There is insufficient evidence from randomized controlled trials to support or refute the use of sodium bicarbonate during resuscitation of infants at birth. On the other hand, basic science and observational studies do not support the use of sodium bicarbonate during resuscitation.

RHL Commentary Ho JJ

1. INTRODUCTION

Perinatal asphyxia is a leading cause of perinatal mortality in developing countries. According to the World Health Organization, in 2004, worldwide there were 133 million live births and 3.7 million neonatal deaths, 98% of which occurred in developing countries (1). About 23% of neonatal deaths were due to perinatal asphyxia (2). It is estimated that about 3% of live births in developing countries require neonatal resuscitation (3), but even in major hospitals in some developing countries resuscitation measures may be inappropriate (4).

Newborn babies that do not start breathing spontaneously have a high concentration of acid in their blood. Intravenous sodium bicarbonate infusion was introduced some thirty years ago to reverse metabolic acidosis. Since then, along with resuscitation, sodium bicarbonate infusion has become the standard treatment for initiating breathing in babies that do not start breathing spontaneously. Sodium bicarbonate entered into neonatal practice after Usher's publication of a report of his experience with the compound compared with historical controls. He reported a reduction in mortality for infants receiving a glucose and bicarbonate infusion of 65 ml/kg of body weight per day compared with no infusion (5). The original data supporting the effectiveness of sodium bicarbonate in newborn resuscitation had come from animal studies (6, 7). The main rationale for this was that acidosis reduces cardiac contractility and hence blood pressure. However, its use has been challenged on the grounds that upon administration the compound is converted into carbon dioxide, which is another acid. Carbon dioxide is excreted through the lungs, so the administration of sodium bicarbonate to a baby without adequate ventilation would result in build up of carbon dioxide, thereby worsening acidosis. The excess carbon dioxide produced by an infusion of sodium bicarbonate diffuses easily to equilibrate between extracellular and intracellular spaces, but there is a delay in diffusion of bicarbonate, resulting in intracellular acidosis and extracellular alkalosis (8). There are now quite a number of observational and some uncontrolled intervention studies in humans and most of these have failed to show a benefit (9). A recent guideline suggests it is only rarely required (10). The primary objective of this review was to determine whether in infants receiving resuscitation in the delivery room at birth the infusion of sodium bicarbonate compared with placebo or no treatment reduces mortality. The secondary objectives were to determine whether sodium bicarbonate reduced long- and short-term morbidity (in particular neurological disability) and whether it is more effective than other alkanising agents.
2. METHODS OF THE REVIEW

The authors included randomized or quasi-randomized studies of newborn infants (both term and preterm) who received any resuscitation in the delivery room. The intervention was sodium bicarbonate compared with placebo, no treatment or other alkalinizing agents such as tris-hydroxymethyl-aminomethane (THAM). The primary outcome was mortality in the delivery room and secondary outcomes included mortality in hospital, long-term neurodevelopmental outcome, neurological outcome at discharge, intraventricular haemorrhage and periventricular leukomalacia, neonatal seizures and other signs of hypoxic ischaemia encephalopathy, and necrotising enterocolitis.

The authors used an extensive and inclusive search of numerous sources to identify studies in any language. This was last done in September 2005. The decision to include individual studies and the quality evaluation was done independently by two authors. Identified studies were evaluated for allocation concealment, blinding of the intervention and outcome assessment and completeness of follow-up.

3. RESULTS OF THE REVIEW

The authors identified three studies in four publications. Two were excluded because the intervention was not carried out at resuscitation. The other remaining study, reported in two separate publications, was included. It involved 55 infants, both term and preterm, needing positive pressure ventilation at 5 minutes of age who were randomized to two groups: sodium bicarbonate or an equal volume of 5% dextrose. There were no differences for the whole population or the term and preterm subgroups for any of the six reported outcomes: mortality (death in the labour room was not reported in the study), abnormal neurological examination, the combined outcome of abnormal neurological examination or death before discharge, seizures, encephalopathy or intraventricular haemorrhage.

4. DISCUSSION

4.1 Applicability of the results

Overall, there is insufficient evidence from randomized controlled trials to support or refute the use of sodium bicarbonate. The one small study included in this review did not provide any evidence to support its use. Since the study was conducted in India, a middle-income country, the findings of the review are generalizable to other low- and middle-income countries.

Generally, if there is no evidence to support an intervention then it is difficult to justify its use. This would apply to sodium bicarbonate. Should evidence come to light to support its use then this conclusion could change. Sodium bicarbonate is not expensive, but nevertheless would involve additional costs which would include the cost of an umbilical venous catheter; even these small extra costs cannot be justified given the lack of evidence.

4.2 Implementation of the intervention
Resuscitation practices increasingly focus on airway management, in particular expansion of the lungs and the application of positive pressure ventilation when needed. Some guidelines recommend the use of sodium bicarbonate, but only after stabilization if significant metabolic acidosis persists in spite of adequate spontaneous respiration or assisted ventilation (10, 11, 12). To do this, facilities for blood gas analysis would be needed, and in many developing countries such facilities are limited. In these situations, the use of sodium bicarbonate after resuscitation would have to be empirically based on the infant’s condition after stabilization. There should be established and adequate respiration or assisted ventilation and other relevant interventions such as adrenalin and a fluid bolus should be completed. Helpful clinical indicators might be continued prolonged capillary refill time or low blood pressure in the presence of adequate ventilation.

4.3 Implications for research

Research into the use of sodium bicarbonate after stabilization and establishment of ventilation in settings where blood gas measurement is not available might be useful - for example, studies to assess the value of certain clinical features present in ongoing metabolic acidosis.

Basic science and observational studies do not support the use of sodium bicarbonate during resuscitation, so although the evidence in this review is insufficient to draw a conclusion, it is difficult to justify further studies. If any further randomized controlled trials were to be done, they would need to be done in countries where use of sodium bicarbonate is continuing and researchers there feel that it is justifiable to carry out further trials. Such trials should include neurodevelopmental outcomes in childhood.

Sources of Support
Penang Medical College, Hospital Pulau Pinang, Malaysia.

Acknowledgement
Dr ML Tan, Penang Medical College, Penang, Malaysia, for helpful comments on the manuscript.

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This document should be cited as: Ho JJ. Sodium bicarbonate infusion during resuscitation of infants at birth: RHL commentary (last revised: 1 February 2010). The WHO Reproductive Health Library; Geneva: World Health Organization.

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