Brit. J. Psychiat. (1968), 114, 859–861

Metronidazole and Alcoholism*

By JULIUS MERRY and ARNOLD WHITEHEAD

Metronidazole (Flagyl) is an established and effective treatment of urogenital trichomoniasis. J. A. T. Taylor (1964) was using metronidazole to treat a husband and wife for this condition, when she observed the following. The husband, who was a chronic alcoholic, seemed to lose his craving for alcoholic drinks. Sometimes he experienced flushing of the face and shoulders and epigastric discomfort when he took metronidazole soon after alcohol, i.e. he experienced a disulfiram type reaction. The wife reported that alcohol drinks tasted unpleasant to her during therapy. Taylor then studied 53 alcoholic patients and concluded that metronidazole (*i*) decreased tolerance for alcohol, (*ii*) diminished craving for alcohol and (*iii*) produced an uncomfortable reaction to alcohol.

We decided to assess the effect of the drug on the drinking habits of chronic alcoholics.

Method

The subjects were volunteer male residents of St. Luke's House, a rehabilitation centre for chronic alcoholics. The residents leave for work after breakfast and return to the House for an evening meal. After this they may enjoy the House facilities or may seek entertainment outside, before retiring in the House for the night.

Experiment 1

The volunteers numbered 20, and their ages ranged from 25 to 55; they all had a history of chronic alcoholism, of the loss of control variety, of more than five years. They had been told the nature of metronidazole and of Taylor's conclusions on it.

The volunteers were given 400 mg. metronidazole at breakfast and 400 mg. at the evening meal. Meals were taken in the small dining room where the residents were clearly observed by the staff, and it was quite certain that the subjects did take the tablets, which are rather unpalatable. The drug was deliberately given at the two meal-times because of the known unreliability of unsupervised medicine-taking (Willcox *et al.*, 1965), and in this way we were reasonably certain of the prescribed medication. The metronidazole was taken over a period of 30 days and its effect on the drinking behaviour recorded. During this period the subjects had no other prescribed medication. A control group was established of 20 other residents, randomly selected from the chronic alcoholic residents of the same age group and with similar length of history; these were having either no prescribed medication or else a variety of drugs, e.g. disulfiram, tranquillizers or anti-depressant drugs in various combinations.

Results (*Experiment 1*)

	Metronidazole Group	Control Group
Abstinent	9	14
Drink on 4 days or less ..	1	4
Drink on 5 days or more..	6	2
Discontinued	4	0
Total	20	20

The four subjects in the metronidazole group who discontinued did so for varying reasons and at different stages of the experiment.

The staff had been worried by the introduction of an unproved drug and the possible disastrous effects on a community where sobriety is the goal. We considered it possible that staff anxiety had been transmitted to the rest of the community and might have influenced the outcome. As it happened, the staff were relieved that a disaster had not occurred, and we therefore decided to repeat the experiment, this time against a background of staff confidence.

* With Appendix on Metronidazole and Heroin Addiction by Julius Merry.

https://doi.org/10.1192/bjp.114.512.859 Published online by Cambridge University Press

Experiment 2

On this occasion, 12 volunteers participated, and the dosage of metronidazole was increased to 600 mg. b.d. over the same period of 30 days. This group was compared with itself (group A) over the preceding 30 days during which they had also been resident, and with another random sample of 12 residents (group B) selected in the same manner as in Experiment 1.

Results (*Experiment 2*)

	Metronidazole	Group A	Group B
Abstinent	10	12	8
Drink on 4 days or less	0	0	3
Drink on 5 days or more	1	0	1
Discontinued	1	0	0
Total	12	12	12

Discussion

Ban *et al.* (1966), reporting a study of 10 alcoholic in-patients, claimed that metronidazole (*i*) was useful for treating withdrawal symptoms (2 out of 3 patients) and (*ii*) produced an unpleasant reaction to alcohol in a proportion of patients, viz. a disulfiram type reaction.

Pearson and Strassmann (1965, unpublished) compared the effect of two almost identical pharmacological regimes, one containing metronidazole and the other disulfiram, on two groups of chronic alcoholic patients in post-withdrawal phase. They found a possible superiority in the metronidazole regime.

Semer *et al.* (1966), in an uncontrolled pilot study on 26 patients with doses ranging from 500–750 mg. daily, obtained good results in 24 patients. There have been other favourable reports on the metronidazole treatment of chronic alcoholics repeating some or all of Taylor's conclusions. However, many of these studies have been on either very small samples or on patients taking other psychotropic drugs concurrently and/or without control groups. Goodwin (1967), in a controlled double-blind trial on 12 patients with dosages of 500–750 mg., failed to confirm Taylor's findings. Rowe and Atkinson (1966, unpublished) conducted an experiment on themselves, and failed to show any significant change in blood ethanol levels or unpleasant reactions from taking 1 gram of metronidazole one hour before the ingestion o 150 ml. of 70° proof whisky.

In our experiment 1, only 16 patients completed 30 days on metronidazole. Thus 9 out of 16 patients were abstinent, and comparison with the control group reveals no significant difference.

In experiment 2, comparison of the metronidazole group with Group A and Group B again revealed no significant difference in the rate of relapse into drinking. No patients reported a reduction in craving, and only one patient reported a reaction to alcohol of epigastric pain and slight flushing.

In experiment 1, of the four subjects in the metronidazole group who discontinued, two left St. Luke's House during the experiment, while two subjects decided to revert to disulfiram, which they felt gave them more confidence in resisting alcohol. In experiment 2, one subject taking metronidazole was discontinued because he left St. Luke's House during the experiment.

Our experiment had the advantage over other investigations that our subjects, by virtue of living in a hostel and going out to work, were subjected to the stresses and strains of everyday life and also had ready access to alcohol. In addition, the administration of the metronidazole was under very close supervision so that we were reasonably certain that our volunteer subjects were taking the prescribed dosage. Finally, the hostel arrangements and the supervision by the experienced staff meant that relapse into drink was immediately detected.

Conclusion

Following reports that metronidazole reduces craving for alcohol, produces distaste of alcohol, and causes an unpleasant reaction when taken with alcohol, controlled trials were conducted on two occasions over a period of 30 days. In the first experiment, 20 subjects took 400 mg. metronidazole twice daily, and in the second experiment 12 subjects took 600 mg. twice daily. These experiments showed that metronidazole

https://doi.org/10.1192/bjp.114.512.859 Published online by Cambridge University Press

in these dosages is as effective as, but not superior to, other treatments of chronic alcoholism, e.g. with no drugs at all, or with disulfiram or citrated calcium carbimide, or with a variety of psychotropic drugs.

ACKNOWLEDGMENTS

We wish to thank Dr. W. S. Marson for his permission to include his patients in the trials. We are indebted to the assiduous staff of St. Luke's House for their invaluable help. Finally, our thanks are due to May and Baker Ltd. for providing the metronidazole (Flagyl).

REFERENCES

BAN, T. A., LEHMANN, H. E., and ROY, P. (1966). *Union Médicale du Canada*, 95, 147.
GOODWIN, D. W. (1967). *Amer. J. Psychiat.*, 123, 1276.
PEARSON, A. W., and STRASSMANN, H. (1965). Unpublished.
ROWE, A. J. E., and ATKINSON, A. A. (1966). Unpublished.
SEMER, J. M. *et al.* (1966). *Amer. J. Psychiat.*, 123, 722.
TAYLOR, J. A. T. (1964). *Bull. Los Angeles Neurolog. Soc.*, 29, 158.
WILLCOX, D. R. C. *et al.* (1965). *Brit. med. J.*, *ii*, 790.

APPENDIX

METRONIDAZOLE AND HEROIN ADDICTION

By JULIUS MERRY

Following a report by Semer *et al.* (1966, unpublished) of the successful treatment of three heroin addicts with metronidazole, I used metronidazole on eight out-patient heroin addicts who were having maintenance doses of heroin. Metronidazole was prescribed in a dosage of 300 mg. t.d.s. Whilst this regime did not help to persuade the addicts to further reduce their intake of heroin, they opined that the metronidazole was as helpful, or unhelpful, as the psychotropic drug which they had formerly taken with the heroin and for which the metronidazole had been substituted. Thus I failed to confirm the observations of Semer *et al.*

REFERENCES

SEMER, J. M. *et al.* (1966). Unpublished.

Julius Merry, M.D., D.P.M., *Consultant Psychiatrist, Lambeth and St. Thomas's Hospitals, London, and West Park Hospital, Epsom, Surrey*

Arnold Whitehead, B.D., *Warden, St. Luke's House, 25a Wincott Street, S.E.11.*

(*Received 23 June, 1967*)

https://doi.org/10.1192/bjp.114.512.859 Published online by Cambridge University Press