Study

Therapeutic trial of sodium antimony gluconate alone and in combination with ketoconazole in post-kala-azar dermal leishmaniasis (PKDL)

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ABSTRACT

Background: Drugs used in PKDL include parenteral sodium antimony gluconate (SAG), amphotericin-B, pentamidine, and ketoconazole (KTZ). SAG is the most effective one. Given alone, SAG has to be given for a long duration, leading to poor patient compliance and treatment failure. This study was carried out to compare the effectiness of SAG alone and a combination of SAG and KTZ for sixty days. **Methods:** Ten patients of PKDL were included in the study. Five patients (Group A) were given SAG intravenously, in the dose of 20 mg/kg per day and five (Group B) were given SAG (intravenously 20 mg/kg per day) and KTZ (200 mg twice daily orally). Both treatment regimens were given for sixty days. **Results:** In Group A, the nodules and/or plaques showed approximate 80-85% clinical improvement, and macules showed 25-30% improvement. In group B (SAG + KTZ), there was 90-95% clinical improvement in the nodules and/or plaques and 25-30% in macules. **Conclusion:** This study suggests the therapeutic superiority of the combination treatment regimen in a shorter duration but is not conclusive as the number of patients was low. Further trials are recommended.

Key Words: Post-kala-azar dermal leishmaniasis, Sodium antimony gluconate, Ketoconazole

INTRODUCTION

Post-kala-azar dermal leishmaniasis (PKDL) is a distinct clinical entity, which follows an attack of visceral leishmaniasis (VL), usually after 6 months to 5 years.[1] *Leishmania donovani* is the causative organism for both PKDL and VL. PKDL is known for its refractoriness to various modalities of treatment. No satisfactory regimen has been developed. Medications generally used in PKDL include parenteral sodium antimony gluconate (SAG), amphotericin-B, nystatin and pentamidine. SAG is the most effective and needs to be given for 120 days as per WHO recommendation.[2] This long duration of treatment leads to incomplete treatment, treatment failure and relapses. Nystatin and amphotericin-B are usually avoided owing to their toxicity. Ketoconazole (KTZ), an antifungal agent, has been tried successfully in the treatment of VL.[3] It has been used alone in PKDL, but the duration required for clinical cure was inordinately long, with no response to short courses.[4,5] In this study, SAG alone and in combination with KTZ were compared to see whether the duration of therapy and toxicity could be reduced.

METHODS

Ten patients with clinical lesions suggestive of PKDL were included in the study. The diagnosis was based

How to cite this article: Rathi SK, Pandhi RK, Khanna N, Chopra P. Therapeutic trial of sodium antimony gluconate alone and in combination with ketoconazole in post-kala-azar dermal leishmaniasis (PKDL). Indian J Dermatol Venereol Leprol 2003;69:392-3.

Received: June, 2003. **Accepted:** July, 2003. **Source of Support:** Nil.

on clinical and histopathological examination. A tissue smear was made to demonstrate *Leishmania donovani* bodies. A slit skin smear was done to exclude acid-fast bacilli. The patients were randomly assigned either of the treatment regimens. Patients in Group A were given only SAG intravenously, in the dose of 20 mg/kg body weight daily, while those in Group B received a combination of SAG intravenously (20 mg/kg body weight per day) and ketoconazole orally (200 mg twice daily). Both the treatment regimens were given for a period of sixty days. Response to treatment, in the form of regression of lesions, was subjectively evaluated by two separate observers.

Complete hemogram, urine examination, and liver and renal function tests were performed before treatment, in between and at the end of the treatment period. All patients had an X-ray chest, ultrasound abdomen and VDRL test performed before treatment and had electrocardiographic monitoring.

RESULTS

The study included 9 males and 1 female aged between 18 and 30 years. All patients gave a history suggestive of VL in the past. Skin manifestations included nodules and/or plaques and hypopigmented macules, distributed mainly on the face, extremities and trunk, and extremities respectively.

Five patients were included in Group A, and were treated with SAG alone. Nodules and/or plaques showed approximately 80-85% clinical improvement after sixty days of treatment. However, in macular lesions 25-30% improvement was seen. In the five patients included in Group B (SAG + KTZ), there was 90-95% clinical response in nodules and/or plaques and 25-30% in macules after sixty days of treatment.

No patients were withdrawn from the study because of laboratory abnormalities. There was a transient rise of serum transaminases in four patients (three were from Group B); these returned to normal within 7-10 days of stopping treatment. Treatment in these patients was restarted without any adverse effects thereafter.

All the patients were followed up for one and half years. Lesions continued to show further improvement and there was no relapse.

DISCUSSION

Various treatment modalities have been tried in PKDL. Sodium antimony gluconate, in the dose 20 mg/kg body weight per day given up to maximum of 120 days, is the most effective of all the chemotherapeutic agents.[2] Ramesh et al observed that ketoconazole was effective in PKDL. They noted complete clinical cure in only one out of four patients treated with KTZ 800 mg/day for nine months.[4] The remaining patients developed side effects related to the drug. We compared the combination of SAG and KTZ at a lower dose to observe the response.

We observed that combination treatment has a slight edge over monotherapy but this difference is statistically not significant. Since the number of patients in both the treatment regimens is rather small, no conclusion can be drawn. The combination of KTZ and SAG does not increase efficacy sufficiently. Therefore, addition of KTZ, which may increase the toxicity as well as cost of the combination therapy, should be further evaluated taking more patients in each group.

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