to progressive renal failure. Plasma phosphate and serum uric acid concentrations and blood pressure, however, were always within the normal range, and a renal biopsy specimen showed no evidence of interstitial nephritis and only minimal arteriolar hyalinisation. In the rat extensive renal ablation is followed by increases in glomerular capillary hydraulic pressure, glomerular capillary plasma flow rate, and single nephron glomerular filtration rate, and these changes may eventually cause glomerulosclerosis.³ Similar processes may have occurred in this case.

Children maintain stable renal function for up to 33 years after unilateral nephrectomy.⁴ Our patient had lost a large proportion of his renal substance 19 years before he developed renal failure, suggesting that the eventual development of glomerulosclerosis in human remnant kidneys depends on both the number of remaining nephrons and the interval since injury.

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Metronidazole and Indian kala-azar: results of a clinical trial

Visceral leishmaniasis is a disease of global importance, yet the choice of drugs available for its treatment is severely limited; so far there has been no satisfactory alternative to pentavalent antimony. Metronidazole is a time honoured drug with a wide margin of safety and a wide range of antiprotozoal activity. Anecdotal reports suggest that it may be effective in visceral leishmaniasis.^{1,2} We report our experience with this drug in Indian kala-azar.

Patients, methods, and results

We studied five men and five women with the disease. Their mean age was 26.7 (SD 9.0) years and mean weight 37.5 (SD 5.0) kg. After a thorough clinical examination and routine investigations bone marrow was obtained by sternal or iliac crest puncture and smears examined for amastigotes of *Leishmania donovani*.

Effect of metronidazole in individual cases

	Case No										Mean
	1	2	3	4	5	6	7	8	9	10	
Liver enlargement (cm):											
Before treatment	2	3	7	4	10	6	7	0	11	5	5.5
After treatment	0	0	3	0	3	4	1	0	6	4	2.1*
Spleen enlargement (cm):											
Before treatment	9	5	7	4	11	17	5	8	7	5	7.8
After treatment	2	2	3	0	4	15	2	4	0	3	3.5*
Total leucocyte count (×10 ⁹ /l):											
Before treatment	1.4	2.5	2.7	3.8	2.5	1.9	2.2	4.6	5.3	5.2	3.21
After treatment	3.9	5.5	6.7	6.6	5.2	1.8	3.3	8.0	10.1	5.7	5.68*
Haemoglobin (g/l):											
Before treatment	64	88	102	90	60	52	78	90	95	85	80.4
After treatment	86	110	115	116	70	72	100	96	120	110	99.5*
Day temperature became normal	6	4	4	4	5	†	†	†	6	5	4.9
Parasitological cure	Yes	Yes	Yes	Yes	No	†	†	†	Yes	Yes	
Follow up:											
Duration (months)	10	6	7	6	1	†	†	†	3	2	
Relapse	No	No	No	No	Yes	†	†	†	No	No	

* Compared with pretreatment value p<0.001.
† Switched to sodium stibogluconate at end of two weeks. In these three cases post-treatment values refer to those at end of two weeks.

Only parasitologically confirmed cases were studied. Patients with complications such as pulmonary tuberculosis, jaundice, and cardiac or renal failure were excluded, as were those who had ever received antimonials or any other specific treatment for kala-azar.

Each patient was given metronidazole for 12 days—25 mg/kg daily by intravenous infusion for five days followed by 40 mg/kg daily by mouth in four divided doses for seven days. Patients were assessed at regular intervals and any who did not show a satisfactory clinical response within two weeks were switched to antimony. In other cases the final assessment was made at the end of four weeks, when the bone marrow was also re-examined. The duration of follow up ranged from one to 10 months.

Student's *t* test for paired data was used to compare pretreatment and post-treatment values.

Six patients showed both clinical and parasitological evidence of cure and remained well for up to 10 months (table). Only two patients did not respond clinically. One patient (case 5) showed clinical but not parasitological evidence of cure, and another patient (case 7) withdrew from the trial just when her temperature had touched almost normal. Possibly a longer period of treatment might have succeeded in these last two cases. There were no appreciable side effects in any patient.

Comment

In six out of these 10 cases the results may be said to have been excellent, while two might be given the benefit of doubt; two cases were clear treatment failures.

Though experimental and in vitro studies^{3,4} must have dampened the enthusiasm of many workers, we decided to pursue this study as clinical results do not always conform to experimental findings. We are reasonably gratified by the results.

In view of the remarkable safety of metronidazole we suggest that it is worth a trial as a first line drug in visceral leishmaniasis; if treatment fails the patient may easily be switched to pentavalent antimony. The optimum dose, duration of treatment, route of administration, and mode of action, however, remain to be defined.

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