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NEW APPROACH FOR TREATMENT OF CUTANEOUS LEISHMANIASIS BY MANNITOL

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SUMMARY

The present study was carried out in Hawija District and surrounding villages. Three villages were chosen (Al-Kadhemia,Sader Al-Naher, Al-Ameniea). The high incidence rate of cutaneous leishmaniasis was during the winter months (December 1996 to March 1997). The total positive cases were 227 (111 males and 116 females). The highest incidence rate was among childeren from 1-10 years old.

Intralesional mannitol solution was shown to be more effective (93.89%) than Hypertonic Sodium Chloride 7% (HSCS) (87.50%) but almost identical to pentostam (96.20%). Most of lesions were cured in first and second injection, in all three treated groups but few of them needed the third injection. In all three treated groups, the scar was absent or minimum after healing. None of the control lesions cured within 6-8 weeks.

It is concluded that 20% mannitol is an effective local method of treatment for acute cutaneous leishmaniasis. The efficacy of 20% of mannitol is identical to pentostam and greater than 7% " HSCS".

INTRODUCTION

Cutaneous leishmaniasis is a granulomatous skin diseases (1) caused by flagellated tissue protozoa of genus

Leishmania which is named Leishmania tropica and commonly seen in tropical and subtropical areas (2,3).

It is transmitted by sandfly from infected persons or animals like cat, dog, rodent and gerbiles. Starting by small nodules which slowly enlarged then ulcerate and end within approximately one year with a characteristic permanent, depressed and disfiguring scar (1,3,4).

Many studies have been established for treatment of cutaneous leishmaniasis in Iraq. Al-Yazachi used many methods for treatment of cutaneous leishmaniasis by infiltration of pentostam, by using cryotherapy with liquid nitrogen and by cautery (1).

Sharquie also used pentostam locally (5) and discovered new approach for treatment of the disease with 7% Hypertonic sodium chloride solution "HSCS" which was infiltered around the edges of the lesion until blanching occurred (6). This was confirmed by Hussains and El-Gorban studies (7,8).

Mannitol is a polyhydric alcohol with 182 molecular weight which is filtered across the glomeruli but not reabsorbed to any significant extent in the tubules. It may be given intravenously or orally, when it includes osmotic diarrhoa (9).

Mannitol has useful effect in neurosurgery for reduction of cerebrospinal fluid pressure and for the reduction of intraocular pressure when it is given intravenously because it encourage the movement of water from inside the cell to the extracellular fluid. Mannitol is contra-indicated in congestive cardiac failure and pulmonary oedema, where there is uncertainty that the drug will be excreted not more than 25 g should be given. It is available at 10% , 20% , in 500 ml containers in Iraq (9).

If the patient acquires an adequate but not excessive cell-mediated immune response to the parasite, healing of lesions and solid protection result, but in an inadequate the result may

be diffuse cutaneous leishmaniasis, and spontaneous cure is less. On the other hand, an excessive cell-mediated immune response produced lupoid recidiva leishmaniasis (10).

The aim of this study was to discover a new approach for effective and safe treatment of cutaneous leishmaniasis which is available locally. Another objective was to compare the effect of 3 types of local therapy for acute cutaneous leishmaniasis (20%) Mannitol, Pentostam , (7%) Hypertonic sodium chloride "HSCS".

PATIENTS AND METHODS

An out break of acute cutaneous leishmaniasis in Hawija town and surrounding villages in Al-Tameem province occurred in winter 1996-1997. This study was carried out on 227 patients from December 1966 to March 1997. Three villages endemic with cutaneous leishmaniasis were chosen and 227 cases with 396 lesions of cutaneous leishmaniasis were examined. The diagnosis was confirmed on clinical ground and laboratory methods.

The clinical bases were:

1. Geographically endemic area.
2. Any nodule of more than one month duration in an endemic area during winter, was regarded as cutaneous leishmaniasis until proved otherwise (11).
3. Exposed parts were the usual site of lesions.

Laboratory method was carried on by examining the direct smear stained with giemsa stain in Al-Tameem Public Health Laboratory.

The total number of patients were 227 of both sexes 111 male (49.90%) and 116 female (51.10%), ranging in age from 1-60 years.

The total number of lesions examined were 396 , both dry (301) and wet (95) types.

The skin lesions were divided randomly into four groups according to the type of therapy used and as follows:

GROUP A: MANNITOL TREATED LESIONS

180 lesions were infiltrated with sterile 20% mannitol Sammara Drug Industry, Iraq) until complete blanching of whole lesion had occurred.

The amount of mannitol solution required was 1-5 ml depending on size of lesion and presence of ulcer, wet lesions required more solution than nodular ones (dry ones) because the first one can not nold the solution.

The solution was injected by ordinary syringes with 23-25 gauge needles without xylocaine. The lesions were examined regularly every 10 days for 6-8 weeks.

GROUP B: PENTOSTAM TREATED LESIONS

79 lesions in 49 patients were locally infiltrated with pentostam (Welcome, England) every 10 days in the same way as mannitol , but with addition of 2% plain xylocaine. The amount of solution needed was 1 ml – 3 ml and the patients were followed up every 10 days for 6-8 weeks.

GROUP C: HYPERTONIC SODIUM CHLORIDE "HSCS" 7%

96 lesions in 46 patients were treated with 7% "HSCS" in same manner as groups A and group B but 2% plain xylocaine was combined with it.

GROUP D: CONTROL SKIN LESIONS

41 lesions (32 dry, 9 wet) in 20 patients were left untreated as control. They were followed up until the end of study.

STATISTICAL ANALYSIS

Chi-square analysis was done to show the significant difference between groups.

RESULTS

The total positive cases of cutaneous leishmaniasis in Hawija District was 227. Their age were ranging from 1-60 years, 111 were males and 116 were females. The highest rate of infection were among 1-10 year followed by 11-20 , 21-30 , 31-40, 51-60 and 41-50 age groups respectively. The infection rate was slightly higher in females than males (Table.1).

The distribution of lesions was mostly on the face (53.54 %), followed by upper limbs (27.77 %), and lower limbs (18.69%) respectively (Table.2).

During period of study which was 4 months, the lesions were examined during 10 days intervals, and treatment was repeated when required.

In mannitol treated group lesions, it found that from 118 dry lesion, 114 cured completely and 4 showed mild improvement. In 62 wet lesions, 55 cleared completely and 7 showed mild improvement (Table.3).

Regarding the number of injections of mannitol required to cure lesions, it was found that one injection was needed to cure 78 dry lesions while two injections were required to clear 36 dry and 44 wet lesions. Three injections were needed to clear 11 wet lesions (Table.4).

In pentostam treated group lesions, it was shown that from 79 lesions, 76 lesions were cured (70 dry and 6 wet), while mild improvement were the outcome in 3 lesions (1 dry and 2 wet) (Table.5).

It was found that 9 dry lesions required one injection, 65 lesions (61 dry and 4 wet) cleared with two injections and only two wet lesions required three injections. (Table.6).

In using hypertonic sodium chloride solution (7%) it was seen that from 96 lesions, 84 lesions (76 dry and 8 wet) were cured, while there was slight improvement in 12 lesions (4 dry and 8 wet) (Table.7).

It was observed that 17 lesions (15 dry and 2 wet) required one injection, 64 lesions (60 dry and 4 wet) required two injections, while third injections was required to cure 3 lesions (1 dry and 2 wet) (Table.8).

In all treated groups, it was seen the scars were either absent or minimum (Figs 1-3).

In control untreated group, 41 lesions (32 dry and 9 wet) showed no improvement till the end of study which was from December to March 1997.

DISCUSSION

The high distribution of infection in this study might be related to poor hygiene, large population of rodents and failure of using insecticidal agents.

The high rate of infection among children may be because of bad habit of children playing outside houses without clothes which expose them to insect bite. This is also reported by Hussain in Baghdad (7) and El-Gorban in Door town (6).

The high incidence of infection in females than males reflects their working habits as woman were working in the farm more than men in this region. This finding is in agreement with that shown by Hussain (7) who carried on his study in Baghdad.

It is well known that many methods had been established in Iraq to treat Baghdad boil. Many studies showed that intralesional injection with pentsotam and 7% "HSCS" were effective (5,6,8,11).

In this study mannitol was used as a new approach for intralesional treatment of cutaneous leishmaniasis. It is believed

that, its mode of action is similar to pentostam and "HSCS" by making the environment of parasite hypertonic, resulting in paralysis and shrinkage of the parasite.

Recently "HSCS" 7% become a Known approach in management of cutaneous leishmaniasis as many medical staff use it in unproper way because of difficulty associated with the use of solution made from table salt as it always presented in a hydrous from rather than unhydrous form. Hence it is decided to use an available solution which should be sterile, pure and with constant concentration, easily available in hospital and approved by Ministry of Health.

Comparing the finding of this study with others, it is shown that the efficacy of mannitol (93.89%) was higher than "HSCS" 7% which was reported by Hussain (7) who found that the efficacy of "HSCS" was (88.9%).

In this study it was found that:

1. There was no resistance or partial healing in dry lesions with 3 types of treatment.
2. Mannitol looks superior to others.
3. Partial healing with mannitol was less than pentostam and "HSCS" 7%.
4. The good response occurred in wet lesions after the second injection was more in mannitol than pentostam and "HSCS".

From the results of this study it is concluded that mannitol is an effective local treatment for acute cutaneous leishmaniasis. Its efficacy is identical to pentostam and greater than 7% "HSCS" .

It is advisable to use 20% mannitol because it is available with pure, sterile and constant concentration and proved by M.O.H. and its efficacy is more than 7% "HSCS".

Fig.1. Lesions of cutaneous leishmaniasis before and after treatment with mannitol.
A- Before treatment.
B- After treatment.

Table.1 The frequency of distribution of cutaneous leishmaniasis according to the age.

Age (years)	Males	%	Females	%	Total	%
1-10	56	50.45	70	60.34	126	55.51
11-20	28	25.23	19	16.38	47	20.70
21-30	22	19.82	13	11.21	35	15.42
31-40	2	1.80	6	5.17	8	3.52
41-50	3	2.70	2	1.73	5	2.20
51-60	0	0	6	5.17	6	2.64
Total	111	100.00	116	100.00	227	100.00

Table.2 Site of lesions of Cutaneous leishmaniasis

Site	No. of lesions	%
Face	212	53.54
Upper limbs	110	27.77
Lower limbs	74	18.69
Total	396	100.00

Table.3 The outcome of 180 lesion treated with intra-lesional Mannitol

Response	Total No.	%	Dry	Wet
Cured	169	93.89	114	55
Mild improvement	11	6.11	4	7
Total	180	100.0	118	62

$\chi^2 = 4.422$ d.f = 1 $P < 0.05$

Table.4 : The number of injections needed in the cured lesions by Mannitol

	Curred lesions			
No. of injection	Total No.	%	Dry	Wet
One injection	78	46.15	78	0
Two injection	80	47.34	36	44
Three injection	11	6.51	0	11
Total	169	100.0	114	55

$\chi^2 = 78.807$ d.f = 2 $P < 0.05$

Fig. 2. Lesions of cutaneous leishmaniasis before and after treatment with pentostam.
A- Before treatment.
B- After treatment.

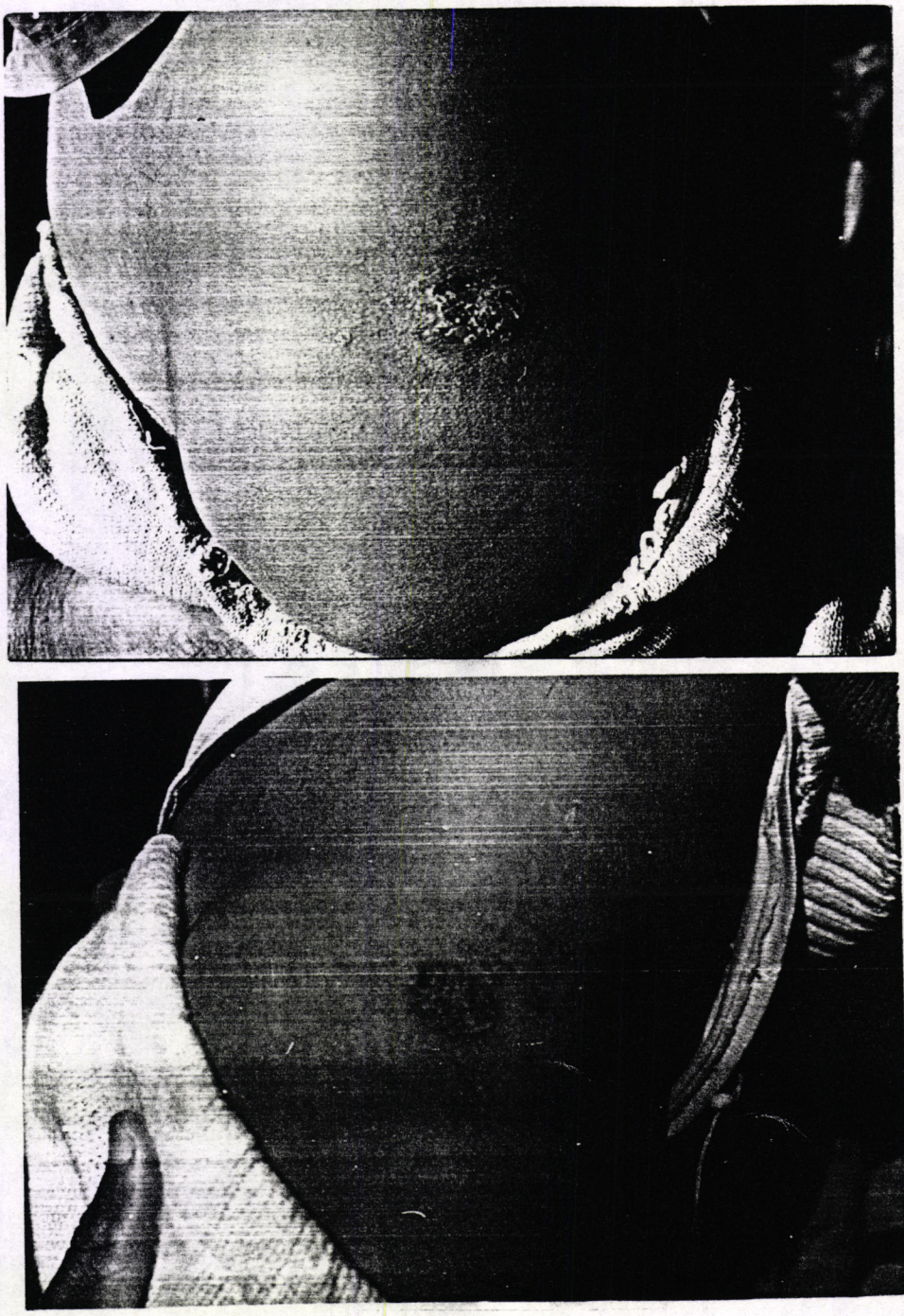

Fig. 3. Lesions of cutaneous leishmaniasis before and after treatment with HSCS 7% .
A- Before treatment.
B- After treatment.

Table.5 The outcome of 79 lesion treated with interlesional Pentostam

Response	Total No.	%	Dry	Wet
Cured	76	96.20	70	6
Mild improvement	3	3.8	1	2
Total	79	100.0	71	8

$\chi^2 = 10.454$ d.f = 1 $P < 0.05$

Table.6 : Number of injections needed in the cured lesions by Pentostam

No. of injection	Total No.	%	Dry	Wet
One injection	9	11.84	9	0
Two injection	65	85.35	61	4
Three injection	2	2.63	0	2
Total	76	100.0	70	6

$\chi^2 = 24.376$ d.f = 2 $P < 0.05$

Table.7 The outcome of 96 lesion treated with interlesional 7% "HSCS"

Response	Total No.	%	Dry	Wet
Cured	84	87.50	76	8
Mild improvement	12	12.50	4	8
Total	96	100.0	80	16

$\chi^2 = 20.743$ d.f = 1 $P < 0.05$

Table.8 : Number of injections needed in the cured lesions by 7% "HSCS"

No. of injection	Total No.	%	Dry	Wet
One injection	17	20.24	15	2
Two injection	64	76.19	60	4
Three injection	3	3.57	1	2
Total	84	100.0	76	8

$\chi^2 = 12.264$ d.f = 2 $P < 0.05$

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محاولة جديدة لعلاج داء اللشمانيات الجلدية بواسطة محلول المانيتول

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الخلاصة

أجريت هذه الدراسة في مقاطعة الحويجة والقرى المحيطة بـــها ، تـــم اختيار ثلاث قرى (الكاظمية ، صدر النهر والامينية). نسبة الإصابة العاليـــة بداء اللشمانيات الجلدية كان خلال اشهر الشـــتاء (كـــانون الأول 1996 اذار 1997). مجموع الإصابة الكلية كان 227 حالة (111 ذكور و 116 اناث) وكان اعلى نسبة الإصابة بين الاطفال الذين يـــتراوح اعمـــارهم مـــن 1-10 سنوات.

وجدت ان استخدام سائل المانيتول عن طريق الحقن الموضعـــي كـــان اكثر فعالا بنسبة (89.93 %) اعلى من محلول كلوريد الصوديوم مفرط التوتـــر (50.87 %) ولكن مشابه لمادة بنتوستام (20.96%).

معظم الافات تم شفائها بالزرقة الأولى والثانية والقليل منها احتاجت إلى الزرقة الثالثة .

في المجاميع الثلاثة المعالجة وجدت ان الندب كانت طفيفة أو معدومـــة عقب الالتئام ، لم يتم شفاء المجموعة الضابطة (غير المعالجة) خـــلال 6-8 اسابيع .

أستنتج من هذه الدراسة بأن محلول المانيتول (20%) هـــي طريقـــة موضعية فعالة لعلاج داء اللشمانيات الجلديـــة الحـــادة وان كفـــاءة 20% مـــن المانيتول مشابهة لمادة البنتوستام واكثر من 7% من محلول كلوريد الصوديـــوم المفرط التوتر.