

# Evaluation of Paromomycin Sulphate Topical Ointment as Effective Therapeutic Agent in Cutaneous Leishmaniasis

Pages with reference to book, From 53 To 55

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## Abstract

This is a prospective open study of randomly selected 35 patients with a single sore of cutaneous leishmaniasis who were treated with paromomycin sulphate topical ointment for 4 weeks. According to the observations made on days 0, 15, 45 and 105 after the careful application twice a day in 2 lengths from one side of the lesion to the other at right angles to each other and then smeared to cover the whole surface of the sore, the overall efficacy of the ointment as therapeutic agent was 91%. There was a mild and temporary adverse reaction in the form of painless, non-itching nodulation around the ulcers in 10(28%) patients after 15 days application which disappeared within 5-7 days of further application. It thus proved a promising, simple and inexpensive remedial agent without any undesirable side effects as compared to other complicated and unpredictable therapeutic regimens (JPMA 46: 53, 1996).

## Introduction

Cutaneous leishmaniasis (CL) famously known in the world by the regional or local names such as Oriental sore, Delhiboil, Aleppo boil, Baghdad Boil, Biskra boil and Quetta/Kandahar Kaldana prevails over several areas with different geographical conditions in the province of Balochistan. There was a time when the natives of Quetta (Provincial capital), Kasi, Pathans and Berahvis and people living in Kandahar (Afghanistan) were recognised in other areas of the region by the presence of disfiguring scars on their faces and other exposed parts of the body. The lesion has since been named Kaldana in Pashto in Balochistan and Afghanistan meaning a sore taking years to heal<sup>1,2</sup>. Balochistan being at the crossroad of Afghanistan in the North, Iran in the West, India in the East and Arabian Sea in South had been in the past and is still exposed to Leishmanial diseases through travellers entering its frontiers from endemic areas. The endemicity of CL has achieved greater dimensions in the recent years in Balochistan and the disease may well be placed on the top of the list of patients with skin disorders attending the dispensaries and hospitals both in government and private sectors in rural and urban areas (unpublished).

Due to lack of effective vector control and other prophylactic measures in a hyperendemic region like Balochistan where poverty, illiteracy and lack of civic sense prevail, these problems became more alarming through the continuous huge influx of Afghan refugees, who entered the province through its northern frontiers for the last 15 years. Besides other sufferings, both CL and visceral leishmaniasis (VL) were introduced on a large scale and the control of the disease has become a major health problem. The unavailability, toxicity, parenteral painful and uncontrolled administration of conventional pentavalent antimonials and other old fashioned therapies in the scarcely populated rural areas here prompted us to resort to the use of a topical ointment containing 15% paromomycin sulphate as a remedial agent which was used in the cases of recurrent cutaneous leishmaniasis (LR) by El-On et al 1985<sup>3-5</sup>. The same ointment is used in the University College Hospital London. The ointment was used in 1990 for CL sores for 3 weeks with apparently complete clinical cure. In another study the same ointment was used in 100 cases of CL with 80% cure rate<sup>6</sup>. The objective of the study, is to assess improved curative measures by exploring the efficiency of the topical ointment and observe any side

effects.

### **Patients and Methods**

Thirty-five adult male patients with a localised single sore less than or equal to 5 cm in diameter, which persisted for less than 4 months and located 3 cm away from the eyes, were included in the study after obtaining a written consent. These patients had not received any treatment before. There was no history of allergy and no concomitant serious disease was present. Their ages ranged from 17 to 39 years.

The diagnosis was made by skin slit preparation technique and after staining the smears with Giemsa stain, when leishmanial amastigotes were seen in the dermal macrophages or dispersed extracellularly. The patients were examined for physical fitness and laboratory investigations such as leucocyte count, haemoglobin, blood urea nitrogen and SGOT were done on day zero, 15, 45 and 105. Photographs of the sores were taken on the same days (Figures Ia. and Ib).

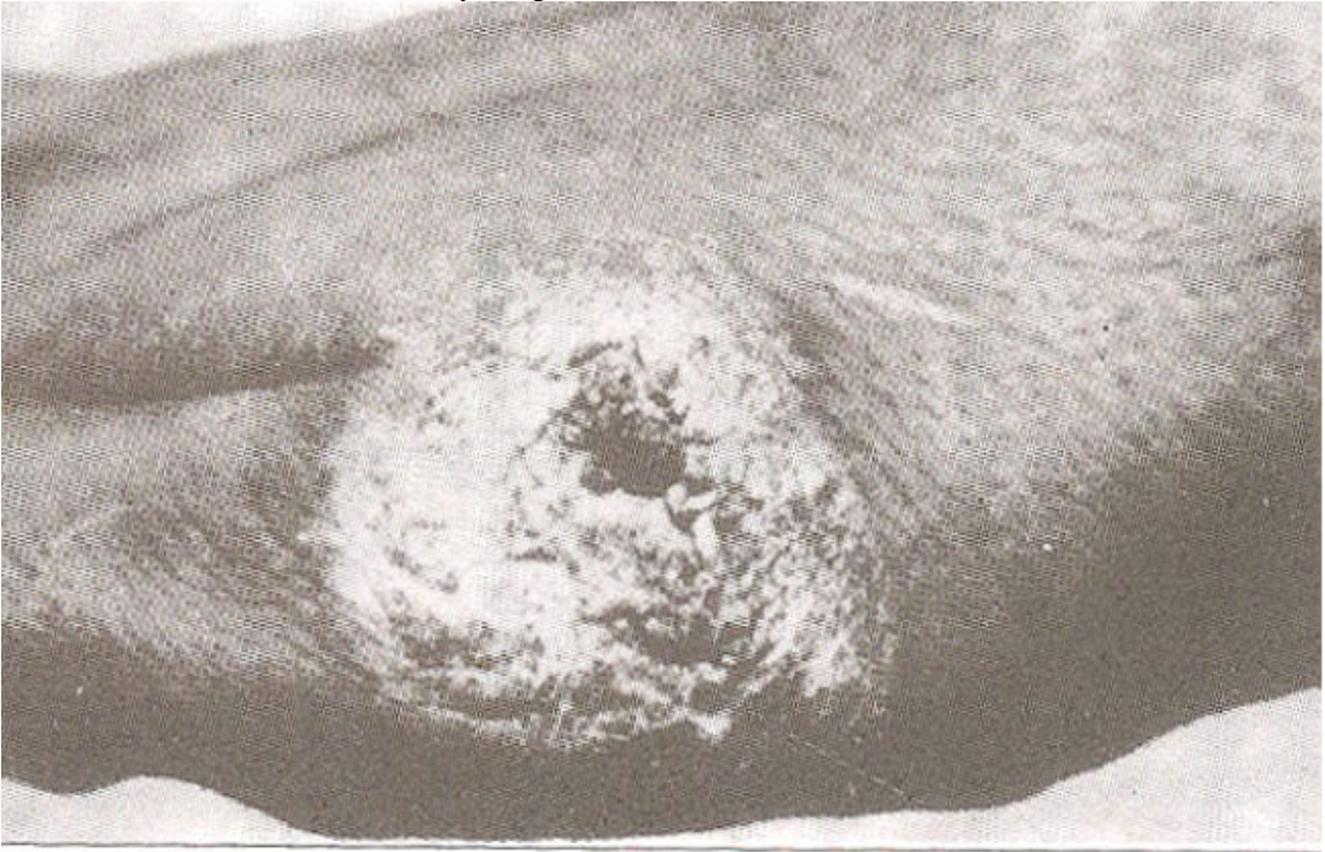


Figure 1a.

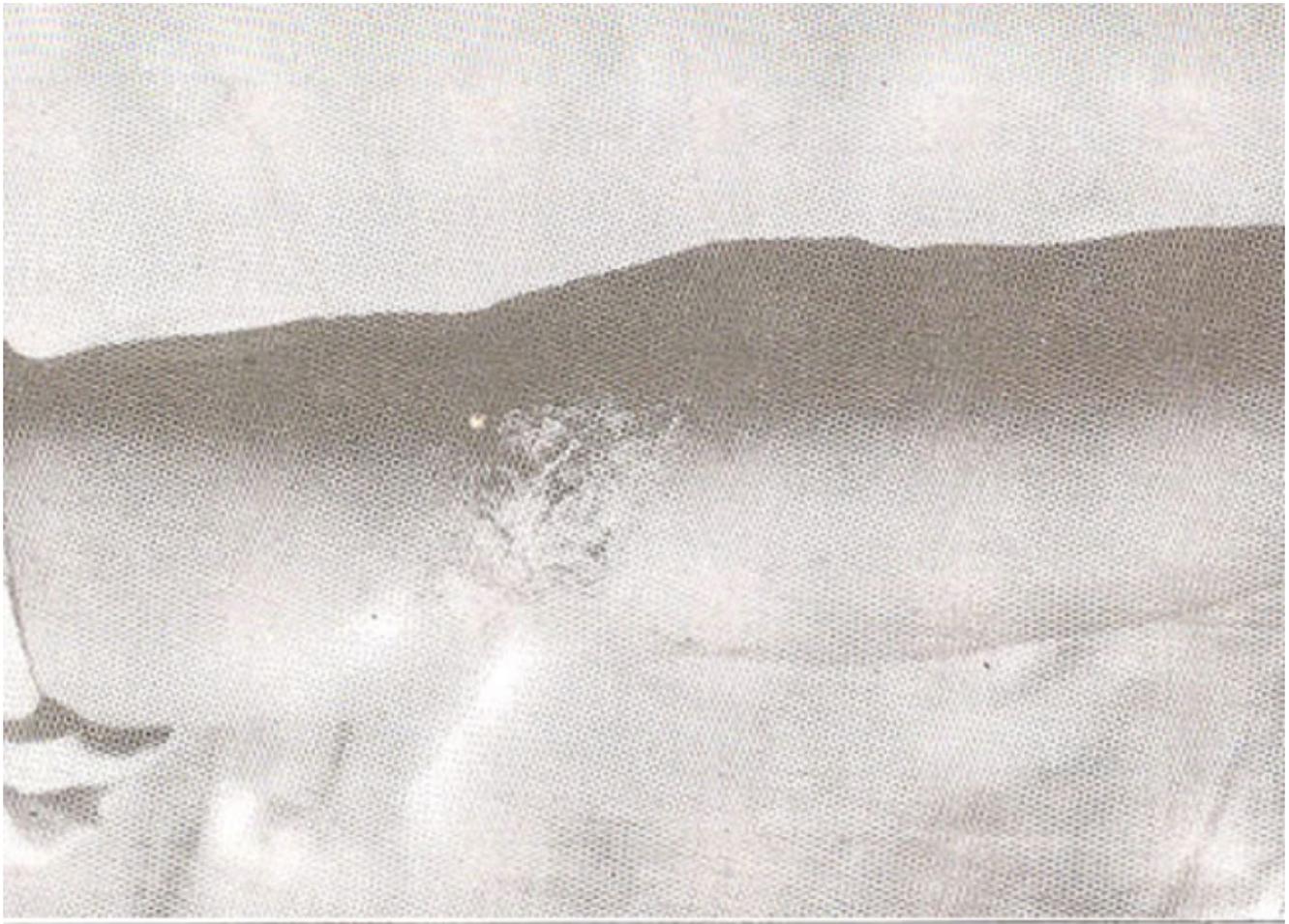


Figure 1b.

Two tubes of topical ointment each containing 30g (11.50% Paromomycin) were labelled for every patient and it squeezingjjfrbm the collapsible tube in2 lengths over the sore airight angle from one another.

Partial response or apparent cure was evaluated by dryness or otherwise of the sore, epithelization, decrease in size and edema and lowering of edges, smear positivity/negativity and tolerability or adverse reaction on days 15,45 and 105.

All of the patients were soldiers in the Pak Army based at Quetta and they were deputed to undergo an exercise for 2 months in a dry river bed (Nari bank) near Sibi which is an L-major hyperendemic region in Balochistan. After the exercise was over they were sent home on leave. Almost all of them belonged to northern districts of the country and they were non-immune to the disease. About 1300 personnel were bitten by the vector and these were notified in the Combined Military Hospital. Quetta during a period of 7 months (March to October, 1993).

Their ages ranged from 17 to 39 years and average duration of the sore development was one and half month. All of them had a localized sore on the exposed parts of the body. less than 5 cm in diameter. The white cell count, hacmoglobin, blood urea nitrogen and SGOT, done on day 0,15,45 and 105 were observed to be within normal limits.

On day 15, partial response of apparent cure was observed as dryness of the sore, epithelization, decrease in size and edema and lowering of edges in 3(9%) patients (Figure 2a and ib).



Figure 2a.



Figure 2b.

There was a mild and temporary adverse reaction in the form of painless and non-itching nodulation around ulcers in 10 (28%) which disappeared within 5 to 7 days of further application (Figure 3a. b and c).



Figure 3a.

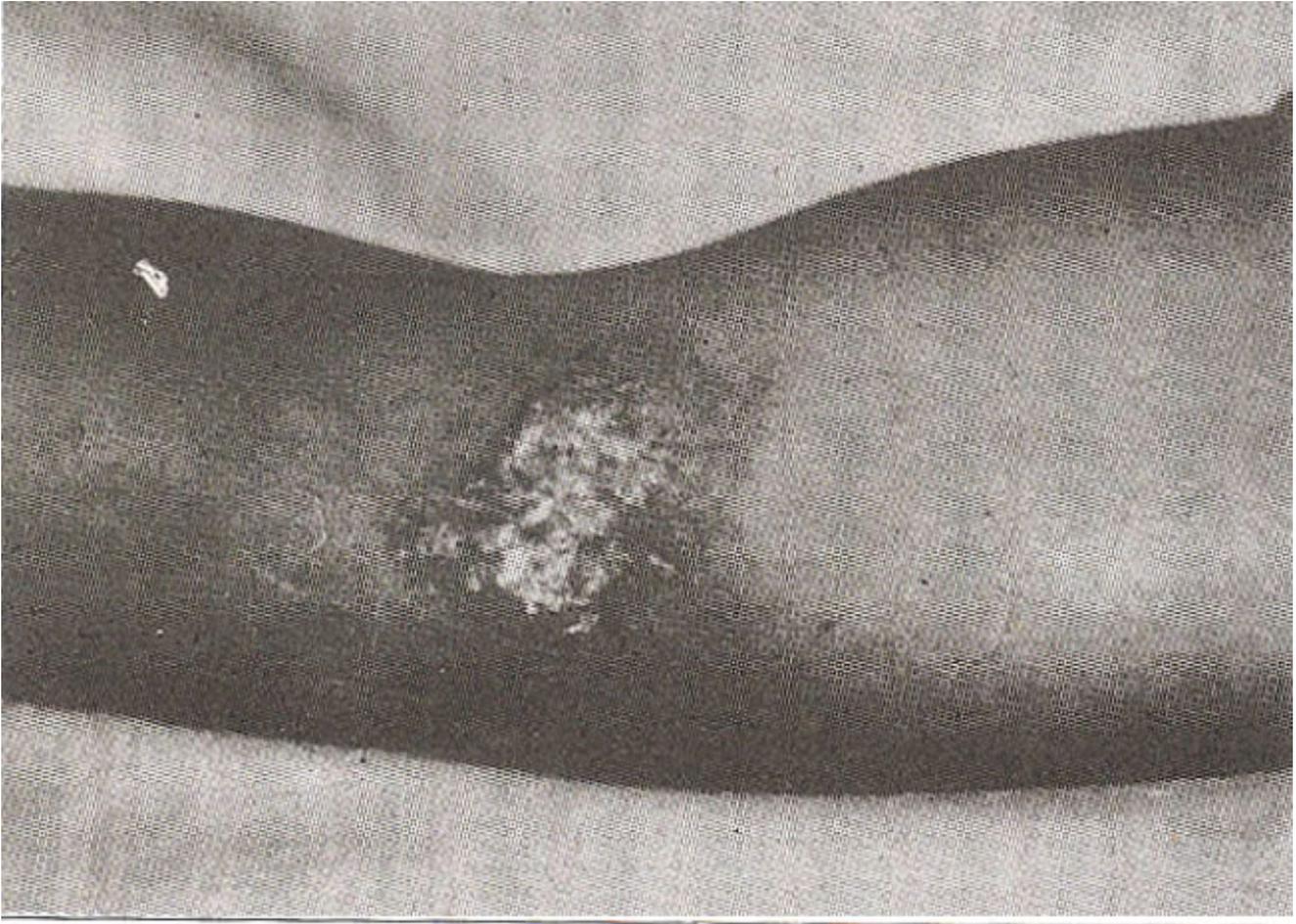


Figure 3b.

The same parameters were evaluated on day 45 with clinical assessment of efficacy revealed by clinical improvement in 26 (74%) patients. On day 105, final observations were made by evaluating the clinical as well as parasitological cure in 32 patients (91%). (Figure 3a and 3b). During the follow-up period of 6 months, no recurrence was observed.

## Discussion

Cutaneous leishmaniasis is widely spread throughout Balochistan due to its strategic geographical situation within Irano-Turanian (40%) and Saharo-Sindian regions of the world where there is maximum distribution of L-major disease. The disease occurs sporadically throughout the year, the explosive human infection occurs in epidemics. First epidemic occurred in 1935, after a dreadful earthquake in Quetta, when thousands of children were affected. The subsequent epidemics occurred in Multan in 1971-72 in which 2500 patients were affected followed by epidemics in the year 1976-77 in Uthal, 1979-80 in Pirkuh (Sibi), 1990 in Quetta and

1993-94 in Sibi when diggings were done on large scale for the development of industry and towns whereby non-immune workers were exposed to the bite of the vector in those areas.

Zoonotic CL due to *L. major* is the main type of leishmanial disease in Balochistan and rest of the country, except in Mirpur in Mangla Dam area and a spot in the extreme south of Balochistan where from ACL due to *L. tropica* has been reported.

The old remedies in this country are intralésional mepacrine, curettage and surgical removal of the non-healing, annoying and incapacitating or mutilating sores, as well as antimonial compounds parenterally

and intralesionally<sup>7</sup>. The results of this study are in partial agreement with that carried out in Iran<sup>8</sup> (Personal communication). Paromomycin is an aminoglycoside antibiotic used under the trade name of humatin in amoebiasis and intestinal tapeworm infection. It has an antibacterial activity against normal and pathogenic microorganisms in the intestinal tract and is ineffective against extra-intestinal disease<sup>8</sup>. As a parasitocidal it inhibits synthesis irreversibly at 3 steps. It interferes with peptide formation initiation complex, it induces misreading of the code on mRNA template resulting in the correct amino acid incorporation into the peptide and it breaks up polysomes in nonfunctional monosomes. By these mechanisms paromomycin sulphate interferes with integrity of the leishmanial parasites. The adverse local reaction in the form of appearance of nodules or blebs around the ulcer and allergic induration of its margins in few cases was transitory, painless and disappeared promptly. It was thus concluded that Paromomycin Sulphate topical ointment is an effective, non-toxic, cost effective and simple to use therapeutic agent for cutaneous leishmaniasis.

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