Blood carbonic anhydrase activity in the newborn

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Logan, R. W., Crooks, S. M., Hutchison, J. H., and Kerr, M. M. (1973). Archives of Disease in Childhood, 48, 256. Blood carbonic anhydrase activity in the newborn. Erythrocyte carbonic anhydrase activity was measured in 7 adults, 12 mature newborn infants, 12 preterm low birthweight infants, 9 'dysmature' infants, 33 infants with the respiratory distress syndrome (RDS), and 5 infants who had received intrauterine transfusions. The mean level of enzyme activity in infants with RDS was 3.6% of normal adult level, 21% of the mean level in mature infants, and 30% of the mean level in dysmature infants. There was, however, no significant difference between the mean enzyme activity found in infants with RDS and in low birthweight, preterm infants without RDS. In 3 of the 5 infants treated by intrauterine transfusion RDS developed while the carbonic anhydrase activity was up to adult levels. It is unlikely that the very low enzyme levels found in premature infants have any aetiological relation to the development of RDS, and there is no indication for treatment by exchange transfusion.

Carbonic anhydrase is a zinc-containing enzyme which catalyses the conversion of bicarbonate to carbon dioxide and water, or the reverse. It has been shown that there is a markedly reduced level of activity of this enzyme in the blood of infants with the respiratory distress syndrome (RDS) (Kleinman, Petering, and Sutherland, 1967), and it has been suggested that this might be related to the aetiology of this disease. The study of Poblete, Thibeault, and Auld (1968) has shown that in premature and term infants, the CO2 gradients existing between alveoli and a systemic artery do not correlate with whole blood carbonic anhydrase activity. Precise interpretation of their results is rendered difficult, however, when consideration is given to such factors as the interval between birth and blood sampling, the relative time spent by blood in the pulmonary capillaries compared with the remainder of the circulation, ventilation–perfusion abnormalities, pulmonary diffusion defects, and the absolute carbonic anhydrase activity. It could reasonably be expected that within certain limits there would be an inverse relation between carbonic anhydrase activity and the Pco2 of blood in the pulmonary arteries which would not necessarily be reflected in blood returning to the systemic circulation. As it seemed important to determine whether the low carbonic anhydrase activity in the blood of infants with RDS had any role in the pathogenesis of this disorder, a study was designed to measure the enzyme activity in various groups of neonates and to compare the levels with those found in healthy adults.

Clinical material

Carbonic anhydrase activity was measured in the packed cells from heparinized whole blood from 7 adult females, 12 preterm (not over 36 weeks' gestation) infants with birthweights below 2.5 kg (550 to 2290 g), 12 mature infants (over 38 weeks' gestation), 9 'dysmature' infants whose birthweights fell below the 10th centile on the Denver intrauterine growth chart (Lubchenco, Hansman, and Boyd, 1966), 33 infants with typical RDS (birthweight over 2.5 kg in 2 cases only), and 5 infants who had received intrauterine transfusions for haemolytic disease of the newborn (3 with RDS, 2 without).

Methods

The blood was obtained from the umbilical vein or artery when catheterization was performed for therapy or monitoring of the blood gases in infants with RDS or haemolytic disease. In the other infants (mature, healthy, premature, and dysmature) the blood was obtained by heel stab or venepuncture when other routine tests (e.g. blood glucose, Dextrostix, serum bilirubin) were being performed. Most specimens were
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Comparison of carbonic anhydrase activities (Wilcoxon)

<table>
<thead>
<tr>
<th>Carbonic anhydrase activity mean value (units/ml packed cells)</th>
<th>(A)</th>
<th>(B)</th>
<th>(C)</th>
<th>(D)</th>
<th>(E)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults (A)</td>
<td>23,809</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mature infants (B)</td>
<td>4086</td>
<td>X</td>
<td>&lt;0.05</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Dysmature infants (C)</td>
<td>2781</td>
<td>X</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Premature infants nonRDS (D)</td>
<td>1071</td>
<td>X</td>
<td>&lt;0.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RDS infants (E)</td>
<td>848</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results

In the Fig. are shown the enzyme activities found in the various groups except those cases requiring intrauterine transfusion.

Table I shows both the mean values of carbonic anhydrase activity for each group and the probability that differences between these groups occurred by chance. As can be seen, there is a high probability that the groups are significantly different with respect to their enzyme activities, though the premature infants without RDS and those exhibiting RDS did not differ at the 5% level of significance.

Table II lists details including individual carbonic

TABLE II

Intrauterine transfusion cases

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Carbonic anhydrase activity (units/ml packed cells)</th>
<th>Birthweight (kg)</th>
<th>Maturity (wk)</th>
<th>Clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21,740</td>
<td>2.04</td>
<td>33</td>
<td>RDS</td>
</tr>
<tr>
<td>2</td>
<td>23,260</td>
<td>2.75</td>
<td>36</td>
<td>RDS</td>
</tr>
<tr>
<td>3</td>
<td>29,400</td>
<td>1.95</td>
<td>33</td>
<td>No RDS</td>
</tr>
<tr>
<td>4</td>
<td>14,600</td>
<td>2.98</td>
<td>38</td>
<td>No RDS</td>
</tr>
<tr>
<td>5</td>
<td>25,000</td>
<td>2.14</td>
<td>34</td>
<td>RDS</td>
</tr>
</tbody>
</table>
anhydrase activities for the cases which received one or more intrauterine transfusions.

Discussion

It is obvious that all newborn infants have carbonic anhydrase activities much below the levels found in the blood of healthy adults. There is presumably a critical level of enzyme activity below which CO₂ cannot be eliminated from the lungs effectively because of the slowed conversion of bicarbonate, and in our infants with RDS the mean level of enzyme activity was only 3.6% of normal adult level and 21% of the mean level found in mature newborn infants. On the other hand, it was 30% of the enzyme activity found in our 'small-for-dates' infants, none of whom showed respiratory distress, and the mean enzyme activity of preterm infants with RDS (848 units/ml) was not statistically significantly different from the mean enzyme activity found in premature infants without respiratory distress (1071 units/ml). It is, therefore, extremely unlikely that the very low levels of carbonic anhydrase activity in infants with RDS had any aetiological significance. This is compatible also with the recent finding that the absence of surfactant from the lungs and the probable development of RDS postnatally can be forecast before birth from measurement of the lecithin/sphingomyelin ratio in the liquor amnii obtained by amniocentesis (Gluck et al., 1971; Whitfield et al., 1972). However, deficiency of carbonic anhydrase activity in infants suffering from RDS and consequent CO₂ retention may worsen an already serious situation by inhibiting the conversion of bicarbonate to CO₂, so that diffusion of CO₂ out of the pulmonary capillaries will not be satisfactory during the rapid passage of the blood through the lungs. In common with others, we have sometimes had the impression that exchange transfusion for haemolytic disease in infants who also suffered from RDS had a beneficial effect on the respiratory disorder. 4 of the 33 infants who suffered from RDS had rhesus incompatibility of a degree requiring exchange transfusion. 3 died despite intensive care, including ventilation. The respiratory problem did not appear to improve during transfusion. The fourth infant (birthweight 2730 g at 36 weeks' gestation) tolerated the procedure of transfusion well. In 3 of the 5 infants treated by intrauterine transfusion and who also suffered from severe RDS (fatal in 2 cases), the carbonic anhydrase activity was up to normal adult levels. It seems, therefore, that, like so many other physiological measurements, the carbonic anhydrase levels in the newborn infant differ from those of the adult, and raising the enzyme activity in the preterm infant with RDS by exchange transfusion is unlikely to prove of much benefit.

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References


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