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Journal of Dermatology & Dermatologic Surgery 19 (2015) 108–113

Original article

Treatment of cutaneous leishmaniasis by topical 25% podophyllin solution (single, blinded, therapeutic, controlled study)

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Received 30 July 2014; accepted 2 October 2014
Available online 19 February 2015

Abstract

Background: There are many therapies that had been used to treat cutaneous leishmaniasis (CL).
Objective: To evaluate the effectiveness of topical 25% podophyllin solution in treatment of CL.
Patients and methods: Sixty-five patients with acute CL enrolled in this study, which was done in the Department of Dermatology, Baghdad Teaching Hospital, Baghdad, during January 2008–April 2009.The total number of lesions was 124 and duration of lesions ranged from 3 to 12(6.84 ± 2.902) weeks. The size of lesions ranged from 0.5 to 3(1.75 ± 1.81) cm. Diagnosis was confirmed by biopsy and smear. Lesions were divided into two groups with matching of type and size of lesions
Group A treated with topical 25% podophyllin solution once weekly for number of sessions ranged from 3 to 6(4.51 ± 0.85) sessions.
Group B was left untreated as a control group. Follow up was every 2 weeks for 8 weeks.
Results: The total number of lesions was 120:79(65.84%) were ulcerated and 41(34.16%) were dry and 25(40.32%) patients had single lesion while 37(59.677%) patients had multiple lesions.
Group A: 51(85%) lesions out of 60 lesions had cure with number of sessions ranging from 3 to 6(5.137 ± 0.9385) sessions.
Group B: no lesion was cured.
Conclusions: Topical 25% podophyllin is a new effective topical therapy for CL, with few side effects.

Keywords: Cutaneous leishmaniasis; Podophyllin; Treatment

1. Introduction

Cutaneous leishmaniasis (CL) is a parasitic disease caused by several species of the genus *Leishmania* . It is an endemic disease in Iraq and other countries in Middle East, with fluctuation in their frequency, sometime reaching an epidemic state (Sharquie et al., 2001; Desjeux, 1992; Neouimine, 1996). Although, CL is self healing disease but spontaneous cure may take several months or even years (Sharquie et al., 2001; Harmay, 1986; Sharquie and Al-Talib, 1988) and can produce a large number of lesions (sometimes up to 200) causing serious disability invariably leaving the patient permanently scared, a stigma which

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Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.jdds.2014.10.001

can cause serious social prejudice (Sharquie and Al-Talib, 1988; WHO, 2001). Several topical therapies had been tested and found to be effective including intralesionally injected pentavalent antimony compounds (Sharquie and Al-Talib, 1988; WHO, 1984) hypertonic sodium chloride (Sharquie, 1995; Sharquie et al., 1994) zinc sulfate (Sharquie, 1995; Sharquie and Al-Azzawi, 1996) and electrotherapy (Sharquie et al., 1998) as well as topically applied paramomycin (El-On et al., 1985). The current recommended systemic treatment which has been in use since the 1950s is parentally administered pentavalent antimony compounds (Desjeux, 1992; Neouimine, 1996; WHO, 1984). Although effective, these can only be administered parentally, are expensive and may cause serious side-effects (Desjeux, 1992; Neouimine, 1996).

Podophyllin is an alcoholic plant extract obtained from dried rhizomes of common plants called emodi (Indian podophyllum) or podophyllum peltatum (May apple or mandrake) which belongs to Berberidaceae (barberry) family (Martin et al., 2004). Since the 1940s, it has been used topically for treatment of various skin lesions, especially for warts, molluscum contagiosum (Ahmed et al., 2008) and as an anti-neoplastic agents (Martin et al., 2004) where it had been used in the treatment of keratoacanthoma (Habif, 2004), oral hairy leukoplakia (James et al., 2006), multiple, superficial of infiltrating basal cell epithelioma, squamous cell epithelioma, seborrheic keratosis, and actinic keratosis (United State Pharmacopeia Committees, 2004) also it has antifungal activity (Rahman et al., 1995).

Podophyllin resin is an anti-mitotic and caustic agent with anti-viral activity (United State Pharmacopeia Committees, 2004; Reynolds, 1993; Sackett, 1993). The possible mechanism of action includes (Oslen and Dart, 2004; Canel, 2000; Moore and Strober, 2008): arresting cellular mitosis in metaphase, this is done by the reversal bind to tubuline which is the protein subunit of the spindle microtubules at a site that is the same of overlaps with the colchicines binding site thereby preventing polymerization of tubuline into microtubules. So it will disturb the cellular cytoskeleton. Also it blocks oxidation enzymes in tricarboxylic acid cycle, so it will interfere with nutrition of cells. In addition, it inhibits the axonal transport, protein, RNA, DNA synthesis and mitochondrial activity with the reduction of cytochrome oxidase activity.

Therefore the aim of the present study was to evaluate the effectiveness of topical 25% podophyllin solution in treatment of CL.

2. Patients and methods

This single, blinded, therapeutic, controlled trial was carried out in the Department of Dermatology, Baghdad Teaching Hospital, Baghdad, Iraq, during the period from January 2008 to April 2009.

A total of 65 patients with typical acute CL enrolled in this study; 35(53.8%) were females and 30(46.2%) were males and their ages range from 3 to 50 years with a mean ± SD of 22.89 ± 14.82 years. The total number of lesions was 124; 83(66.93%) ulcerated and 41(33.06%) dry and the size of lesions ranged from 0.5 to 3 cm in diameter with a mean ± SD of 1.75 ± 1.81 cm. The duration of lesions ranged from 3 to 12 weeks with a mean ± SD of 6.84 ± 2.902 weeks.

Full history and examination were performed including: age, sex, residence, job, duration, type, site.

Any patients with the following criteria were excluded from this study: Pregnancy (United State Pharmacopeia Committees, 2004), chronic diseases like diabetes mellitus, peripheral neuropathy, poor peripheral circulation, immune compromised patients and other severe illnesses and patients on prolonged corticosteroid therapy (Podophyllin in benzoin tincture, 1999), lesion with surface area more than 10 cm^2 or lesions close to eyes(United State Pharmacopeia Committees, 2004). Also, patients who received anti-leishmanial treatment either local or systemic and lesions of more than 12 weeks duration to exclude the possibility of self healing during follow-up period (Sharquie et al., 2001). Patients with re-infestation were also excluded.

Formal consent was taken from each patient after full interrogation and explanation to each patient about the nature of the disease, course, treatment modalities and complications, follow up, prognosis and the need for pre and post treatment photographs.

Also the ethical approval was performed by the Scientific Committee of the Scientific Council of Dermatology and Venereology-Iraqi Board for Medical Specializations. All the patients had been diagnosed by history and clinical examination, and confirmed by biopsy and smear.

In many patients, some lesions, which were located in the covered area, were untreated and left as a control after obtaining the consent of the patient. This is also beneficial to the patient as it gives long lasting immunity (WHO, 1984).

Regarding the therapy, lesions had been divided into two groups with matching of type and size of lesions.

Group A: treated with 25% topical podophyllin solution in tincture benzoin. It was prepared by dissolving 25 g of podophyllin resin powder, purchased from Merck Company, Germany, in 100 ml of tincture benzoin. This solution was applied with cotton-tipped applicator. The amount of solution that was used in each session did not exceed 0.5 ml and the surface area treated did not exceed 10 cm^2, in order to minimize the local and systemic side effects of the drug. The podophyllin solution was allowed to dry in approximately 2 min and patients were instructed to wash off it after 6–8 h. The solution was applied once weekly for maximum 6 weeks.

Group B: the lesions in this group received no treatment and left as a control group.

Follow-up of patients in two groups was every 2 weeks for 8 weeks and on each visit; all lesions were re-assessed to record the degree of the response and any local and