Measurement of ionised calcium concentration in neonates

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Abstract

Whole blood ionised calcium concentration was measured simultaneously in capillary and arterial blood from neonates being nursed on an intensive care unit using an ion selective electrode. The mean arterio-capillary difference was -0.027 mmol/l (95% confidence intervals -0.041 to -0.012 mmol/l) and the limits of agreement between the two measurements were 0.034 and -0.088 mmol/l. Measurement of ionised calcium in capillary blood is acceptable for clinical purposes.

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The overall incidence of neonatal hypocalcaemia is unknown, but it is reported to occur in 30-90% of cases depending upon the population under consideration.¹ In 1935 McLean and Hastings showed that the physiologically active form of calcium in body fluids is the 'free' or ionised fraction.² The predictive value of ionised calcium concentration determination from total plasma calcium concentration, plasma protein concentration, and blood pH is poor.^{3,4} With ion selective electrodes becoming more widely available, rapid and accurate measurement of ionised calcium in a variety of neonatal disorders is now possible.

In the absence of an indwelling arterial catheter, blood samples from neonates are commonly obtained by means of heelprick. Factors that influence ionised calcium include plasma concentrations of total calcium, lactate and bicarbonate, mass fraction of albumin in total protein, plasma ionic strength, pH, and temperature. Theoretically, some of these factors may differ between capillary and arterial blood resulting in different measured ionised calcium in the same patient, dependent upon the sample site. Therefore, we conducted this study to test whether there was sufficient agreement between capillary and arterial ionised calcium to validate the use of capillary measurements for clinical purposes.

Methods

Neonates receiving care in the regional neonatal medical unit, St Mary's Hospital, Manchester were enrolled into the study. For ethical reasons, only those infants receiving a glucose solution through an arterial line were chosen. When a heelprick was done for routine determination of blood glucose a 150 μ l capillary blood sample was collected in heparinised capillary tubes (Radiometer, Copenhagen) for measurement of ionised calcium. Almost simultaneously, and only if a blood sample was

required for other laboratory tests as part of the management of the infant, a 150 μ l arterial blood sample was obtained for the same measurement. Infants with low blood pressure (mean arterial pressure <30 mm Hg) or poor peripheral perfusion (delayed capillary filling after blanching) were not studied so that the effect of vascular stasis on pH and ionised calcium was minimised. Blood samples were analysed within 15 minutes and ionised calcium measured at actual pH using an ion selective ionised calcium electrode (ICA-1, Radiometer, Copenhagen). According to the manufacturer, the analytical error for this electrode is 0.01 mmol/l, which is in agreement with independent observations.⁴ The degree of agreement between the two sets of measurements was assessed by the method described by Bland and Altman.⁵

Results

A total of 19 paired measurements of ionised calcium were made on 14 neonates. The median (range) gestational age, birth weight, and age at which ionised calcium was measured was 26.5 weeks (24-32 weeks), 873 g (480-1635 g), and 1 day (1-20 days), respectively. The figure shows the arterio-capillary difference of ionised calcium between the two sets of measurements plotted against the mean ionised calcium in each patient; the dashed lines represent the mean (2 SD) difference (limits of agreement).⁵ The mean difference was -0.027 mmol/l with 95% confidence intervals of -0.041 to -0.012 mmol/l. The limits of agreement between the two measurements were 0.034 and -0.088 mmol/l. As expected, capillary and arterial ionised calcium was highly correlated ($r=0.99$, $p<0.001$).

Difference in arterial and capillary ionised calcium plotted against mean ionised calcium. Dashed lines represent mean (2 SD) difference.

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Discussion

Calcium in body fluids exists in three forms: approximately 40% is bound to proteins (mainly albumin), about 10% is complexed with anions such as bicarbonate, and about 50% is free or ionised and physiologically active. Ionised calcium is dependent on several factors and, therefore, its prediction from nomograms which allow for only some of these factors is poor.^{3,4} With the introduction of semiautomated ion selective electrodes it is recommended that ionised calcium be measured directly whenever knowledge of the active calcium concentration is required.

Neonatal hypocalcaemia, which has a diverse aetiology and pathogenesis, may be commonly encountered in infants who are premature, asphyxiated, born of diabetic mothers, or who require exchange transfusions.¹ Furthermore, it is a recognised cause of neonatal convulsions. Capillary blood samples are easily obtained and would be helpful in the measurement of ionised calcium if this measurement reflected accurately arterial ionised calcium. To our knowledge the agreement between capillary and arterial ionised calcium in neonates has not been assessed before.

In the present study, although the number of patients and paired measurements of ionised calcium was small, it is clear that ionised calcium in capillary samples is greater than in arterial samples by a mean value of 0.027 mmol/l (capillary sample values were greater in

15/19 paired measurements). As shown by the limits of agreement, capillary ionised calcium may be 0.088 mmol/l above or 0.034 mmol/l below arterial values. This difference is unlikely to be solely due to the analytical error of the ICA-1 electrode. However, we believe that the difference between capillary and arterial ionised calcium is unlikely to be of clinical significance in infants with normal blood pressure and peripheral perfusion. Furthermore, the ease with which capillary blood can be obtained makes capillary ionised calcium measurement particularly attractive.

In conclusion, direct measurement of ionised calcium is the method of choice whenever an accurate knowledge of the active concentration of calcium is required. Capillary blood samples may be used but it should be remembered that ionised calcium in capillary blood might be, on average, slightly greater than in arterial blood.

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