

Short reports

Suckling stimulation test for neonatal tremor

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SUMMARY The response of neonatal tremor to a suckling stimulation test was investigated in 102 healthy neonates born at full term. In 84 the tremor resolved immediately; none had hypocalcaemia and only one had mild hypoglycemia. Eighteen in whom the tremor continued had either hypocalcaemia (n=13) or hypoglycaemia (n=5).

Neonatal tremor is common, and has various causes including neurological damage and some biochemical deficiencies. These infants are usually otherwise normal on physical examination, and the batteries of tests to which they are often subjected cause much distress to the infant and to the parents. A review of published reports failed to disclose a simple method for differentiating between physiological and pathological tremor. This study was designed to test the hypothesis that cessation of the tremor by the suckling stimulation test indicates a physiological tremor.

Patients and methods

Of 9408 newborn infants born at the Hadassah Medical Centre between August 1984 and February 1988, 143 were found to have neonatal tremor at the routine physical examination carried out during the first 72 hours of life and before the morning meal. Neonatal tremor was defined as repetitive movements of both hands (with or without movement of the legs or jaws) at a frequency of 2-5/s and lasting more than 10 minutes. A total of 102 infants who fulfilled the following criteria were included in the study: gestational age ≥ 37 weeks; birth weight ≥ 2500 g; Apgar score ≥ 8 at five minutes, and a physical examination that was otherwise normal. Forty one neonates were excluded from the study because they were premature, or small for gestational age, or had diabetic mothers, or had other abnormalities on physical examination. Twenty five healthy babies born at full term without tremor were selected sequentially after each infant enrolled in

the study to serve as a reference group. Characteristics of the patients and the reference group are shown in table 1.

Infants were examined on the first and third day of life at a mean (SD) of 30 (17) minutes before their morning meal (range 6-66 minutes). The suckling stimulation test consisted of the examiner putting his middle finger into the mouth of the infant who was lying supine with the head straight and both hands free. Each test was performed twice, the second time by another examiner. A test was positive if the tremor stopped instantly and returned when the examiner's finger was removed.

A Dextrostix plastic reagent strip test was carried out, and venous blood was taken for estimation of glucose and calcium concentrations from all infants with tremor, before the next meal. Blood from the reference group infants was taken on the third day before the 10.00 am meal from the same heel puncture that had been used to take blood for thyroid function and phenylketonuria screening tests. Plasma glucose and calcium concentrations were measured by a Technicon SMAC 11.

Hypoglycaemia was defined as a concentration of less than 1.66 mmol/l, and hypocalcaemia as a concentration of less than 1.79 mmol/l.

Informed consent was obtained from all mothers. Statistical analysis was by the unpaired Student's *t* test and 2×2 contingency tables.

Table 1 Characteristics of patients with neonatal tremor and reference group. Figures are given as mean (SD)

	Birth weight (g)	Gestational age (weeks)
Group in which the suckling stimulation test was positive (n=84)	3280 (510)	39.0 (0.9)
Group in which the suckling stimulation test was negative (n=18)	2980 (620)	38.1 (1.1)
Reference group (n=25)	3120 (320)	38.3 (0.7)

There were no significant differences between the neonatal tremor group and reference group.

Results

Two distinct groups of infants were identified from the responses to the suckling stimulation test (table 2). The first comprised 84 infants (82%) in whom the test was positive. They were all normocalcaemic and all but one had normal blood glucose concentrations. The infant whose blood glucose concentration was 1.5 mmol/l was asymptomatic except for the tremor, and the mild hypoglycaemia was corrected by oral feeding. Although the values were within normal limits, plasma glucose concentrations were significantly lower in this group of infants than in the reference group ($p < 0.006$), but there was no difference between the two groups in plasma calcium concentrations.

The second group comprised 18 infants (18%) in whom suckling failed to interrupt the tremor. Thirteen of these had mean (SD) plasma calcium concentrations of 1.44 (0.18) mmol/l (range 1.12–1.75). The other five had a mean glucose concentration of 0.71 (0.29) mmol/l (range 0.5–1.2). None had both abnormalities. The tremors resolved completely after correction of the hypoglycaemia in five infants and hypocalcaemia in 10 infants. In three of the hypocalcaemic infants the tremor continued to occur occasionally, but responded to the suckling stimulation test.

The sensitivity of the suckling stimulation test was 95% with a specificity of 100%.

Discussion

The suckling stimulation test enabled us on the one

hand to offer prompt treatment to the infants whose tremor was of true pathological origin, and on the other hand set our minds at rest when we were dealing with physiological tremors. Significantly low concentrations of calcium or glucose as found in 18 infants were detected with a high sensitivity (95%). Only one infant with a positive test was hypoglycaemic.

The response of the infants with positive reactions to the suckling stimulation test were different. Although within 'normal' limits,¹ their mean glucose concentration was significantly lower than that of the reference group (3.16 (0.7) and 3.84 (0.9) mmol/l, respectively; $p < 0.006$).

Clinical symptoms and signs of neonatal hypoglycaemia may be divided into two main categories; the first comprises those resulting from lack of glucose for central nervous system metabolism such as irritability, bizarre behaviour, convulsions, and coma. The second comprises signs resulting from increased adrenaline secretion such as tremor, jitteriness, pallor, sweating, and tachycardia. Though symptoms of excess adrenaline secretion usually occur with transient mild hypoglycaemia, symptoms arising from central nervous system depression tend to predominate as the severity or duration of the hypoglycaemia increases.²

Our results may indicate that the infants responding to the suckling stimulation test had excess adrenaline secretion, which by some unknown mechanism was corrected by suckling. A possible explanation is that the act of suckling raises the concentration of some gastrointestinal substance (a neurotransmitter such as the 14 amino acid gastrin) acting as an adrenaline antagonist.³ Another explanation is that brain gut peptides may have a direct effect on the neurones in the extrapyramidal system.⁴⁻⁶ Tremor caused by hypocalcaemia that did not respond to the suckling stimulation test results from a direct effect of low calcium concentration on neuromuscular transmission.

In conclusion we suggest that the suckling stimulation test should be applied to any newborn presenting with neonatal tremor of unknown origin. A positive response to the test combined with a normal plasma glucose concentration measured by Dextrostix plastic reagent strip testing would define the physiological tremor and spare the infant from further investigation.

Table 2 Calcium and glucose concentrations in the three groups. Figures are given as mean (SD) and range

	Calcium (mmol/l)	Glucose (mmol/l)
Group in which the suckling stimulation test was positive (n=84)	2.11 (0.15), 1.79–2.67	3.16 (0.72),* 1.5–5.2
Group in which the suckling stimulation test was negative:		
Hypocalcaemic subgroup (n=13)	1.44 (0.18),† 1.12–1.75	3.65 (0.37), 2.3–4.1
Hypoglycaemic subgroup (n=5)	2.18 (0.19), 1.90–2.32	0.74 (0.29),† 0.5–1.2
Reference group (n=25)	2.28 (0.12),† 1.89–2.54	3.81 (0.9),*‡ 2.4–5.1

* $p < 0.006$; † $p < 0.001$.

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Effects of ethamsylate on cerebral blood flow velocity in premature babies

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SUMMARY Cerebral blood flow velocity and cardiac output were measured with ultrasound before and 30 minutes after the administration of ethamsylate in a double blind placebo controlled study of 19 very low birthweight infants. No differences were found before or after treatment in either group.

Ethamsylate (diethylammonium 2,5-dihydroxybenzenesulphonate) is a non-steroidal drug that reduces bleeding from small vessels. The results of a double blind multicentre study showed that there were fewer severe periventricular haemorrhages among the survivors of a group of very low birthweight infants treated with this drug shortly after birth.¹ The mode of action remains to be clearly elucidated but experimental evidence shows an inhibition of the products of the prostaglandin pathway.² A group of very low birthweight infants with respiratory distress syndrome treated with ethamsylate had lower serum concentrations of immunoreactive prostacyclin metabolite than an untreated control group,³ and one interpretation was that the drug limited prostacyclin release from ischaemic brain, perhaps preventing bleeding secondary to the presence of this potent vasodilating and platelet disaggregating substance.

Prostaglandins are known to play a part in cerebral blood flow. Indomethacin inhibits prostaglandin production although at a different enzymatic point than that thought to be affected by ethamsylate. Studies in animals, adult humans, and babies attest to the reduction in cerebral blood flow velocity after treatment with indomethacin.⁴ Although inhibition of the prostaglandins produced by metabolism of arachidonic acid are not as complete after treatment with ethamsylate as after treatment with indomethacin, it seems plausible that this drug may also reduce cerebral blood flow

velocity in the newborn. Periventricular haemorrhages develop early in postnatal life in most infants, therefore a common approach to prevention entails prophylactic administration of the drug to a cohort of babies defined as 'high risk'. Sixty per cent of very low birthweight infants will be given treatment for a condition that they will never develop if this approach is adopted; proposed agents therefore need to be fully investigated.

Patients and methods

Nineteen very low birthweight infants admitted to the Cambridge neonatal intensive care unit who did not have periventricular haemorrhages were studied at a postnatal age of less than 12 hours. Mean (SD) birth weight was 1105 (265) and mean gestational age 28 weeks (range 26-31). Approval for the investigation was granted by the ethical committee of Addenbrooke's Hospital. Measurements of cerebral blood flow velocity and cardiac output were made before and 30 minutes after administration of a solution containing either ethamsylate or saline. Infants were treated with 0.1 ml/kg of solution that contained either 12.5 mg/kg of ethamsylate, or saline alone. The solution was prepared in identical vials by the manufacturers who held the identification code until the end of the study.

Measurement of cerebral blood flow velocity and cardiac output were made by duplex Doppler ultrasound (ATL Mk 600). Doppler signals from the anterior cerebral artery were identified using the real time image and the Fourier transform of the frequency shift was sampled using an Apple IIe microcomputer. This was used to estimate time averaged mean velocity from several consecutive cardiac cycles and also used to calculate the Pourcelet resistance index.⁵ This was expressed as the peak systolic velocity minus the diastolic velocity divided by the peak systolic velocity. The same computa-