. Neither a severe nor serious ADE occurred with DIM. No skin damage was observed. These findings are at variance with the opinion that all topical antihistamines are both ineffective and sensitizing. Some of these preconceived notions need to be reconsidered.

In conclusion, it is obvious from the results of the present study that the antihistaminic and antipruritic dimethindene maleate 0.1% (Fenistil® Gel) is of practical value in everyday use and especially suitable against itching from mosquito bites.

Acknowledgements

The authors are indebted to Mr Rouquet for editing and tailoring the English version.

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