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Original Article

Comparison of efficacy of intralesional meglumine antimoniate vs. combination of 50% trichloroacetic acid and intralesional meglumine antimoniate in patients of cutaneous leishmaniasis

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Abstract

Objective is an endemic disease. This study was done to compare the efficacy of intralesional meglumine antimoniate (MA) with combination of 50% trichloroacetic acid (TCA) and intralesional meglumine antimoniate in patients of cutaneous leishmaniasis (CL).

Methods It was a randomized controlled trial conducted in department of dermatology, Military Hospital, Rawalpindi over six months i.e. 02-08-2016 to 01-02-2017. A total of 210 patients (105 in each group) were taken in this study. Group A received 50% TCA fortnightly with intralesional meglumine antimoniate and group B was treated with intralesional meglumine antimoniate alone.

Results Efficacy was observed in 91 (86.7%) patients of group A and in 78 (74.3%) patients of group B (p=0.024).

Conclusion Combination therapy with TCA 50% and intralesional MA accelerated the resolution of CL lesions with significant difference in complete resolution rate in comparison to the patients treated with intralesional MA alone.

Key words
Cutaneous leishmaniasis, intralesional injection, meglumine antimoniate, trichloroacetic acid, topical therapy.

Introduction

Cutaneous leishmaniasis (CL) is an endemic disease in 88 countries. The estimated annual incidence of new cases is 1.5 to 2 million cases per year globally. More than 350 million people are at risk world wide.[1]

Pakistan is one of the countries where CL is becoming an epidemic disease. And because of its morbidity and disfiguring scars, it is emerging as a major public health problem especially alongside regions bordering the neighboring Afghanistan and cities that have had the maximum influx of Afghan refugees.[2]

Treatment of leishmaniasis is often difficult. Many physical, topical, intralesional and systemic modalities have been suggested for cutaneous leishmaniasis. Although pentavalent antimonial compounds are still considered the standard treatment, their side effects and increasing rate of resistance have motivated

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researchers to seek safer and alternative modalities.[3]

Trichloroacetic acid (TCA) peeling is a long utilized procedure in dermatology. TCA is an analogue of acetic acid. It works by precipitating proteins and inducing coagulative necrosis of epidermis and/or papillary dermis followed by sloughing off of necrotic layers and re-epithelization, and promotes dermal collagen remodeling.[4] Topical TCA is not significantly absorbed and, therefore, does not produce systemic complications. Considering the TCA potential to induce collagen synthesis, it can be used as an adjuvant in treatment of CL.[5]

Different studies have shown variable effectiveness of TCA and meglumine antimoniate (MA) in treatment of CL. A study done in Iran showed an accelerated resolution rate with combination therapy of intralesional meglumine plus topical TCA, with 85.7% showing complete resolution in 8 weeks time as compared to 79.2%[3] of with intralesional meglumine alone. In another similar study success of MA alone was 70.9%.[6]

The present study was designed to evaluate the efficacy of intralesional meglumine antimoniate versus combination of 50% TCA and intralesional meglumine antimoniate (Glucantime®) in patients of CL. If found effective, then in future, topical 50% TCA could be suggested as an adjuvant therapy to accelerate the healing process and decrease the healing time of the lesions in patients of CL.

Methods

This study was a randomized controlled trial done in department of dermatology, Military Hospital, Rawalpindi, over a period of six months from August 2016 to February 2017. Sample size was calculated by using WHO sample size calculator for two proportions based on outcome variables, level of significance 5%, power of test 80%, anticipated population proportion (P1) 85.7%,[1] anticipated population proportion (P2) 70.9%.[6]

Considering 10% for loss to follow-up total sample size of 210 (105 in each group) was calculated. Patients in group A received intralesional MA twice weekly for 8 weeks and topical 50% TCA applied by cotton swab fortnightly for 8 weeks. Patients in group B received intralesional MA alone twice weekly for 8 weeks.

Efficacy was calculated in terms of clinical response (more than 75% reduction in size and induration of lesion) achieved at 8 weeks' time, which was measured by palpation and ruler using two largest perpendicular diameters. Measurements done before treatment and weekly till the end of eighth week.

Non probability consecutive sampling was done. Patients included in the study were clinically and histopathologically confirmed cases of CL from either gender, aged 15-40 years, with no visceral involvement and no previous history of systemic or topical therapy for CL. Patients with less than 5 skin lesions and less than 3cm diameter and of less than 12 weeks duration with no superimposed bacterial infection (culture negative) were included. Patients having any major concomitant illnesses like hepatic, renal or cardiac diseases and immunocompromised patients were excluded. Similarly, pregnant or nursing women were not included in the study group as well. Lesions located within 2cm distance of palpebral margin were excluded.

Patients of CL fulfilling the inclusion criteria were admitted in dermatology inpatient department (ward) at Military Hospital Rawalpindi after informed consent and

permission from Hospital Ethical Committee. Random allocation of patients was done into two groups: those reporting on even dates fallen in first group and those reporting on odd dates fallen in second group.

Response to treatment was graded as complete cure (complete re-epithelization of lesion, lack of induration and size reduction more than 75%), partial cure (partial improvement in erythema, induration and size reduction 50% to 75%), and non-cure (no significant improvement in lesion and size reduction less than 50%). All data was recorded on a proforma.

SPSS version 20 was used for analysis of the data. Qualitative variables like gender, efficacy, site of lesion were measured by frequency and percentage. Quantitative variables like age, number of lesions and duration of lesions were measured as mean±SD. Chi square test was applied to compare efficacy between two groups. P value ≤0.05 was taken as significant. Effect modifiers like age, gender, site, duration of lesion and number of lesions were controlled by stratification.

Results

Mean age of the patients was 31.38±4.64 years and 31.48±3.92 years in group A and B, respectively. There were 102 (97.2%) males in group A and 100 (95.2%) males in group B. Only 3 females (2.8%) were in group A and 5 (4.8%) in group B. Mean number of lesions in group A was 1.06±0.23 and in group B 1.08±0.26. In group-A mean size of lesion was 3.08±1.19cm^2 and in group-B mean size of lesion was 2.99±1.30cm^2. Mean duration of lesion was 8.87±1.77 weeks in group A and 7.87±1.72 weeks in group B. Sites of upper extremity were involved in 61 (58.1%) patients of group A and 55 (52.4%) patients in group B while sites of lower extremity were involved in 44 patients (41.9%) of group-A and 50 patients (47.6%) of group-B. Efficacy was observed in 91 (86.7%) patients of group A and in 78 (74.3%) patients of group B **(Table 1)**.

Table 1 Comparison of efficacy of intralesional meglumine antimoniate (MA) with trichloroacetic acid (TCA) vs. intralesional MA alone.

Efficacy	*Group A* *50% TCA with MA*	*Group B* *MA alone*
Yes	91 (86.7%)	78 (74.3%)
No	14 (13.3%)	27 (25.7%)
Total	105 (100%)	105 (100%)

Chi square = 5.122, P value = 0.024

Stratification was carried out with regard to age, gender, site of lesion, duration of lesion, size of lesion and number of lesions.

Discussion

Majority of leishmaniasis cases are more geographically concentrated, as 90% cases of visceral leishmaniasis (the most severe form of leishmaniasis) occur in six countries. 90% of CL cases (the most common type of leishmaniasis) occur in seven countries. It is very prevalent in Pakistan and has been reported from all provinces and almost all major cities. It is endemic in Baluchistan, Interior Sindh, North West Pakistan and Multan.[7]

CL has a huge social and economic burden.[8] Different treatment strategies have been described. The choice of treatment is often determined by the characteristics of the patient (age, gender, location of lesion, and immunity) and parasite (species variation). The treatment efficacy is also dependent on the geographical area.

The pentavalent antimonial meglumine antimonate (Glucantime®, Aventis, France, 85 mg $Sb5^+$/mL) for intramuscular and intralesional administration and sodium stibogluconate (Pentostam®, 100 mg $Sb5^+$/mL) for intravenous

and intramuscular administration have been used for decades for the treatment of CL, and are the gold standard for other new investigational drugs.[10]

The World Health Organization (WHO) recommendations for the treatment of CL are intralesional or systemic antimonials, according to the species and the clinical features.[11]

Topical TCA has different indications in dermatology. It is reported as a safe and effective treatment for benign pigmented lesions such as seborrheic keratosis, solar lentigines, melasma, and freckles with no significant complications.[12] El-Domyati *et al*.[13] reported epidermal and dermal rejuvenation in four patients with photodamaged skin treated with TCA.[13] Yug *et al.*[14] reported the treatment of three patients with acne scars by topical application of TCA 95%, resulting in cosmetic and histologic improvement of the depth of acne scars. Treatment of atrophic scars with TCA was associated with activation of dermal fibroblasts and increased collagen contents.[14] The same mechanism of new collagen formation and elastic fibers degradation might contribute to the accelerated healing process of CL lesions after topical application of TCA in combination therapy group.

Results of present study showed that combining topical TCA treatment with intralesional MA improves the efficacy of intralesional alone (86.7% vs. 74.3%). Topical application of TCA 50% have advantages when used as an adjuvant therapy to accelerate the healing process and decrease the healing time of the lesions in patients with CL. Further studies to assess the mechanism of action of TCA in the treatment of CL, its possible efficacy as combination therapy with other treatment modalities of CL, and assessment of its long-term usage side effects are warranted.

Conclusion

Combination therapy with TCA 50% and intralesional MA accelerated the resolution of CL lesions with significant difference in complete resolution rate in comparison to the patients treated with intralesional MA alone. Topical application of TCA 50% as an adjuvant therapy have advantages in decreasing the resolution time of the lesions in patients with CL.

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