

Lack of efficacy of liposomal glucantime in the treatment of cutaneous leishmaniasis

Sir,

Pentavalent antimony compounds are known to be the main anti-leishmania modalities prescribed either intralesionally or systemically, although pain due to injection and systemic toxicities pose major limitations to their use. Liposomal formulations are among the new methods used to enhance transcutaneous absorption, increase penetration into the macrophages and delay clearance from the site of action.^[1-3] In this pilot study, we sought to evaluate the efficacy and safety of a new topical formulation of liposomal meglumine antimoniate for the treatment of old world cutaneous leishmaniasis.

The study was approved by the ethical committee of the Mashhad University of Medical Science. Twenty patients with cutaneous leishmaniasis attending

the leishmaniasis clinic of Imam Reza Hospital were enrolled in this study based on the following inclusion criteria: (1) parasitological confirmation of the disease (2) no previous history of treatment (3) duration of disease <6 months (4) largest diameter of the lesion <80 mm (5) refusal to receive conventional intralesional injection of glucantime and (6) informed consent. Exclusion criteria were: (1) antimoniate sensitivity (2) irregular attendance (3) secondary infection of the lesion (4) concomitant use of other treatments.

Liposomal meglumine antimoniate was prepared locally using small unilamellar liposomes with an approximate diameter of 110 nanometers by fusion method. Shape and sizes of the nanoliposomes were checked by particle size analyzer. Furthermore, the particles were checked for stability, zeta potential and meglumine antimonite content. Patients were asked to apply the formulation 3 times a day for eight weeks. Follow-up visits were scheduled weekly and two largest perpendicular diameters of the lesion in millimeters were recorded. Potential local adverse effects of the treatment were also recorded.

After 8 weeks of the treatment, decrease in induration was recorded and clinical efficacy of the formulation was defined as: (1) significant response (>75% decrement) (2) moderate response (50–75% decrement) (3) mild response (25–50% decrement) (4) slight response (<25% decrement) (5) no response (no change or increase of indurated area). Patients were followed up at 1.5, 3 and 6 months after the end of the treatment to evaluate disease progression and suspected adverse effects. All the data was analyzed with SPSS version 11.5 (IBM Corp., Armonk, NY) for Windows, New York, USA. Eight men and 12 women were enrolled and a total of 55 lesions were studied. The mean age (= SD) of patients enrolled was: 23.2 ± 18.48 years. (range 2-52 years). Initial induration was calculated as the product of two perpendicular diagonals of the lesion. Accordingly, the largest lesion was 4118 mm² and the smallest was 12 mm² (mean 349.85 mm²). In four patients, allergic contact dermatitis to liposomal glucantime occurred at the treatment site. Among them, two patients showed adverse reactions at week 6 of treatment resulting in treatment withdrawal. and two other patients at weeks and at week 3 respectively. In the last patient the dermatitis resolved with continued treatment. Three patients were excluded from the study, two patients with a total of 19 lesions because of local adverse effects and one patient with a single lesion because of irregular attendance. Finally, 17 patients with a total lesion count of 35 were statically analyzed. Since the improvements calculated as mentioned above did not have a normal distribution, non- parametric tests such as Kruskal–Wallis and Spearman’s test were used to analyze the data.

Clinical response rates of the lesions at 8 weeks are summarized in Table 1. The most common outcome was no response which was noted in 24 (68.6%) lesions. Significant response was noted in only 3 (8.6%) lesions.

Spearman’s test showed no statistically significant correlation between the duration of the lesion and response rate and between the initial size of the lesion and improvement rate ($r = 0.117$, $P = 0.505$). Contrary to our expectation, in this pilot study liposomal formulation of glucantime was not effective in the treatment of cutaneous leishmaniasis. The lack of efficacy could be due to the low penetration of the formulation through skin considering that most treated

Table 1: Frequency distribution of the lesions according to clinical response

Clinical response	Number of lesions	Percentage
Significant	3	8.6
Moderate	2	5.7
Mild	3	8.6
Slight	3	8.6
None	24	68.6
Dropped out	20	-
Total	55	100

lesions were not ulcerated. This was unexpected since penetration of the formulation and its efficacy in the treatment of cutaneous leishmaniasis in BALB/c mice has been previously studied.^[4] However, it failed to be clinically effective in humans in this pilot study, in contrast to liposomal amphotericin which was effective in another clinical trial reported from our country.^[5] Instability of the drug in these formulation is also another concern. The main limitations of this study are the small sample size and lack of a control group.

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Conflicts of interest

There are no conflicts of interest.

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