Effects of Intragastric and Intravenous Sodium Bicarbonate on Rate of Recovery from Post-asphyxial Acidosis in the Neonate

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Evans, R. S., Olver, R. E., Appleyard, W. J., and Newman, C. G. H. (1970). *Archives of Disease in Childhood*, 45, 321. **Effects of intragastric and intravenous sodium bicarbonate on rate of recovery from post-asphyxial acidosis in the neonate.** A trial was carried out on acidotic infants recovering from neonatal asphyxia, on the relative effects of intragastric and intravenous sodium bicarbonate on acid/base balance.

Intragastric bicarbonate caused an increased rate of correction of metabolic acidosis within 30 minutes of administration. However, the PCO_2 remained higher in these patients than in the controls, so that the effect of the bicarbonate on rate of pH correction was negligible. The rise in PCO_2 occurred despite apparently normal respiratory function.

A similar limitation of pH rise by a sustained rise in PCO_2 was evident in the intravenously treated patients.

Treatment of metabolic acidosis in neonates with sodium bicarbonate may not produce the desired correction of pH.

Sodium bicarbonate is widely used in the treatment of neonatal acidosis, particularly in cases of asphyxia and respiratory distress syndrome (RDS). For these purposes it is usually given by the intravenous route, either by single injection or as an infusion. Dramatic clinical and biochemical improvement may follow its use in severely asphyxiated newborn infants. Since this response might be the result of changes either of a biochemical nature, or involving the pulmonary vasculature, we decided to measure the actual effect on acid-base metabolism of currently used doses of intravenous sodium bicarbonate.

In 1967 Abraham and Brown suggested that in cases of RDS, bicarbonate given intragastrically was as effective in the correction of acidosis as bicarbonate given intravenously. We have followed up this observation with a trial of intragastric and intravenous bicarbonate given to acidotic infants recovering without complication from neonatal asphyxia. The trial was designed to show the relative rate and extent of correction achieved by the two routes.

Material and Methods

Observations were carried out on newborn infants recovering from moderate to severe degrees of asphyxia as judged clinically. Infants who had required urgent alkali therapy during the resuscitation procedure were excluded from the trial. Also excluded were those infants showing any clinical evidence of impairment of pulmonary function during the recovery period, in order to minimize the possibility of inadequate oxygenation causing variations in the rate of spontaneous correction of acidosis.

Those infants qualifying for the trial were randomly allocated treatment by a system of sealed envelopes and were given intravenous bicarbonate, intragastric bicarbonate, or intragastric water.

Cases allocated to intravenous treatment were given sodium bicarbonate 1.3 mEq/kg. injected over two minutes via an umbilical vein catheter. This dosage, though generally insufficient for full correction, may be safely used for emergency treatment of asphyxiated infants before acid-base measurements.

Cases allocated to intragastric treatment were given either sodium bicarbonate 2.6 mEq/kg. by nasogastric tube or, in control cases, water 4 ml./kg. The intragastric contents were first aspirated, and there was no vomiting or noticeable distension. All doses were given at approximately one hour after the onset of effective

ventilation in order to avoid the more marked and unpredictable acid-base changes which occur in the first 30 minutes (James, 1963).

1 ml. umbilical venous blood samples for acid-base analysis were withdrawn into 2 ml. heparinized plastic syringes, and kept in iced water until estimated (within 1 hour). A separate study (Evans and Olver, to be published) has shown that samples stored in this manner showed negligible changes.

Blood samples were taken immediately before treatment, and at 10 minutes, 30 minutes, 1 hour, and 2 hours after treatment. Estimation of pH, PCO_2 , and standard bicarbonate was carried out by standard Astrup technique (Astrup *et al.*, 1960).

Results

In the analysis of results, infants with pretreatment PCO_2 levels of greater than 45 mm. Hg were excluded, in order to minimize further the effects of differences in pulmonary function. Those with mild metabolic acidosis, i.e. those with pretreatment standard bicarbonate levels over 17.5 mEq/l., were also excluded.

Readings obtained on 5 cases in each treatment group were analysed. Clinical data and mean values, together with standard deviations, of acid-base parameters in the three groups immediately before treatment are shown in the Table. No significant difference between these initial readings for the three groups was found.

Changes in standard bicarbonate after treatment, expressed as a percentage of the initial values, are shown in Fig. 1. The intragastric bicarbonate group showed a greater percentage rise in standard

bicarbonate than the control group and this difference was significant at both 30 minutes and 1 hour. There was a large rise in standard bicarbonate in the intravenous group at 10 minutes, and this rise remained significantly greater than that of the control group at 30 minutes and after 60 minutes after administration.

FIG. 1.—Changes in standard bicarbonate: (a) after intragastric bicarbonate; (b) after intravenous bicarbonate.

Fig. 2 shows changes in pH in the three groups following treatment.

It will be seen that there was little difference in rate of pH rise between the intragastric group and the control group, and at no stage was this difference statistically significant. The pH rise in the intravenous group was of only short duration.

Changes in PCO_2 , expressed as a percentage of initial values, are shown in Fig. 3.

TABLE
Clinical Data and Initial Acid-base Status; Mean Values and Standard Deviations

	Control Group Intragastic Water	Intravenous 5% Bicarbonate	Intragastric 5% Bicarbonate
No. of cases	5	5	5
Birthweight (g.)	2182 ± 610	3040 ± 1029	2694 ± 466
Gestational age (wk.)	39 ± 2.4	39.6 ± 1.8	39 ± 2.4
Time from effective oxygenation to treatment (min.)	51 ± 15	61 ± 19.3	67 ± 9.2
Initial pH	7.20 ± 0.08	7.22 ± 0.03	7.19 ± 0.07
Initial PCO_2 (mm. Hg)	34 ± 8	36 ± 8	31 ± 7
Initial standard bicarbonate (mEq/l.)	14.4 ± 2.0	14.4 ± 1.3	13.0 ± 2.0

FIG. 2.—Changes in pH: (a) after intragastric bicarbonate; (b) after intravenous bicarbonate.

FIG. 3.—Changes in PCO_2 : (a) after intra-gastric bicarbonate; (b) after intravenous bicarbonate.

The intra-gastric bicarbonate group showed a mean rise in PCO_2 , while in the intra-gastric water group the PCO_2 values initially tended to fall. The difference in PCO_2 between the two groups was statistically significant at 30 minutes and 1 hour, and provides an explanation of the failure of the pH to rise more rapidly in the intra-gastric bicarbonate group compared with controls, despite a more rapid rise in standard bicarbonate,

A similar phenomenon was seen after the use of intravenous bicarbonate. There was a sustained and significant rise in PCO_2 values in the bicarbonate group compared with the intra-gastric water controls.

A comparison of the intra-gastric and intravenous bicarbonate groups showed a significantly greater percentage rise of pH at 10 minutes after intravenous injection, but the reverse (intra-gastric pH rise greater than intravenous) at 60 minutes. There was no significant difference between the two groups at 30 and at 120 minutes. At 60 minutes there was a significantly greater rise of PCO_2 in the intravenous group, and the reverse at 120 minutes. The percentage rise of standard bicarbonate in the intravenous group was significantly greater at 10 minutes only; there was no significant difference subsequently. The dose of bicarbonate given into the stomach was twice that injected intravenously.

Discussion

Intra-gastric sodium bicarbonate has been used in the treatment of metabolic acidosis in the respiratory distress syndrome with varying reported degrees of effectiveness. Abraham and Brown (1967) found evidence that bicarbonate was well absorbed and corrected the pH as effectively as bicarbonate given intravenously. Stoneman and

Owens (1968) found that though an accelerated recovery from metabolic acidosis could be achieved by giving intra-gastric sodium bicarbonate, there was little effect on rate of pH correction, for while in the untreated patient CO_2 levels tended to fall, in the treated patients high CO_2 levels tended to be maintained.

The results of the present study of the short-term effects of intra-gastric bicarbonate administration on moderately acidotic infants tend to agree with the latter view. Though there was evidence of an increased rate of correction of metabolic acidosis within 30 minutes of treatment, the PCO_2 remained higher in this group than in the controls, so that the effect on rate of correction of pH was negligible. It was of interest that this effect occurred despite apparently adequate pulmonary function.

In the group treated with intravenous bicarbonate there was an immediate correction of metabolic acidosis, but the levels of CO_2 again remained higher than the controls, so that the correction of pH achieved was rather less than might be expected. A similar effect was noted by Sinclair, Engel, and Silverman (1968) when using rapid arterial sodium bicarbonate infusion in low birthweight hypoxaemic acidaemic infants. In our series, the rise of PCO_2 that modified the rise of pH reached its peak in the intravenous group at 60 minutes, but not until 120 minutes in the intra-gastric group.

In contrast, Russell and Cotton (1968) found that after injection of sodium bicarbonate into the umbilical vein of infants with early RDS, the PCO_2 tended to fall. This was attributed to improvement in pulmonary function after release of pulmonary arteriolar spasm. This may well be a mechanism responsible for the sudden improvement in some severely asphyxiated newborn infants after the use of intravenous sodium bicarbonate. Berg, Mülling, and Saling (1969) showed a rise of pH associated with a rise of PCO_2 on injecting 1–2 mmole/kg. sodium bicarbonate into 7 rabbits, in a comparison of the effects of THAM and sodium bicarbonate. There was a considerable hyper-ventilatory response in the rabbits which were not, however, asphyxiated or acidotic before the injection of bicarbonate. The stimulation of respiration was probably a response to the rise in PCO_2 and only indirectly attributable to the bicarbonate. The relative effects of a low pH and of a raised PCO_2 *per se* are reviewed in Berg *et al.*'s article.

In the present state of knowledge of the indications for, and the optimal route, dose, and rate of infusion of bicarbonate, its effects are not entirely predictable. In many cases intended correction

of the metabolic component of acidosis in the circulating blood may not be followed by the desired correction of pH.

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