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TREATMENT OF URBAN CUTANEOUS LEISHMANIASIS IN IRAN WITH CYCLOGUANIL PAMOATE

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In its urban form, cutaneous leishmaniasis in Iran lasts for a considerable period of time and the methods of treatment available at present are either ineffective or time-consuming, expensive and sometimes even dangerous. Clinicians in this country are always looking for new drugs which are harmless and more effective.

After noticing the regression of early lesions of dermal leishmaniasis in malaria patients treated orally with chloroguanide hydrochloride, Péna Chavarria et al (1965) decided to evaluate the efficacy of cycloguanil pamoate which has the same active agent, in the treatment of dermal lesion caused by **L.braziliensis**. They treated 30 patients, 26 of whom were cured. Beltran et al (1966) used the same drug in the treatment of 83 cases of dermal leishmaniasis in Mexico; 63 (76 %) of them had complete recovery within two to four weeks. Some of these patients had had their lesions for more than 20 years; they were resistant to all available methods of treatment.

Péna Chavarria in 1968 and Johnson in 1968 used cycloguanil pamoate in the treatment of, respectively, 50 and 26 cases of dermal leishmaniasis in Costa Rica and Panama. They have reported cure rates of 88 and 73 per cent respectively.

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Johnson indicates that the time required for healing ranges from 38 to 138 days and that more than half of the cases require more than 90 days, but Péna Chavarria indicates that the majority of patients become parasitologically negative by the tenth day after treatment.

In the old world this drug has been experimentally used in the treatment of cutaneous leishmaniasis by several investigators. Helmy Salem et al (1969) in Iraq reported a cure rate of 47.9 per cent with an average cure time of six weeks. They also reported improvement in 31 per cent of the patients; only 21.1 per cent did not respond.

Kurban et al tested the efficacy of the drug in Lebanon in 1969. Sixty per cent of their patients were cured or showed improvement; and the rest showed no response after two months. In 1968 Bryceson reported the ineffectiveness of this drug in the treatment of cases of dermal leishmaniasis in Ethiopia.

The present paper shows the results of a clinical trial for the effectiveness of Cycloguanil pamoate (Camolar; CI-501) in thetreatment of urban cutaneous leishmaniasis in Iran.

MATERIALS AND METHODS

One hundred one patients were put under treatment, 86 of them were patients from Mashad in north-eastern part of the country, and the rest from Tehran. The patients from Mashad were aged from 4 to 55 years, median 7 years. Thirty-eight were male and 48 were female. The 15 patients from Tehran were schoolchildren from two elementary schools of Yoosef-Abad in the north of the city, aged from 7 to 12; 12 were male and 3 female.

Cycloguanil pamoate was used as a suspension in 40 per cent benzyl benzoate and 60 per cent castor oil in vials, 25 ml, 1 ml contained 140 mg of the base. The dosage was as follows:

140 mg (1 ml) for subjects less than 5 years of age

280 mg (2 ml) for subjects 5 to 10 years, and

350 mg (2.5 ml) for subjects 11 years and older.

A total of 26 patients received two simultaneous injections. The vials containing 2.5 ml of suspension, were warmed to body temperature and shaken vigorously before injection in order to get an even suspension.

Scrapings of the lesions were examined before treatment and on days 10, 20, 30, 40, 50, 60, 90, and 120. Reaction at the injection site was recorded on days 2, 4, 7, 30 and 60. Complete blood counts were also carried out in the course of observation up to day 120.

Results

Out of 101 patients thus treated, 96 were followed up to day 120. Thirty-one of them recovered within 60 days, 23 recovered after 60 up to 120 days and 42 did not recover (Table 1).

If healing within two months from the time of dispensing of the drug is accepted as attributable to cycloguanil pamoate, the total cure rate is 32 per cent.

Table 1 shows that the failure rate is the highest in 1 ml dose group (children less than 5 years of age). In the rest of the patients who received a higher dose, the observed cure rate is 37 per cent (30 out of 80 available up to day 120).

We also noticed that a higher recovery rate was achieved in cases treated in Tehran (eight out of 15 recovered within 60 days with a cure rate of 53 per cent.

This may be due to the age group of the patients treated in Tehran who were also school children of 7 to 12 years of age, or it may be due to differences in susceptibility to Camolar in strains of leishmania from Mashad and Tehran.

Cure rates were a little higher in those receiving two simultaneous injections than in those who received only one injection.

We could not select a true control group in our trial but previous studies on urban cutaneous leishmaniasis in this country shows an average duration of 11-12 months (Nadim et al, 1969). The cases we selected for treatment

had mostly their lesions for less than six months; thus recovery within 60 days does not seem to be related to the natural course of oriental sore, but is due to the effect of the drug. Comparing the efficacy of the drug to others used in the chemotherapy of the disease, it may be concluded that it is not as effective as pentavalent antimony compounds. (We have had a cure rate of about 70 per cent with Glucantime (antimoniate N-methyl glucamine). However, it still has some beneficial effects. Although our results are not as brilliant as those report from Latin America, we think that the drug is worth trying, especially in older children and adults who may receive higher doses.

The most commonly observed side effects were tenderness at the injection site (83 per cent), induration (27 per cent), fever (6 per cent), and abscess (2 per cent). The incidence of adverse reactions was higher in those patients who received two CI-501 injections than in those receiving a single one. Adverse symptoms gradually decreased up to days 26-31, but tenderness was observed in a longer period of time (up to 63 days) in one patient.

We did not observe any notable change in the complete blood counts of the patients in this study.

Table 1
Effectiveness of CI-501 (Camolar) in the Treatment of Urban Cutaneous Leishmaniasis in Iran

CI-501 Dose Group		No. of Patients Treated	No. recovered within 60 days	No. recovered within 60-120 days	No. who did not recover after 120 days	No. lost because of change of address	Recovery rate within 60 days
1 ml	Single Injection	14	—	1	11	2	0%
	Double Injection	4	1	—	3	—	25%
2 ml	Single Injection	41	14	10	16	1	34%
	Double Injection	16	6	4	4	2	37%
2.5 ml	Single Injection	20	7	6	7	—	35%
	Double Injection	6	3	2	1	—	50%
Total	Single Injection	75	21	17	34	3	28%
	Double Injection	26	10	6	8	2	38%
All Patients		101	31	23	42	5	31%

SUMMARY

One hundred one cases of urban cutaneous leishmaniasis from Mashad and Tehran were placed under treatment with either one or two simultaneous standard doses of cycloguanil pamoate. Out of 101 patients, 96 were followed until the 120th day; 31 (31 per cent) recovered within 60 days, 23 (23 per cent) recovered after between 60 and 120 days, and 42 (42 per cent) did not respond. A higher recovery rate was observed in subjects who received two simultaneous doses of the drug (38 per cent cithin 60 days).

Recovery rate was also higher in the patients from Tehran who were children aged 7 to 12 years. However, our results indicate that Camolar is less effective than pentavalent animonial (Glucantime). The side-effects of the drug were tenderness (83 per cent), induration (27 per cent) fever (6 per cent) and abscess (2 per cent). No changes in complete blood count were observed. The incidence of adverse drug reactions was higher when two simultaneous doses were given.

RESUME

101 cas de Leishmaniose cutanee urbain de Mashad et Téhéran sont traités par une ou deux injections (simultanées) de doses standards de cycloguanil pamoate.

Parmi ces 101 cas, 96 sont suivi jusqu'à 120 jours; 31 (31 %) étaient completement guéris dans moins de 60 jours, 23 (23 %) dans 60 à 120 jours et 42 (42 %) n'ont pas réagit.

Taux de guérison était plus élevé dans les cas traités par deux injections simultanées. (28 %, dans 60 jours). Taux de guérison était aussi plus elevée dans les malades de Téhéran qui étaient agées de 7 à 12 ans. Mais nos résultats indiquent que Camolar est moins effective que les antimoniaux pentavalents.

Les incidents de médicaments étaient:

douleur (83 %) induration (27 %) fièvre (6 %) et abcès (2 %).

On n'a pas remarqué aucun changement dans la numération globulaire

et la formule sanguine. L'incidence des complication était plus elevée dans les cas recevant deux injections simultanées.

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