Correspondence

Br Heart J 1980; 44: 604-5

Effect of intravenous propranolol on QT interval

Sir,

We read with interest the study of Milne *et al.* (*Br Heart J* 1980; 43: 1-6) dealing with a new method to assess the effects of intravenous propranolol on QT interval and wish to comment on some aspects of their paper.

(1) The QT interval of the electrocardiogram can be interpreted only after correction for the cardiac cycle length. Bazett's formula is frequently used for this purpose and expressed as the symbol QTc: an absolute value of QTc exceeding 440 ms means prolongation.¹ Previous reports indicate that a prolonged QTc may represent a significant risk index for major cardiac arrhythmias in acute or healed myocardial infarction.²⁻³ On the other hand, antisymptomatic drugs are used in such clinical situations and may help prevent sudden death.⁴⁻⁵ Propranolol,⁶ alprenolol,⁷ and bretylium tosylate⁸ shorten the QTc interval and this may be how they reduce the incidence of major arrhythmias.

The conclusions drawn by Milne *et al.* do not apparently support this view.

(2) It is surprising however that such a relevant point is not supported by an unbiased statistical analysis.⁹ Furthermore, when comparing (variance analysis) the QTc of all 15 patients with measurements obtained in sinus rhythm and during atrial pacing, before and after propranolol (0.1 mg/kg over three minutes) it is evident (see Table) that: (a) propranolol induces a marginally significant ($p < 0.065$) reduction of QTc when infused in patients in sinus rhythm; (b) the lengthening of QTc after propranolol during atrial pacing is statistically not significant; (c) there is a highly

significant ($p < 0.00001$) lengthening induced by the proposed new method, irrespective of whether the drug was given.

(3) While the method described by Milne *et al.* deserves to be validated in a larger and more homogeneous series, it does not seem that the suggested action of propranolol in prolonging the QT interval duration during atrial pacing is substantiated.

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References

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Table QTc before and after propranolol (mean $\pm$ SD) in 15 patients

	QTc = $\frac{QT}{\sqrt{RR}}$ (ms)	
	Sinus rhythm Before After	Atrially paced Before After
	416 $\pm$ 18 401 $\pm$ 23	485 $\pm$ 39 498 $\pm$ 40
F=35 $p < 0.00001$	x x x — x x x	x x x — x x x
F=3.67 $p < 0.065$	x x x — x x x	
F=0.81 NS		x x x — x x x
F=38 $p < 0.00001$	x x x —	x x x
F=65 $p < 0.00001$		x x x — x x x

This letter was shown to Dr Milne and his colleagues who reply as follows:

Sir,

Puddu and his colleagues point out many of the difficulties in the interpretation of the QT interval, and of the changes of the QT interval occasioned by atrial pacing and by physiological or pharmacological manoeuvres. Though physiological changes in the QT interval can possibly be corrected for concomitant rate changes by the use of correction factors such as Bazett's formula, there is no evidence that changes of rate induced by atrial pacing or by drugs can be similarly corrected. Indeed the results of our research suggest that in the case of atrial pacing, in which rates were used which extended beyond the physiological range assessed by Bazett, simple hyperbolic correction was completely inaccurate as implied in paragraph 2c of the letter by Puddu and his colleagues.

In order to compensate for the bradycardia induced by propranolol, a comparison of pre- and post-propranolol QT intervals can be made by correcting both values for rate according to Bazett's formula. Alternatively, rate can be controlled by atrial pacing at identical frequencies both before and after drug administration. Our results indicated that, when using Bazett's correction the QTc usually shortened after propranolol, but when fixing the rate by atrial pacing, the QT tended to lengthen. As is pointed out by Puddu and colleagues, this result was not statistically significant.

These combined results suggest that one or other method is inappropriate and we are, as yet, pre-

pared to accept that making comparisons at non-physiological atrial paced rates may lead to incorrect results. We are also very unsure, however, about the validity of assuming that Bazett's correction can be applied to pharmacologically induced changes of rate. Rickards *et al.*¹ confirm our belief that simple hyperbolic correction should be not applied to QT interval changes induced by atrial pacing. Their results, like ours, lead to the conclusion that Bazett's correction would seriously overestimate the QTc at atrial driven rates above 100 a minute.

We should also point out that the results of our work do not necessarily apply to the effects of rate changes or beta-blockade on the QT interval in abnormal repolarisation syndromes. The QT interval response to the imposition of an artificial rate, abnormal depolarisation sequence, or pharmacological intervention may be characteristically different from the results in our "normal" series.

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Reference

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