Plasma Concentration and Antihypertensive Effect of β -Receptor Blockers

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In the past years, several attempts have been made to correlate dosage, plasma concentration and effect of certain drugs to their pharmacological activity. Among others, such attempts have also been made with β -receptor antagonists. Whereas Zacest and Koch-Weser (1972) found a linear relationship of β -blockade to the logarithm of the plasma concentration of propranolol, Sundquist et al. (1974) could not find any correlation between the dosage and serum concentration of practolol on one hand, and a reduction of both systolic and diastolic blood pressure and of heart rate in patients with mild to moderate hypertension on the other.

In order to test patient compliance and to compare the antihypertensive effect and the reduction in heart rate, due to β -receptor blockers, to blood levels, the plasma concentrations of propranolol, oxprenolol and timolol were measured in three groups of patients with mild to moderate hypertension. These measurements were carried out gas-liquid-chromatographically, according to the method of Jack and Riess (1974), modified by Horwatitsch (unpublished method).

20 patients treated in our out-patient clinic with propranolol and 18 patients treated with oxprenolol and 6 patients treated with timolol were examined. Blood was drawn casually in the morning approximately 2–3 h after the reported ingestion of the drug, and the concentrations were compared to the reduction in systolic and diastolic blood pressure and in heart rate regarding the blood pressure and heart rate values before the beginning of treatment.

Since the number of patients on timolol was too small to evaluate the results statistically the following tables and graphs will only show the results with propranolol and with oxprenolol.

Figures 1 and 2 show the correlation

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Fig. 1. Correlation between daily dose of propranolol and plasma concentration.

Fig. 2. Correlation between daily dose of oxprenolol and plasma concentration.

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Plasma concentration of propranolol, ng/ml

Fig. 3. Correlation between plasma concentration of propranolol and change in systolic (o) and diastolic (•) blood pressure.

Fig. 4. Correlation between plasma concentration of oxprenolol and change in systolic (o) and diastolic (•) blood pressure.

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Plasma concentration of propranolol, ng/ml

Fig. 5. Correlation between plasma concentration of propranolol and change in heart

Fig. 6. Correlation between plasma concentration of oxprenolol and change in heart rate.

Table I

Propranolol (n = 20)

Oxprenolol (n = 18)

mean mean blood pressure, mm Hg		dose		plasma concentration		mg/day		mean		heart rate	
beats/min		dose		plasma		mg/day		concentration		systolic diastolic	
113.5	51.56	171/106	-8.5	-3.74	-14	± 62.6	± 7.18	± 37/15.9	± 21.89	± 12.13	± 15.83
216.47	292.76	± 47.03	± 258.98								
177/108	-23.22	-11.75	-7.51	± 32/12.74	± 25.32	± 12.76	± 9.60				

heart rate
blood pressure, mm Hg
mean lowering of beats/min
systolic diastolic

113.5 51.56 171/106 -8.5 -3.74 -14
± 62.6 ± 7.18 ± 37/15.9 ± 21.89 ± 12.13 ± 15.83
216.47 292.76 ± 47.03 ± 258.98
177/108 -23.22 -11.75 -7.51 ± 32/12.74 ± 25.32 ± 12.76 ± 9.60

(range: (range: 30–240) 0–168*)

(range: (range: 80–240) 0–1,040**)

p < 0.01

p < 0.01

Bad compliance: plasma concentration * 0–7 (n = 3); ** 0–26 (n = 3).

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between prescribed doses and plasma concentrations. Figures 3 and 4 show the correlation between the reduction in blood pressure (systolic and diastolic) for propranolol and oxprenolol and figures 5 and 6 show the reduction in heart rate for propranolol and oxprenolol. As can readily be seen there is no correlation to be found between the plasma concentration of the respective drugs and their effect on blood pressure or heart rate.

Table I shows the average dose, plasma concentration, systolic and diastolic blood pressure, reduction of systolic and diastolic blood pressure and reduction of heart rate for both drugs. The table shows that the mean prescribed dose for propranolol was significantly lower than the dose for oxprenolol and so was the plasma concentration. Nevertheless, the height of blood pressure, the reduction of systolic and diastolic blood pressures and the reduction of heart rate did not differ significantly in both drug groups.

The compliance turned out to be quite satisfactory. Only 3 patients in either group had lower concentrations of the respective drug than could be expected from the prescribed dosage.

The results of our study show that the antihypertensive effect and the effect on heart rate (at least at rest) depend not only on plasma concentration but must be due to other factors also.

References

Jack, D.B. and Riess, W.: Determination of low levels of oxprenolol in blood or plasma by gas-liquid chromatography. *J. Chromat.* 88: 173–176 (1974). Sundquist, H.; Anttila, M.S., and Arstila, M.: Antihypertensive effects of practolol and sotalol. *Clin. Pharmac. Ther.* 16: 465–472 (1974). Zacest, R. and Koch-Weser, J.: Relation of propranolol plasma level to β -blockade during