

Oxprenolol and Ventricular Ectopic Activity of the Heart

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SUMMARY

Oxprenolol (Trasicor), a beta-receptor blocking agent widely used in angina pectoris, was evaluated for its possible arrhythmogenic or antidysrhythmic effects. In a randomised double-blind within-patient trial, 44 physically active postmyocardial infarction patients completed the trial. Ventricular ectopic activity was evaluated on a magnetic tape and recorded over 7-hour periods while the patients were active at work. No deleterious effects were noted in 73%, an increase in electrical stability was noted in 23% and only one patient was evaluated as being worse while on the drug.

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The widespread use of beta-receptor blocking agents in ischaemic heart disease is presently well established. As it is currently believed that the high incidence of sudden death in these high-risk patients is related to electrical instability of the myocardium,¹ the negative chronotropic effect of these agents might theoretically lead to ventricular escape rhythms with deleterious results. This study reports the effect of oxprenolol on ventricular ectopic activity in active postmyocardial infarction patients. From the beta-receptor blocking agents currently available, oxprenolol was selected because of its beta-stimulating and its local anaesthetic properties on the myocardium.²

PATIENTS AND METHODS

Fifty patients who had suffered an acute myocardial infarction (AMI) more than one month previously and on normal daily activity, were studied. They were divided into two groups according to the time elapsed since infarction. Group I included 36 patients studied less than 3 months after infarction, and group II included 14 patients 3 months or longer after infarction.

Detailed documentation in regard to hospital course and functional status at the time of evaluation was available in all cases. No patient was suffering from angina pectoris and no-one was on anti-arrhythmic drugs at the onset of the trial. The purpose of the study was

explained and the patients' co-operation ascertained. They were required to keep a diary and to log assessments on visual analogue scales. Special emphasis was placed on general feeling of well-being, chest pain and the awareness of palpitations.

The trial was designed as a randomised double-blind within-patient study. Oxprenolol in a fixed dose of 40 mg *t.d.s.* for 2 weeks and then placebo, or vice versa, was evaluated. On day 1, a history, physical examination, resting ECG, chest X-ray films, fasting blood sugar, serum lipids, uric acid and thyroxin, and a control 7-hour ECG on magnetic tape³ were obtained. On day 2, therapy was initiated and the above-mentioned investigations repeated on day 14. On day 15 the alternative therapeutic regimen started and a similar evaluation was performed on day 28. The magnetic tapes were recorded with the patients active at work, but they were instructed, to the best of their ability, to see that their activities remained the same on the days of monitoring. The quanta of ventricular ectopic beats (VEB) were graded from 0 to 4 (Table I), and a positive or negative result was documented only when the quantum changed by one or more grades.

TABLE I. GRADING OF NUMBER OF VENTRICULAR ECTOPIC BEATS

Grade	No. of VEB per hour	Total No. of VEB over 7 hours	Approximate No. of VEB per normal sinus beat
0	0	0	0
1	<1	1 - 6	<1/3 600
2	1 - 7	7 - 49	1/3 600 - 1/500
3	8 - 50	50 - 350	1/500 - 1/70
4	>50	>350	>1/70

RESULTS

In group I, 6 patients did not complete the trial—for reasons which were not drug-related. The results, in regard to the change in the absolute number of VEB while on oxprenolol, are shown in Table II. It is evident that in most cases no impressive change occurred. A definite decrease in the quantum of VEB was observed in 11 (25%) of the cases on oxprenolol. Only one patient in the entire group was evaluated as being worse. This patient had 17 VEB over the control 7-hour testing period, >1000 VEB while on oxprenolol and zero VEB while on the placebo, and was thus graded as 2-4-0, according to the classification.

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TABLE II. NUMBER OF VEB WHILE ON OXPRENOLOL

Patients	Unchanged	Decreased	Increased	Total
Group 1 (1 - 3 months after AMI)	22 (73%)	7 (23%)	1 (3%)	30
Group 2 (3 months after AMI)	10 (71%)	4 (29%)		14
Total	32 (73%)	11 (25%)	1 (2%)	44

TABLE III. PATIENTS' SELF-ASSESSMENT WHILE ON OXPRENOLOL

Patients	Unchanged	Better	Worse	Total
Group I	14 (47%)	12 (40%)	4 (13%)	30
Group II	9 (64%)	1 (7%)	4 (29%)	14
Total	23 (52%)	13 (30%)	8 (18%)	44

The patients' preference in regard to a feeling of well-being while on oxprenolol versus placebo is depicted in Table III. The subjective assessment regarding palpitations proved to be unrealistic. Even although they were specifically asked to assess the incidence of palpitations, most patients were quite unaware of them. No statistically significant change was observed in the patient's functional status, resting ECG, heart size on X-ray film, fasting blood sugar, serum lipids, uric acid or thyroxin determination.

DISCUSSION

It has been shown that in patients with ischaemic heart disease, the manifested VEB tend to remain remarkably constant in individual patients. This behaviour is reflected in both the total number of VEB over extended periods of time as well as in the configuration of these VEB, thus bringing about a valid model for the evaluation of a drug's possible effects on the rhythm of the heart.⁴ It is also evident that the wide variation in coupling

periods of VEB with identical configuration strengthens the possibility that an automatic firing focus is operating in many.⁴ Thus any drug with negative chronotropic qualities would theoretically potentiate manifestation of such a focus.

In the present study no significant difference in the total number of VEB was noticed in 73% of patients, a decrease in 25%, and an increase in only 2% while on oxprenolol. Admittedly a slower heart rate was not aimed at with the dose employed. On the other hand, the relative influence of the supposedly detrimental negative chronotropic effect versus the beneficial membrane anaesthetic effect of the drug, is still unexplained. Also the suggestion that bradycardia predisposes to malignant ventricular dysrhythmia⁶⁻⁷ may not be totally correct, and, in fact, a relative bradycardia *per se* may exert a protective function.^{8,9} In contrast with an automatic firing focus, if a re-entry mechanism is implicated in these patients, again the change in rate, whether faster or slower, must be very critical for the manifestation of ectopic beats.¹⁰

Although the exact significance of VEB in the presence of ischaemic heart disease remains enigmatic and a definition of life-threatening arrhythmias still lacks precision, drugs having an effect on rhythm must be treated with suspicion until more information becomes available. Oxprenolol, a potent beta-receptor blocking agent, does not appear to have deleterious rhythm properties.

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