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Detection of early onset neonatal hypocalcaemia in low birth weight infants by Q—T_c and Q—$_oT_c$ interval measurement

by

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In 26 infants born in the 28th to 34th (mean 32nd) week of gestation, with a weight ranging from 1130 to 1980 (mean 1560) g, the correlation between the plasma level of total calcium and the Q—T_c and Q—$_oT_c$ ECG intervals was studied within 72 (mean 12.5) hours after birth.

The Q—T_c interval correlated with the total calcium ($r = -0.41$, $p \leq 0.01$) and so did the Q—$_oT_c$ interval ($r = 0.56$, $p \leq 0.01$). Sensitivity of the detection of hypocalcaemia when using the Q—T_c interval was 50% and specifity was 93.7%, while with the use of the Q—$_oT_c$ interval sensitivity was 77% and specifity 94.4%. After administration of calcium to five infants suffering from an early form of symptomatic hypocalcaemia, a shortening of the corrected intervals occurred in four cases, while in one a paradoxical prolongation ensued.

The changes were not seen on the display. The use of Q—$_oT_c$ is suitable for the screening of early hypocalcaemia in low birth weight infants and it allows a timely initiation of therapy without delay.

The incidence of the early form of hypocalcaemia in low birth weight infants is about 30—50% [3, 6, 8]. The diagnosis is based on the direct measurement of plasma ionized or total calcium. The determination takes a certain time and thus causes a delay in prescribing an appropriate therapy. The quick method of screening for hypocalcaemia is the measurement of the Q—T_c interval which correlates with the total or ionized plasma calcium level [4, 7]. Until now, these relations have not sufficiently been studied in low birth weight infants, only Coletti et al. [1] concluded that the Q—$_oT_c$ interval is a reliable indicator of hypocalcaemia in the high risk newborn. Their conclusions have not, however, been supported, by data which would show a greater than twofold variation in the calcium level at given Q—$_oT_c$ intervals.

The purpose of the present work was to study in low birth weight infants the detection of hypocalcaemia by the use of the Q—T_c and the Q—$_oT_c$ intervals as a routine method in neonatal intensive care units and to judge the usefulness of these intervals for monitoring the adequacy of treatment.

Methods

A group of 26 low birth weight infants was studied within the first 72 (mean 12.5) hours after birth. The newborns whose weight ranged from 1130 to 1980 (mean 1560) g, were born in the 28th to 34th (mean 32nd) week of gestation. During the study, nine were suffering from RDS and were treated by CNDP therapy and FiO_2 = = 0.4—0.9.

At the time of the study, five babies displayed seizures or a symptomatology compatible with neonatal hypocalcaemia which later was verified in the laboratory. The ECG was always recorded immediately following blood sampling for calcium determination, at a paper speed of 50 mm/sec and a sensitivity calibration of 1 mV = = 1 cm and 2 cm, for the exact determination of the onset of the T wave. The lead with the longest Q—T interval and the best visible T wave onset, usually standard limb lead II, was chosen. $Q—T_c$ and $Q—{}_oT_c$ intervals were measured in five consecutive complexes and in five consecutive R—R intervals (Fig. 1). Results were corrected for frequency by the use of Bazzet's formula (Fig. 2).

$Q—T_c$ means the interval measured from the onset of the Q-oscillation to the end of the T-wave and corrected for the corresponding frequency.

$Q—{}_oT_c$ denotes the interval measured from the onset of the Q-oscillation to the onset of the T-wave and corrected for the corresponding frequency. This interval is not influenced by the duration of the T wave that can be affected by a series of non-specific influences.

In the cases where the onset of the T wave was not clearly visible because of an elevation of the ST—T interval, T wave onset was determined as the point farthest from the line connecting the RS—T junction and the peak of the T wave (Fig. 2). Care was taken not to include the U wave in the $Q—T_c$ interval. During the study the infants were kept in a thermoneutral environment and were not receiving any therapy that might prolong the electric systole. Unfortunately, in ten cases a CNS injury could not be excluded.

Plasma total calcium was estimated by

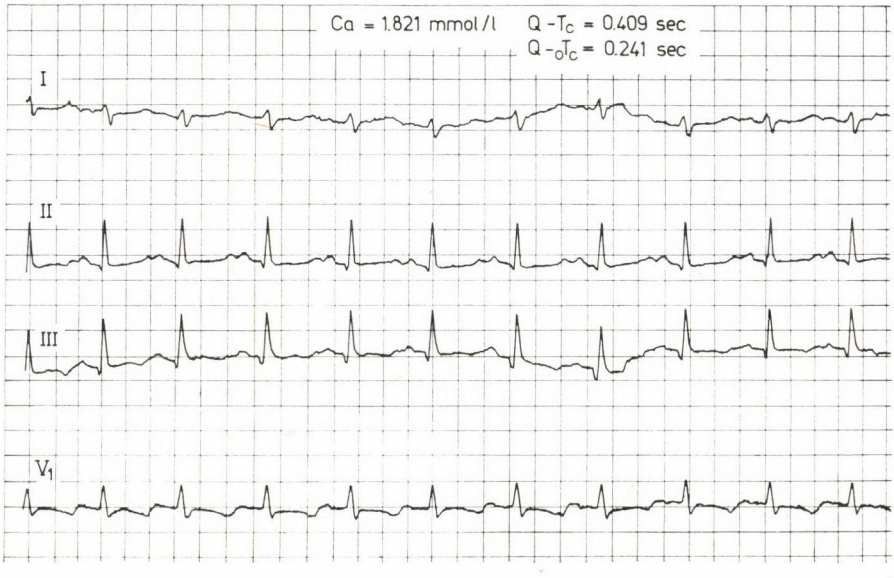
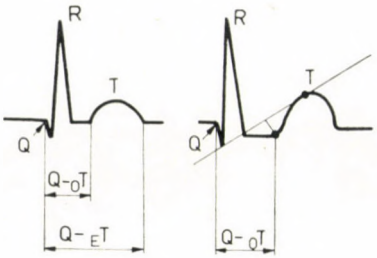


Fig. 1. Typical hypocalcaemic ECG tracing



$$Q\text{-}_E T_C = \frac{Q\text{-}_E T}{\sqrt{R\text{-}R}}$$

$$Q\text{-}_o T_C = \frac{Q\text{-}_o T}{\sqrt{R\text{-}R}}$$

FIG. 2. Determination of Q—T_c and Q—$_oT_c$
Onset and end of the T-wave were determined exactly and the Q—$_oT$ and Q—$_oT_c$ intervals were measured in 5 successive QRS-complexes and R—R-intervals. The obtained intervals were used for the calculation of the corrected intervals Q—T_c and Q—$_oT_c$ according to Bazzet's formula. In some cases the onset of the T-wave could not be determined exactly, mostly because of the depression of the ST—T-section. In these cases we connected the R—ST-junction with the T-wave peak. For the T-wave onset that point was taken into consideration which was most distant from the imaginary line connecting the R—ST point and the peak of the T-wave

photometry [9] with a variation coefficient of 3.6% and $\delta \pm 0.0873$ mmol/l.

The five low birth weight infants who had seizures ascribed to hypocalcaemia were given 1 ml/kg calcium gluconate IV after a 1 ml blood sample was taken and a standard ECG recorded. The ECG was repeated 15 minutes after the injection. The plasma calcium assay was not repeated to avoid repeated venipuncture; we were satisfied with the disappearance of seizures.

Regression lines were calculated from the total calcium values and the values for Q—T_c and Q—$_oT_c$. The variation coefficient was calculated, the results were tested for determination of sensitivity specificity. We chose 0.43 sec and 0.23 sec for the upper normal limits of Q—T_c and Q—$_oT_c$, respectively, because in the first hours the Q—$_oT_c$ interval amounts to 0.42 sec [11], and in newborns with late clamping of the cord even to 0.44 sec [12], thus being somewhat longer than in older infants. Hypocalcaemia was defined as a plasma total calcium level below or equal to 1.996 mmol/l [2].

RESULTS

Correlation (Fig. 3)

Both the Q—T_c and Q—$_oT_c$ intervals correlated with the total calcium value ($p \leqq 0.01$ for both) but the correlation to Q—$_oT_c$ was closer than to Q—T_c ($r = -0.56$ vs).

Sensitivity and Specifity

The explanation of sensitivity and specificity testing is seen in Table I. Results are presented in Table II.

When the Q—T_c interval was used for screening of hypocalcaemia, sensitivity was 50% and specificity 94.7%. With the use of the Q—$_oT_c$ interval, sensitivity increased to 77.7% and specificity was practically unchanged, 94.4%.

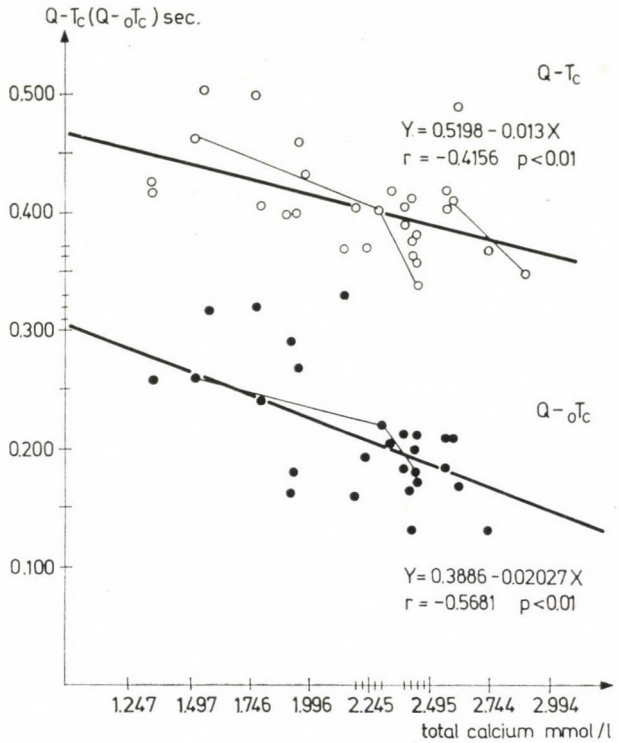


FIG. 3. Correlation of the Q—T_c and Q—$_oT_c$ intervals with total serum calcium in group of 27 low birth weight infants. Lines mean a repeated investigation in the same infants. In 2 cases the Q—$_oT_c$ interval could not be read from the tracing

TABLE I

Test for determination of sensitivity and specificity

$$\text{Sensitivity (\%)} = \frac{A}{A + C} \times 100 \qquad \text{Specificity (\%)} = \frac{D}{B + D} \times 100$$

Hypocalcaemia (based on ECG. measurement) + means, 0.43 sec for Q—T_c 0.22 sec for Q—$_oT_c$	Hypocalcaemia (based on laboratory determination) + means = 1.996 mmol/		
	+	−	
+	positive with both methods A	false positive ECG. diagnosis B	A + B
−	false negative ECG. diagnosis C	negative with both methods D	C + D
	true hypocalcaemic newborns A + C	true normocalcaemic newborns B + D	A + B + C + D

TABLE II

Determination of sensitivity and specificity

with Q—T_c interval		+	−	Hypocalcaemia (laboratory)	
	+	5	1	6	sensitivity 50%
	−	5	18	23	specificity 94.7%
Hypocalcaemia (Q—T_c interval)		10	19	29	

with Q—$_oT_c$ interval		+	−	Hypocalcaemia (laboratory)	
	+	7	1	8	sensitivity 77.7%
	−	2	17	19	specificity 94.4%
Hypocalcaemia (Q—$_oT_c$ interval)		9	18	27*	

* — in 2 cases it was not possible to determine the Q—$_oT_c$ interval because of indistinctness of the origin of the T wave

False positive findings occurred in 5% with both methods; measurement of Q—$_oT_c$ proved more reliable for the screening of hypocalcaemic infants.

Q—T_c and Q—$_oT_c$ intervals after IV administration of calcium (Fig. 4)

After IV administration of calcium there occurred a shortening of both intervals in three cases and a shortening of only the Q—T_c interval in one case because of inability to measure the Q—$_oT_c$ interval. In one case, an unexpected and paradoxical prolongation of both intervals was observed. These small changes cannot be read directly from the display or the ECG tracing, but the changes of the ST—T segment can easily be seen on the display (Fig. 5).

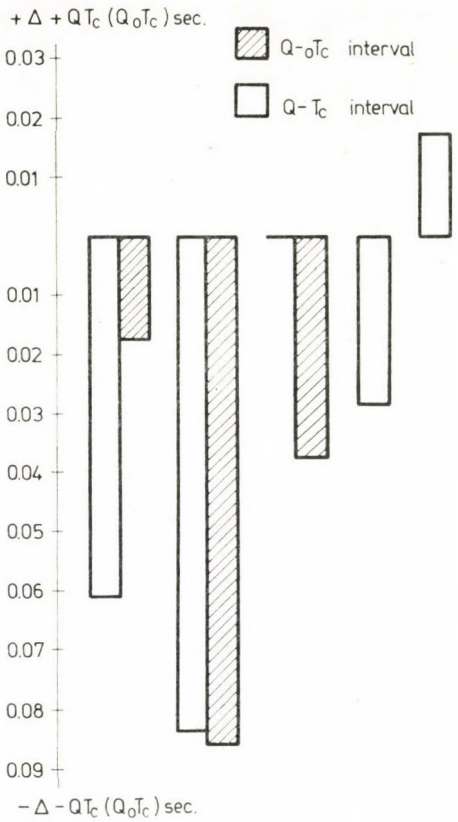


FIG. 4. Q—T_c and Q—$_0T_c$ intervals 15 minutes after the IV administration of 100 mg/kg Ca-gluconate. In 4 infants a shortening, and in one a paradoxical prolongation, of the Q—T_c interval occurred

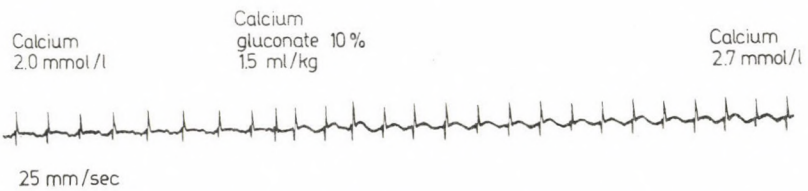


FIG. 5. Changes of the ST segment are clearly seen but exact determination of the shortening of the Q—T_c interval was not possible from the display

DISCUSSION

The plasma calcium level affects the plateau phase of the myocardial transmembrane action potential in the first place. Changes in the extracellular calcium level can therefore be measured by corrected Q—T intervals.

Generally, the changes of corrected intervals are not precise at hypercalcaemic levels and thus ECG measu-

rement is not recommended for the detection of hypercalcaemia. The correlation, however, is sufficiently high in normocalcaemia and hypocalcaemia.

The closest correlation was found between the ionized calcium level and the $Q-{}_oT_c$ interval [4], i.e. from Q to the apex of the T wave, but because of the many errors associated with determination of the apex we have abandoned this procedure.

Coletti et al. [1] were the first to point to the use of the $Q-T_c$ and $Q-{}_oT_c$ intervals for the detection of neonatal hypocalcaemia in fullterm and preterm babies. The correlation between plasma total calcium and the $Q-{}_oT_c$ interval was $r = -0.49$, and with plasma ionized calcium, $r = -0.59$. They recommended the method for the early screening of hypocalcaemia, and their results were practically the same as ours. The method is not time consuming and is non-invasive, and the results are available immediately at the bedside. We recommend to define only values over 0.22 as a prolongation of the $Q-{}_oT_c$ interval, because values between 0.20 and 0.22 are common shortly after birth in normocalcaemic low birth weight infants.

We cannot give a satisfactory answer to the question of whether a correct treatment of hypocalcaemia prolongs both $Q-{}_oT_c$ and $Q-T_c$ intervals, and whether it is possible to monitor by the method the adequacy of treatment. After the injection of calcium we waited for 15 minutes before repeating the ECG, because the chronotropic response to calcium in the isolated heart requires four minutes for its activity [5], and it is possible that a similar period is necessary for the manifestation of ECG changes. We expected a shortening of the interval to occur in all cases and we do not know the reason for the paradoxical prolongation of $Q-T_c$ in one child. In any case, such changes in interval length are too small to be seen on the visual display or the ECG tracing, and also because the heart rate varies after calcium administration.

Some uncertainty exists about the therapy of early neonatal hypocalcaemia, but we believe that screening by measurement of the $Q-T_c$ interval, especially in high risk low birth weight infants, with follow-up by direct measurement of plasma calcium in positive cases, holds promises for early therapy.

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