

the Bence Jones proteins resulted in excellent recovery of renal function with survival much longer than expected on conventional treatment alone.

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Reprint requests should be sent to SLC.

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Comparison of effects of metoprolol and propranolol on asthmatic airway obstruction

Propranolol, which acts unselectively on cardiac (β_1) and bronchial (β_2) adrenoceptors, may cause bronchoconstriction in asthmatic subjects. This risk is less with the cardioselective beta-adrenoceptor blocking drugs practolol or acebutolol.¹ Practolol has been in use the longer of the two and until recently was thought not to cause adverse reactions, but as more patients have been treated with it in the long-term some have developed serious side effects.²

Metoprolol is a recently introduced beta-blocking drug which is cardioselective in animals.³ We report here the effect of intravenous metoprolol and propranolol on airways obstruction in asthmatic subjects.

Patients, methods, and results

Twelve asthmatic outpatients were studied. They understood that their asthma might temporarily worsen, and the study was approved by the local ethical committee. The mean age of the patients was 35.3 years (range 20-46) and their mean weight was 61.4 kg (range 52-70). Only patients with mild airways obstruction were selected, because this was unlikely seriously to worsen as a result of the experiment. They visited the laboratory on three different days at about the same time, to exclude the effect of diurnal variation in ventilatory function. They took no bronchodilator drugs for 12 hours beforehand. At each visit baseline measurements of the forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), specific airways conductance (SGaw), and resting pulse rate were made, and the mean values were closely similar on each occasion. The FEV_1 and the FVC were recorded in litres (ambient temperature and pressure saturated with water vapour (ATPS)) from the best of three forced expiratory spiograms obtained with a dry wedge spirometer. Specific airways conductance (SGaw) was measured in a constant volume body plethysmograph and each reading was the mean of three determinations (normal range 1140-4140 ml s⁻¹ kPa⁻¹ l⁻¹). The logarithms of SGaw were used for statistical analysis since the

distribution of this measurement is log normal. After the baseline measurements intravenous metoprolol 8 mg, propranolol 5 mg, or placebo (saline) was given over 60 seconds in a double-blind randomised sequence. These doses were chosen because, when given intravenously, they had been found to cause a similar decrease in resting heart rate.⁴ Measurements of FEV_1 , FVC, and pulse rate were repeated at 5, 10, 15, 30, and 45 minutes after the injection and measurement of SGaw was repeated at 15 minutes after the injection. Salbutamol was given by pressurised aerosol at 45 minutes.

The table shows the mean differences between the average of all the readings at 5, 10, 15, 30, and 45 minutes from baseline for FEV_1 , FVC, and pulse rate and for log SGaw from baseline and at 15 minutes.

Mean changes (\pm SE) in 12 asthmatics in FEV_1 , FVC, pulse rate, and log SGaw between averages of 5, 10, 15, 30, and 45 minutes after placebo, metoprolol, and propranolol

	FEV_1 (l ATPS)	FVC (l ATPS)	Pulse rate	Log SGaw (ml s ⁻¹ kPa ⁻¹ l ⁻¹)
Placebo	-0.06 \pm 0.04	-0.09 \pm 0.04	-4.13 \pm 2.10	+1.03 \pm 1.06
Metoprolol	-0.28 \pm 0.08	-0.37 \pm 0.14	-12.0 \pm 1.74	-1.35 \pm 1.27
Propranolol	-0.44 \pm 0.07	-0.55 \pm 0.13	-12.0 \pm 1.98	-6.21 \pm 1.74

FEV_1

Placebo v metoprolol P < 0.05.

Placebo v propranolol P < 0.001.

Metoprolol v propranolol P < 0.01.

Pulse rate

Placebo v metoprolol P < 0.01.

Placebo v propranolol P < 0.05.

Metoprolol v propranolol NS.*

FVC

Placebo v metoprolol P < 0.05.

Placebo v propranolol P < 0.01.

Metoprolol v propranolol P < 0.05.

Log SGaw

Placebo v metoprolol P NS*.

Placebo v propranolol P < 0.01.

Metoprolol v propranolol P < 0.05.

*Not significant.

Comment

When given intravenously to asthmatic subjects metoprolol caused less bronchoconstriction than propranolol in doses that lowered the resting pulse rate to the same extent, but although the mean effect of metoprolol on bronchial calibre was slight the FEV_1 fell over 500 ml in two patients, which could well be clinically significant. This was also seen with propranolol, and the response to each of the two drugs tended to be similar in any one patient. Thus, cardioselective beta-adrenoceptor blocking drugs must be used with caution in patients with airways obstruction because their response to β_2 -blocking is unpredictable. The bronchoconstriction resulting from both drugs was readily reversed by salbutamol. Therefore in asthmatics in whom metoprolol causes bronchoconstriction it may be combined with a selective β_2 -receptor-stimulating drug such as salbutamol, which will not diminish the desired β_1 -blocking action of metoprolol.

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Requests for reprints should be sent to Dr K N V Palmer.

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