

## A DOSE REGIMEN FOR METOPROLOL IN THE TREATMENT OF MYOCARDIAL INFARCTION

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Recent studies suggest that beta adrenoreceptor drugs have the potential to reduce infarct size as well as acting as antidysrhythmic agents in post myocardial infarction. (Norris et al 1978; Yusef et al 1980). In these emergency situations induction of beta blockade will require intravenous medication in order to achieve rapid onset of action. Reports in normal volunteers suggest that effective beta blockade is attained in man with metoprolol plasma concentrations of 50-100ng ml<sup>-1</sup> (Jennings et al 1981). This study was undertaken to evaluate the pharmacokinetics of metoprolol after intravenous dosing in patients with cardiac disease, in order to design a dose regimen for the rapid attainment and maintenance of beta blockade in the post infarction patient. The kinetics were determined after 5mg and 10mg bolus doses in 5 and 3 patients respectively and after a 0.025mg kg h infusion and a 0.05mg kg<sup>-1</sup>h<sup>-1</sup> infusion in 5 and 4 patients respectively. Plasma concentrations were determined at suitable times using a G.C. method based on that of Ervick (1976). The disposition parameters obtained after data analysis using standard methods are given in Table 1. Based on these results a regimen of a bolus dose of 5mg with simultaneous commencement of an infusion of 0.05mg kg<sup>-1</sup>h<sup>-1</sup> plus a second bolus dose at 15min of 5mg was proposed. This regimen was investigated in six patients. The regimen attained a concentration of 80±18ng ml<sup>-1</sup> after 30 min, 50±14ng ml<sup>-1</sup> after 2h, 63±19ng ml<sup>-1</sup> after 4h and 57±18ng ml<sup>-1</sup> after 6h. These concentrations would give adequate beta blockade and the regimen is, therefore, recommended for the use of metoprolol in prophylactic treatment of post myocardial infarction.

Table 1. Mean disposition parameters of metoprolol after i.v. dosing in patients with cardiac disease.

Dose	Clearance (L/h)	Volume of Distribution (L)	Half Life (h)
10mg bolus	66	146 ± 42 (a)	1.5 ± 1.7
3.25mg h <sup>-1</sup> infusion (b)	54	102 ± 24	1.28 ± 0.43

(a) Standard Deviation  
(b) Based on average weight of 65kg

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