Topical Paromomycin/Methylbenzethonium Chloride Plus Parenteral Meglumine Antimonate as Treatment of American Cutaneous Leishmaniasis: Controlled Study

SIR—We congratulate Soto and colleagues [1] for their interesting study, because to our knowledge it is the first controlled trial assessing the effect of topical paromomycin/methylbenzethonium chloride (MBCL) in combination with meglumine antimonate as treatment of New World cutaneous leishmaniasis. This study did not show any additional therapeutic effect of the ointment in combination with parenteral meglumine antimonate, which contradicts findings of earlier studies in which high cure rates were associated with treatment with the ointment alone or in combination with meglumine antimonate [2, 3]. Soto et al. argue that this difference may be due to a better controlled study design. Although this point is undoubtedly true, a number of concerns should be kept in mind.

Our experience is that MBCL causes pain of the lesion so that even applying placebo ointment would not allow an adequate blinded control [3, 4]. Paromomycin/MBCL is well known to initially cause enlargement of the lesion probably due to the MBCL component [3–5]. Keeping this factor in mind, it seems problematic to define enlargement of the lesion as a treatment failure. Unfortunately, Soto et al. do not indicate how many of the treatment failures were due to this factor and how many were due to low reepithelialization rates after 1.5 months. Enlargement of the lesions during and shortly after treatment is not necessarily a sign of worsening of the disease but a well-known side effect of the treatment. Furthermore, it seems doubtful to limit the healing time to 1.5 months, as it has been observed that many lesions will heal between 6 and 9 weeks after topical treatment [3, 6].

Soto and colleagues claim that their ointment was prepared under good manufacturing conditions. However, locally prepared ointments in the first study by Soto et al. [2] as well as in our study [3] seemed to be very effective.

Finally, it should be discussed if the combination of topical and parenteral treatment is desirable. Even if this combination was proven to be effective, the disadvantages of both drugs add up. On the one hand, there are the potential systemic toxicity, logistic problems of intramuscular application, and high price of parenteral antimonates. On the other hand, there is the pain due to application of the ointment. From a public health perspective, topical treatment of a disease that is particularly prevalent in remote rural areas would be highly desirable. Our group (B. Arana and colleagues, Universidad del Valle de Guatemala) is presently undertaking a controlled trial with the same ointment in Guatemala.

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References

Reply

SIR—We appreciate the comments of Krause and Kroeger. We too were disappointed that we could not demonstrate the efficacy of topical paromomycin/methylbenzethonium chloride (MBCL) as treatment of cutaneous leishmaniasis.

Krause and Kroeger are concerned about several aspects of our study design. Local side effects of an active topical agent would obviate blinding. The active topical ointment may indeed have side effects, but in our previous report [1], 60% of topical ointment recipients did not report local side effects. Thus, subjects in our present report [2] who had no side effects would not know if they had received the active topical ointment or the placebo topical ointment. At any rate, for cutaneous leishmaniasis, treatment success or failure is based on the objective criterion of lesion size.

Lesions may initially enlarge before healing; therefore, by declaring enlargement of lesions at the end of therapy as treatment failure, we may declare treatment failure prematurely. Herein, we break down the total of 68 treatment failures into enlargement of lesions at the end of therapy, lesions that were not cured by 1.5 months after therapy, and lesions that relapsed (table 1). In the key experimental group (patients who were treated with topical paromomycin/MBCL b.i.d. for 10 days plus injectable meglumine antimonate for 7 days), treatments of only three patients were declared failures at the end of therapy, and enlargement of their lesions was huge: from 182, 64, and 64 mm² before therapy to 918, 495, and 225 mm² after therapy, respectively.

Lesions may heal beyond 6 weeks after initiation of therapy, and we should observe patients for longer periods before declaring treatment failure. Experimental groups were compared...