

Dynamic assessment of the electrocardiographic QT interval during citrate infusion in healthy volunteers

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Abstract

Objective—To investigate changes in the electrocardiographic QT interval during rapidly induced, sustained hypocalcaemia in healthy volunteers.

Design—Serial rate corrected QT measurements were made during and after a variable rate trisodium citrate infusion designed to “clamp” the whole blood ionised calcium concentration 0.20 mmol/l below baseline for 120 min.

Subjects—12 healthy teetotallers aged 19–36 years who were not receiving medication known to influence calcium homeostasis.

Main outcome measures—Whole blood ionised calcium concentration and QaTc intervals (onset of the Q wave to T wave apex divided by the square root of the RR interval).

Results—Mean (SD) ionised calcium concentration decreased from 1.18 (0.03) mmol/l preinfusion to values close to target (0.98 mmol/l) between 10 and 120 min. The QaTc interval lengthened from a baseline of 0.309 (0.021) to a maximum 0.343 (0.024) s^{0.5} at 10 min before returning to a stable level from 15 to 120 min (0.334 (0.023) and 0.330 (0.023) s^{0.5} respectively). The change from baseline of both variables expressed as a ratio ($\Delta\text{QaTc}/\Delta[\text{Ca}^{2+}]$) was greater during rapid induction of hypocalcaemia (at 5 and 10 min) than at other times during and after the infusion ($P < 0.02$).

Conclusions—The disproportionate prolongation of QaTc interval during prompt induction of hypocalcaemia suggests rate dependency which can be represented by a hysteresis relation between (ionised calcium, QaTc) coordinates. This finding may have clinical implications.

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Keywords: QT interval; hypocalcaemia; hysteresis

The effect of changes in serum calcium on the electrocardiographic QT interval was first described over 70 years ago.¹ Several more recent studies have involved detailed electrocardiographic investigation of groups of patients with underlying diseases (including parathyroid dysfunction and malignancy) or undergoing therapeutic procedures (such as blood transfusion and renal dialysis) which

produce measurable disturbances of calcium homeostasis.^{2–14} Despite the lack of a significant association in a number of studies in neonates^{2–4} a simple inverse relation between steady state serum calcium (usually total rather than ionised) and the QT interval has been observed in most of these reports. As QT prolongation is associated with sudden death in a variety of illnesses as well as in apparently healthy individuals,¹⁵ this relation could be useful in clinical situations in which prompt and reliable measurement of serum calcium is indicated but not possible.

The QT interval can be measured from a common starting point at the beginning of the QRS complex to the onset (QoT), apex (QaT) or end (QeT) of the T wave. Although correction for heart rate using Bazett's formula (in which the raw QT interval is divided by the square root of the RR interval to give QTc¹⁶) was developed for QeT, QoTc and QaTc intervals have also been used in a variety of electrocardiographic studies including the majority of those concerned with calcium homeostasis.^{2–8 11–14} QoTc and QaTc correlate better with total¹³ and ionised¹⁴ serum calcium than QeTc. Rumancik *et al.*¹⁴ used pooled patient data to conclude that a hyperbolic relation exists between the serum ionised calcium concentration and each of the three QTc intervals. Nevertheless, such an assumption does not take into account the possibility that the rate of change of serum ionised calcium may also be an important determinant of changes in QTc, in a way analogous to the dynamic parathyroid hormone response to the same stimulus.¹⁷

Intensive electrocardiographic monitoring was performed in healthy volunteers during a 2 h period of controlled hypocalcaemia induced using the previously reported citrate ‘clamp’ technique^{18,19} to assess the effect of a rapid change in serum ionised calcium on the QTc interval.

Subjects and methods

SUBJECTS

Twelve healthy teetotal Malaysian adults (eight males and four females) of mean (SD) age 33 (5) years were studied. None of the subjects was taking regular medication and none had a history of illnesses known to influence calcium homeostasis. All had given witnessed informed consent to participation as controls in a study of calcium metabolism in acute malaria. The study protocol was approved by the ethics committee of the Ministry of Health, Malaysia.

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