CAN ISA COMPENSATE FOR BRADYCARDIA DUE TO β -ADRENOCEPTOR BLOCKADE?

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Bradycardia due to β -adrenoceptor blockers without intrinsic sympathomimetic activity (ISA) may improve by changing therapy to a β -adrenoceptor blocker with ISA. Twenty patients, who presented with asymptomatic bradycardia (heart rate < 50 beats/min) after chronic (> 4 weeks) treatment with either atenolol ($n = 10$, cardioselective, no ISA) or propranolol ($n = 10$, non selective, no ISA) were studied. Ambulatory 12 h ECG and a standardized exercise ECG were done before and 1 week after changing treatment to pindolol (non-selective, ISA), in a fixed dose ratio (one-tenth atenolol dose, one-eighth propranolol dose, 5-30 mg pindolol/day). In 10 patients the initial tests were repeated 1 week later without change of treatment to assess the reproducibility of the method.

The results are shown in Table 1. Basal heart-rate was 42 ± 5 beats/min (mean $\pm$ s.d., $n = 10$) on atenolol and 40 ± 9 beats/min ($n = 10$) on propranolol treatment. Change to pindolol therapy induced a definite increase in heart rate, by 13 beats/min in the atenolol group ($2P < 0.001$) and

8 beats/min in the propranolol group ($2P < 0.005$).

Reduction of atenolol or propranolol dosage (average 200 mg) by half produced only a slight increase in heart rate (Table 1), the heart rate still being lower than later on pindolol treatment in all five cases. Doubling the dose of pindolol (from 11.5 to 23 mg) induced no change in nocturnal heart rate, as expected.

As compared with the initial result after 1 week, no additional change occurred on long term treatment with pindolol.

Compared with placebo, pindolol did not alter the lowest heart rate at night (Table 1), but reduced exercise heart rate by 24 beats/min.

Mild asymptomatic bradycardia due to β -adrenoceptor blocking drugs without ISA can usually be resolved by change to a β -adrenoceptor blocking drug with ISA, such as pindolol. It seems premature to extend these results to severe symptomatic bradycardia on treatment with β -adrenoceptor blocking drugs without ISA or to bradycardia which occurs without β -adrenoceptor blocker therapy.

Table 1 Results of the study

First treatment	Changed to	Dose ratio	n	Mean change in heart rate (beats/min)	s.d.	2P <
Atenolol	Pindolol	10:1	10	+ 13	5	0.001
Propranolol	Pindolol	8:1	10	+ 8	6	0.005
Atenolol or Propranolol	No change, repeated study		10	- 2	3	NS
Atenolol or Propranolol	Dose $\times \frac{1}{2}$		5	+ 4	3	0.05
Pindolol	Dose $\times 2$		5	+ 1	3	NS
Atenolol	Propranolol	10:8	5	+ 3	3	NS
Pindolol	1 week $\rightarrow$ 6 months		5	- 3	4	NS
Pindolol	Placebo		5	± 0	4	NS