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

S. K. Rathi, R. K. Pandhi, N. Khanna, P. Chopra*
From the Departments of Dermatology & Venereology and *Pathology, All India Institute of Medical Sciences, New Delhi, India.

Address for correspondence: Dr. Sanjay Rathi, 143, Hill Cart Road, Siliguri - 734401, India. E-mail: srathi2@rediffmail.com

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 effectiveness 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...
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.

REFERENCES

1. Acton HW, Napier LE. Post-kala-azar dermal leishmaniasis.
in the treatment of visceral leishmaniasis. Lancet
4. Ramesh V, Saxena U, Misra RS. Efficacy of ketoconazole in
post-kala-azar dermal leishmaniasis. Arch Dermatol
dermal leishmaniasis in the Sudan: clinical features, pathology