

## A double-blind trial of metronidazole versus oxytetracycline therapy for rosacea

E.M.SAIHAN\* AND J.L.BURTON

Department of Dermatology, Bristol Royal Infirmary, Bristol

Accepted for publication 17 July 1979

### SUMMARY

Forty patients with papulo-pustular rosacea were treated for 12 weeks on a random double-blind basis either with oxytetracycline 250 mg twice daily or with metronidazole 200 mg twice daily. Both drugs produced an improvement which was greater after 12 weeks than after 6 weeks, but there was no significant difference between them. Metronidazole appears to be a safe and effective drug for the treatment of rosacea.

The antibiotic metronidazole (Flagyl) has been shown to be significantly better than a placebo in the treatment of rosacea (Pye & Burton, 1976) but it has not been tested against conventional therapy; we have now performed a double-blind trial of metronidazole versus oxytetracycline.

### MATERIALS AND METHODS

Forty patients with papulo-pustular rosacea were treated either with oxytetracycline 250 mg twice daily (30 min before meals) or with metronidazole 200 mg twice daily on a random double-blind basis, coded tablets being issued by the pharmacist. None of the patients had received antibiotics for 4 weeks prior to the trial. Each patient was assessed before treatment by one author (E.S.), the severity of the papulo-pustules being graded as mild, moderate or severe. The patients were assessed again after 6 weeks' and 12 weeks' treatment and the patients' condition relative to the initial visit was independently recorded as 'worse', 'unchanged', 'slightly improved', 'moderately improved' or 'much improved', by the same doctor and by the patient. The patients were photographed in colour under standard conditions at each visit and after their final visit the three photographs were evaluated by the second author (J.L.B.). The two photographs taken during therapy were compared with the initial photographs and the changes noted were recorded in the same way. The independent opinions of the patient and two doctors were thus obtained at 6 and 12 weeks for each subject and a numerical value was assigned to each of the three opinions, as follows: worse (-1); unchanged (0); slightly improved (1); moderately improved (2); much improved (3). The mean of the three opinions was then recorded and only then was the treatment code broken for the further analysis of the results.

\* Present address: The London Hospital, Whitechapel, London.

TABLE 1. Degree of improvement in rosacea, expressed on an arbitrary numerical scale (mean  $\pm$  s.d.) described in the text

	Oxytetracycline	Metronidazole
6 weeks	1.8 $\pm$ 0.9	1.6 $\pm$ 0.9
12 weeks	2.6 $\pm$ 0.7	2.3 $\pm$ 1.0

#### RESULTS

Twenty patients receiving oxytetracycline and eighteen patients receiving metronidazole completed the trial. The results (Table 1) show that both drugs produced an improvement, and there was no significant difference between them. Both drugs produced significantly more improvement after 12 weeks than after 6 weeks ( $P < 0.05$ ). No side-effects were reported in either group, but two patients taking metronidazole failed to attend for follow-up after the initial visit.

#### DISCUSSION

Several groups have shown that metronidazole is an effective treatment for rosacea (Pye & Burton, 1976; von Braun, Koester & Taube, 1978; Guilhou *et al.*, 1978) and the present double-blind study has shown that the response to metronidazole does not differ significantly from that produced by oxytetracycline.

The beneficial effect of metronidazole in rosacea cannot be explained since the cause of the disease is unknown. Metronidazole acts against a wide variety of protozoa and anaerobic bacteria, but it also has anti-inflammatory and immunosuppressive effects (Tanga, Antami & Kabade, 1975; Grove, Mahmoud & Warren, 1977).

Metronidazole is a relatively safe drug, although it can occasionally cause alcohol-induced headaches by a disulfiram-like effect (Penick, Carrier & Sheddon, 1969) and neuropathy has also been reported (Coxon & Pellis, 1976). It has mutagenic effects in some bacteria (Voogd, van der Stell & Jacobs, 1974) but the significance of this in man is uncertain.

Oxytetracycline is probably a safer drug than metronidazole for long-term use but the latter has the advantage that it is tolerated well during pregnancy and has no adverse effects on the offspring (May & Baker, 1979) whereas tetracycline administered in the last trimester causes discoloration of the fetal teeth.

We conclude that metronidazole is a worthwhile drug for the treatment of papulo-pustular rosacea, especially in patients who have not responded to tetracyclines, or for pregnant women in whom systemic treatment is essential.

#### REFERENCES

- VON BRAUN, W., KOESTER, H. & TAUBE, K.M. (1978) Metronidazole bei Rosacea. *Dermatologische Monatsschrift Bildung*, **164**, 197.
- COXON, A. & PALLIS, L.A. (1976) Metronidazole neuropathy. *Journal of Neurology, Neurosurgery and Psychiatry*, **39**, 403.
- GROVE, D., MAHMOUD, A.A.F. & WARREN, K.S. (1977) Suppression of cell-mediated immunity by metronidazole. *International Archives of Allergy and Applied Immunology*, **54**, 422.

- GUILHOU, J.J., MEYNADIER, J., GUILHOU, E. & MALBOS, S. (1978) Traitement de la rosacée par le metronidazole. *Nouvelle Press Medicale*, **7**, 1960.
- MAY & BAKER LTD (1979) *Flagyl, Data Sheet Compendium 1979-80*, p. 558. Pharmind Publications, London.
- PENICK, S.B., CARRIER, R.N. & SHEDDON, J.S. (1969) Metronidazole in the treatment of alcoholism. *American Journal of Psychiatry*, **125**, 1063.
- PYE, R.J. & BURTON, J.L. (1976) Treatment of rosacea by metronidazole. *Lancet*, **i**, 1211.
- TANGA, M.R., ANTAMI, J.A. & KABADE, S.S. (1975) Clinical evaluation of metronidazole as an anti-inflammatory agent. *International Surgery*, **60**, 75.
- VOOGD, C.E., VAN DER STELL, J.J. & JACOBS, J.J. (1974) The mutagenic action of nitroimidazoles. I. Metromidazole, nimorazole, dimetridazole and ronidazole. *Mutation Research*, **26**, 483.