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TREATMENT OF CUTANEOUS LEISHMANIASIS WITH METHANOL EXTRACT OF ALLIUM SATIVA (GARLIC), AZADIRACHTA INDICA (NEEM) AND ACCACIA NILOTICA (GARAD) IN GEZIRA CENTRAL OF SUDAN

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ABSTRACT

Objective: To assess the in vivo treatment of cutaneous leishmaniasis using certain medicinal agents and non medicinal agents in Gezira State, Sudan.

To evaluate the in vivo anti-lesihmanial activity of certain plant extracts that used traditionally in Sudan (Azadirachta indica (neem), Accacia nilotica (garad), Allium sativa (garlic, Thoum)).

Methodology: A total of 72cases with cutaneous leishmanisis were studied in Wad Madani Dermatology Teaching Hospital (September 1999 - December 2000). They were from different parts of the Gezira state.

The patients were interviewed and examined followed a special designed questionnaire .The cases showed different types of lesions with different duration and appeared in different areas of the body. The cases divided equally into six main groups (12 for each) for treatment with different agents including medicinal agents and plant methanol extracts.

Results: All cases showed good response (90.3%).The medicinal agents to plant methanol extracts response ratio was 1.0: 1. 03. Garlic had a 100% response it showed no significant difference with pentostam (control) (P= 0.75). Also Neem showed no significant with pentostam (p= 0.09). Leishmanol and garad showed significant differences with the control (p= 0.05 & 0.04 respectively).

Conclusion: According to the results we conclude that garlic and neem methanol extract have a good potential activity on leishmania parasite compaired to other studied agents.

Key words: leishmaniasis, Allium sativa, azadirachta indica, accacia nilotica

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INTRODUCTION

Cutaneous leishmaniasis is a skin involvement by leishmania parasite in which the amastigotes multiplication is restricted to the skin macrophages. In the Old World the disease is caused by the spp in the L. tropica complex and by L. mexicana in the New World.

In Sudan cutaneous leishmaniasis was first reported by Thomson and Balfour [1], and then the disease was reported in different parts of the country [2, 3]. Abdalla & Sharif [4] reported the first outbreak of cutaneous leishmaniasis in the Sudan in Shendi and Atbra area. The most severe outbreak was reported by (EL Safi and Peter [5] . Abdalla et al [6] who studied 21 cases of cutaneous leishmaniasis classified the lesions into three main types: nodular. Ulcerative and diffuse infiltrative types.

Different modes and/ or drugs (chemicals, acids anti-biotics, cryotherapy and medicinal plants) are used for cutaneous leishmaniasis treatment [7] . They showed either a slight or high effect on the parasites [8]. Pentavalent antimonial compounds are the first line-treatment. They are available in the form of sodium stigoglocunate (pentostam) and meglumine.

MATERIALS AND METHODS

The study was carried in the department of Dermatology, Wad Medani Teaching Hospital, Gezira State, Sudan (September 1999- December 2000). A specialized cutaneous leishmaniasis clinic was established and held for one day /week. 72 cases from different areas of Gezira State were included in the study.

The objectives of the study were clearly explained to the patients. All cases gave a written concents before their participation in the study. Each patient was interviewed and examined following a special designed questionaire. This includes age, sex, locality, site, types, size, number of lesions and their duration and treatment, follow up and observation.

Clinial diagnosis was confirmed by a definitive laboratory diagnosis in which the Leishman Donovan bodies (LD bodies) were demonstrated microscopically.

The study population (72 cases) had been divided equally into six categories . The first one, which is a reference or control group, was admitted to hospital and treated with

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intravenous pentostam. The starting dose was one mL, then one mL. was added daily up to 5mL (building dose), and then the patient was injected with 5mL daily or alternatively for 10 days. In every case an electrocardiogram and a full blood counts were done before the drug was administered.

The remaining groups were treated as out-patients orally or topically as followed:- The first group was subjected to metronidazole orally (750 mg/day) with cotrimoxazole (960 mg twice daily).The second group used leishmanol topically twice a day.The third group was treated with Neem methanol extract (100mg/mL) twice/ day. The fouth and fifth groups were treated in the same manner of Neem by using Garad and Garlic methanol extracts. All patients were followed up weekly for two months.

Assessment of treatment

Criteria for the efficacy of the treatment were diminution or absence of parasite and macroscopic resolution of the lesion. The following definitions were use according to Abdalla [6] .

Complete healing: smooth scar and parasite not detectable.

Partial healing: complete or almost complete re-epetilization and parasite not detectable.

Active lesion: the lesion with raised, reddish edges regardless the presence or absence of parasites.

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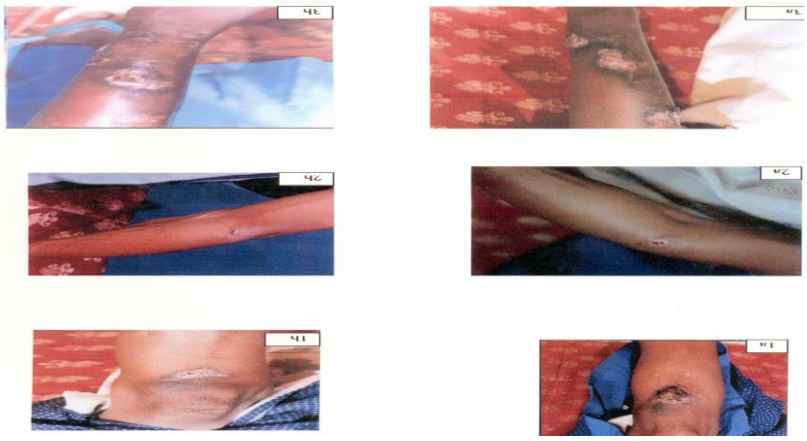
Photos: these phoograph show the progress of improvement.



RESULTS

The age of studied group (72 cases) was ranging between 3-63 years (mean= 28.2 years). The majority of them (31.9%) were in the group age 21-30 years

Males were 52.8% and females were 47.2% they were from different regions of Gezira State, (43.1% were from rural and 56.9% were from urban area).

31.9% of the cases had nodular lesions. Ulcerated lesions were noticed in 63.9% of cases (most common type). Nodular and ulcerated lesions were noticed in 2.8% of cases and only 1.4% of case had fungating-ulcerative lesion. These lesions were in different parts of the body but most of these lesions were located on unclothed areas. 87.5% of cases had at least one lesion on the lower or upper limb. The number of lesions varied from one patient to another. The total number of lesions was 402 with a mean of 5.5. Multipe lesions were very common. 61.1% of cases had number of lesions ranging from 1-5 lesion (s), the majority of this group had one lesion (22.2%). 25% of cases had (6-10) lesions, 8.3%of cases had (1115) lesions, and only 5.6% of patients had a number of lesions more than 15.

The lesions varied in size from few millimeters to more than three centimeters. Also their duration varid from few days to more than one year but in most of these cases (91.6%) the duration ranged from few days to three months.

Treatment

Over all cases (90.3%) showed good response while in 9.7% of cases there was no improvement lesions. Of cases which showed therapeutic treatment response 36.1% healed completely while the rest partially healed.

The response to pentostam and garlic was 100%. Of a single drug regimens there were 16.7% of cases failure in treatment for each of leishmanol, Neem and Garad and 8.3% for metrinodazole with co tri-mixazole. With standard treatment with pentostam ,the

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mean duration of effective treatment was 24.08 days while the shortest mean duration for effective treatment with garlic (19.75 days), and the longest mean was with metrinodazole (27.4 days).

DISCUSSION

Our study showed that all age groups and both sexes were exposed to leishmanial infection. The highest infection was observed in the group aged 21-30 years (31.9%). This fact was in agreement with Elsafi et al [5] and Gaafar et al (1995) studies [9]. The infection was widely spread in all regions of Gezira State involving urban and rural citizens, urban to rural ratios 1.3:1. This may be due to the agricultural nature of the State and its situation a long the bank of the Blue Nile in addition to the presence of canals in areas, which are remote from the river. Similar results had been reported by El Safi & Peter [5] , Abdalla and Sharif [4] .The variation in morphology of lesions indicated that the majority of cases reported late after ulceration (63.9%), this might be due to the fact that cutaneous leishmaniasis is painless. Patients seek for the treatment after ulceration and complications by secondary infection. Elsafi [5] study confirmed this finding. The study proved that infection could involve all parts of the body. The most infected parts are the limbs (87.5%). This may be due to the fact that the limbs are the most exposed areas to sandflies bite particularly at night. Elsafi et al [10] and gaafar et al [9] reported similar observations.

The duration of the lesions varied from few days to more than one year. Most cases showed duration between 1-3 months (91.6%). This goes with Elsafi et al [5] study. (2.8%) of cases in our study showed a duration more than five months. This result indicates that cutaneous leishmaniasis lesion can remain up for more than one year if patients were not treated. According to Abdalla et al [6] study, which indicates that (4.7%) of cases had a duration of lesions up to 18 months.

The size of lesions varied from few millimeters to more than three cm .This in accordance with Elsafi [5] results and Abdalla et al [6] who showed variations of lesions size from 1cm to 6 cm.

The number of leisons varied from one to sixteen lesions in one patient with a mean of (5.5) .El Safi et al [5] study reported that multiple lesions were very common among patients (80% of studied cases). Bell [11] reported that the number of leisons ranged from 1-25. WHO (2000) reported that, the disease can produce a large number of lesions

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some times up to 200 lesions causing serious disability leaving the patient permanetly scared, a stigma which can cause serious social prejudice.

Infection with leishmaniasis varies in site, extent, severity and prognosis and have different requirements for treatment [12] . So different agents were used for the treatment.

The agent used for treatment in our study showed a response in 90.3% of cases and only 9.7% of cases showed no response or complete failure. The response varied from complete healing to partial healing in period ranging from 15 to 45 days. The response ratio of medicinal agents to plant metanol extract was 1.03: 1 . This indicates the importance of considering folk Sudanese plants in the treatment of cutaneous leishmaniasis and other parasitic disease. This was supported by the study of Khalid et al [13] and Ibrahim et al [14] who showed that medicinal Sudanese are rich and diversified in the treatment of some diseases. However few studies investigated the potential usage of these plants.

Our study showed that the combination of metronidazole and co-trimoxazole cause response in 91.6% (11/ 12) of CL cases, but only 16.6% (2/12) showed complete healing. While the rest just showed a partial healing in period ranging from 15-37 days (mean 27.4 days). This result reflected that the combination of metronidazole and co tri-moxazole had an effectiveness of anti- leishmanial activity on cutaneous leishmaniasis with no significant difference with control (P= 0.195).

Leishmanol showed a response rate in 10 out of 12 cases (83.3%) ranging from 15 to 37 days mean (26days) however only 25% of cases showed compelet healing. One patient who had already been treated with leishmanol and showed complete healing showed a second leihmanial infection, which appeared at new sites after 5 weeks. This could be due to new infection or due to the development of previously very small lesion, which had not been noticed early. Recurrence was noted by El-kadaro et al [15] in Elizeragab Moreover another patient who had been treated with leishmanol showed dermatitis and exofoliative dermatitis as side effects. The methanol extracts of all studied plants were used topically twice a day with a concentration of 0.1g/ mL. Neem showed response in 83.3% (10/12) in period ranging from 15- 37 days (mean 21.67 days). From the responded cases 33.33% showed complete healing (see picture) and 50% showed partial response. The failure of treatment was shown in two cases. This

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may be due to the location of lesion (joint area). This result indicates that Neem can be considered as antileishmanial agent. Neem is used traditionally worldwide, in both the maintenance of general health and skin care [16] .It is clinically proven to be anti-parasitic, antifungal, anti-viral anti-bacterial and anti-inflammatory. Also it is proven to be effective against some seriou skin conditions like eczyma [16] .

The extract of garad showed response in 83.3% of cases but only 16.6% of cases showed complete healing. Garad showed significance with the standard (P= 0.04). However, it may be accepted as anti-parasitic according to El-Taher study [17] . Garad can not be accepted as approperiate anti-leishmanial agent according to our study result.

All cases treated with garlic methanol extract showed response (100%). In 91.6% (11/ 12) of cases this response occurred within 15-22 days (mean 19.75 days) (see pictures). However one case showed response within 30 days. It showed no significant difference with pentostam. 66.67% of cases showed complete healing in case of garlic while pentostam showed complete healing in 58.3% of cases only. This result indicates tat garlic can be considered as a powerful antileishmanial agent. It might be better than pentostam in the treatment of cutaneous leishmaniasis. There is no published work in the field of usage of garlic invivo against cutaneous leishmaniasis. However aquaeous extract of garlic was tried in the treatment of 10 children infected with Hymenolepis nana and 26 infected with Giardia lambia. It was foud to be efficient and safe and needs a short period of treatment. Also Venugopal and Venugopal [18] studied the ability of garlic to treat ringworm. They concluded that garlic could be used as an effective antidermatophytic agent and even more it may better than the standard anti-fungal drugs.

RECOMMENDATION

According to the above results we recommended garlic and neem extracts for treatment of cutaneous leishmaniasis. More research is needed to determine the active ingredient of the crude extract of garlic and neem.

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