

RPA Newborn Care Guidelines

Royal Prince Alfred Hospital

Acidosis

Introduction

Acidaemia is common in neonates especially in association with prematurity and perinatal asphyxia. It is essential to establish whether the acidaemia is respiratory with a raised PaCO₂, or metabolic with a normal PaCO₂ but a negative base excess, or a combination of both. Metabolic acidosis in preterm infants may be associated with hypoxaemia, hypotension or poor tissue perfusion, anaemia, infection or sepsis, or strenuous activity (respiratory distress).

A late metabolic acidosis may develop in premature infants that receive high protein or amino acid intakes. This may be exacerbated by reduced reabsorption of bicarbonate from the proximal tubules and reduced new base formation by the kidneys of premature infants.

This guideline deals with postnatal acidosis. See resuscitation for acidosis at birth.

Incidence and risk factors

Goldaber¹ studied 30,000 consecutive deliveries and found a cord pH < 7.2 occurred in 3506 infants (11.7%), pH < 7.1 in 472 (1.6%), and pH < 7.0 in 87 (0.3%). The incidence of postnatal acidosis has not been documented in the overall population of neonates born at KGV Hospital. In a cohort of preterm infants born at KGV the incidence of postnatal acidosis in the first 48hr of life by gestation were:

Gestation (weeks)	pH < 7.20	Base excess < -10
23 to 25	18%	26%
26 to 27	28%	19%
28 to 29	11%	14%

Important causes of acidosis in neonates:

- Perinatal asphyxia
 - Sepsis
 - Respiratory distress
 - Hypovolaemia
 - Low cardiac output and poor tissue perfusion
 - Hypothermia
 - Anaemia
 - Renal bicarbonate losses
 - Cardiac failure / congenital cardiac anomalies
 - Inborn error of metabolism
-

Consequences

There is an association between acidosis, acute physiological dysfunction in the neonate and longer term neurodevelopmental abnormalities. Whether the acidosis is causative or only associated with acute organ dysfunction and abnormal neurodevelopment is less certain. The following associations with acidosis have been documented:

Short term:

Acidaemia associated with asphyxia inhibits surfactant production^{2,3} and increases pulmonary vascular resistance⁴. A pH < 7.15 is associated with reduced myocardial contractility⁵ and diaphragmatic activity (in dogs⁶). EEG documented abnormal cerebral function has been shown in preterm infants < 32 weeks gestation in relation to episodes of acidosis⁷.

Hydrogen ions cause the precipitation of bilirubin acid. Acidosis may exacerbate kernicterus. This should be taken into account in the treatment of hyperbilirubinaemia

Longer term:

There is an association between neonatal acidosis and evidence of end-organ damage from perinatal asphyxia including hypoxic ischaemic encephalopathy. In the series of 30 000 infants of Goldeber¹, the incidence of neonatal death and neonatal seizures did not increase until a pH < 7.05 was reached. The absolute incidence of otherwise unexplained neonatal seizures was 1.1% for pH < 7.05 and 9.2% for pH < 7.00. The mortality increased to 1.1% for pH < 7.05 and 8% at a pH < 7.00.

In preterm infants there is an association between a low umbilical arterial pH and subsequent abnormal neurodevelopmental outcome in extremely low birth weight infants⁸.

Diagnosis

Determination of acid-base status may be made by:

- Arterial blood gas - cord umbilical artery at delivery, umbilical arterial line, or peripheral arterial line or arterial puncture post delivery.
- Capillary blood gas - more accurate at determining pH, less accurate for PCO₂ and

inaccurate at predicting arterial PO₂. Results should be used with caution⁹.

It is essential to establish whether the acidaemia is respiratory with an elevated PaCO₂ or metabolic with a normal PaCO₂ but a negative base excess, or a combination of both.

Acidosis may be:

- Respiratory: low pH, high PaCO₂, and high HCO₃
- Metabolic: low pH, negative base excess
- Mixed metabolic and respiratory: low pH, high PaCO₂ and negative base excess most frequent in premature infants)
- Compensated respiratory: near normal pH, high PaCO₂, high base excess and near normal HCO₃
- Compensated metabolic: near normal pH, low PaCO₂, negative base excess and low HCO₃

Establishing the underlying cause of the acidosis may be assisted by:

- History - evidence of fetal distress, risk factors for sepsis, prematurity
- Examination - respiratory distress, cardiac disease, poor peripheral perfusion, pallor (anaemia), hypotension, unusual odours (metabolic disease),
- Serum Na, K, Cl, and bicarbonate (on ABG) to determine anion gap = $([Na + K] - [Cl + HCO_3])$
- Blood lactate to confirm lactic acidosis
- Metabolic screen: urine and serum for amino acids and organic acids
- Blood count - sepsis, anaemia
- Blood cultures - sepsis
- ECHO - low cardiac output

Interventions

Respiratory acidosis should be corrected by manipulation of the ventilation. Normocarbica (PaCO₂ 35-45 mmHg) should be the aim of ventilatory management. Bicarbonate therapy given to a hypercarbic baby may worsen the hypercarbia as well as increase cerebral acidosis (animal and adult data reviewed by Howell¹⁰).

Metabolic acidosis is most often corrected by attention to its cause. **Hypocarbica should not be produced when treating a metabolic acidosis.**

- **Bicarbonate therapy:**

Consider treatment with alkali in infants if pH < 7.20 and a metabolic acidosis is present (low pH and high base deficit). The evidence for use of alkali therapy in premature infants with respiratory distress is equivocal. Several studies have attempted to demonstrate the effect of treatment of early acidosis in infants (usually pH < 7.25) with RDS and shown differing results^{11, 12, 13}.

Whether correction of severe acidosis improves outcomes has not been studied in a randomized trial.

Give bicarbonate therapy over 30-60 minutes. Sinclair¹¹ studied rapid (<5 minutes) versus slow bicarbonate therapy (over 24 hours) and found a trend to increased mortality in the rapid group and no benefit in terms of time to correction of pH. In view of experiences with rapid infusions of bicarbonate resulting in an increased incidence of intraventricular haemorrhage^{14, 15, 16} (non-randomised studies) and animal data suggesting harmful effects (reviewed by Howell¹⁰) rapid infusions of bicarbonate should be avoided where possible.

- **Alkalinisation of total parenteral nutrition:**

Acetate should be added to total parenteral nutrition of infants with a base deficit \geq 5. Premature infants with late metabolic acidosis have better weight gain and higher nitrogen assimilation if given NaHCO_3 compared to saline¹⁷, and the use of acetate in total parenteral nutrition for premature infants reduces the severity of the acidosis and incidence of hyperchloraemia¹⁸.

- **Bicarbonate therapy for resuscitation:**

See resuscitation.

- **THAM (tris-hydroxymethylaminomethane):**

THAM is not available in Australia. This alkali has the potential advantages of not causing hypernatraemia and hypercarbia. However, it provides a higher osmolar load in equimolar doses to sodium bicarbonate and caused depression of ventilation and hypoglycaemia. It has not been subjected to randomised trials.

If a decision is made to correct the metabolic acidosis using base, sodium bicarbonate is used in the following amount. Remember that repeated infusion of sodium bicarbonate may cause hypernatraemia. Half correction should be aimed at and repeated if necessary. Use sodium bicarbonate 8.4% and dilute 50:50 with water (= 4.2%).

For half correction:

$$4.2\% \text{ NaHCO}_3 \text{ (ml)} = \text{weight (kg)} \times \text{base deficit} \times 0.3$$

Administer over 30-60 minutes.

Key Points

Key points	Level of evidence
Treat acidosis to keep pH \geq 7.20	★
Avoid giving rapid infusions of bicarbonate (<5minutes)	★★★★★ ¹¹

Use bicarbonate 4.2% (1:1 dilution of 8.4% NaHCO₃ and water)

★ ★ 14, 15, 16

References

1. Goldaber KB, Gilstrap LC III, Leveno KJ. Pathologic fetal acidemia. *Obstet Gynecol.* 1991; **78**: 1103-.
2. Linderkamp O, Versmold HT, Fendel H, Reigel KP, Betke K. Association of neonatal respiratory distress with birth asphyxia and deficiency of red cell mass in premature infants. *Eur J Pediatr.* 1978; **129**: 167-173.
3. Thibault DW, Hall FK, Sheehan MB, Hall RT. Postasphyxial lung disease in newborn infants with severe perinatal acidosis. *Am J Obstet Gynecol.* 1984; **150**: 393-399.
4. Rudolph AM, Yuan S. Response of the pulmonary vasculature to hypoxia and hydrogen ion changes. *J Clin Invest.* 1966; **45**: 399-411.
5. Beierholm EA, Grantham N, O'Keefe DD, Laver MB, Daggett WM. Effects of acid-bas changes, hypoxia and catecholamines on ventricular performance. *Am J Physiol.* 1975; **228**: 1555-1561.
6. Howell S, Fitzgerald RS, Roussos C. Effects of uncompensated and compensated metabolic acidosis on canine diaphragms. *J Appl Physiol.* 1985; **59**: 1376-1382.
7. Eaton DG, Wertheim D, Oozeer R, Dubowitz LM, Dubowitz V. Reversible changes in cerebral activity associated with acidosis in preterm neonates. *Acta Pediatr.* 1994; **83**: 486-492.
8. Gaudier FL, Goldenberg RL, Nelson KG, Peralta-Carcelen M, Johnsini SE, DuBard MB, Roth TY, Hauth JC. Acid-base status at birth and subsequent neurosensory impairment in surviving 500 to 1000 gm infants. *Am J Obstet Gynecol.* 1994; **170**: 48-53.
9. Courtney SE, Weber KR, Breakie LA, Malin SW, Bender CV, Guo SM, Siervogel RM. Capillary blood gases in the neonate. A reassessment and review of the literature. *Am J Dis Child.* 1990; **144**: 168-172.
10. Howell JH. Sodium bicarbonate in the perinatal setting - revisited. *Clin Perinatol.* 1987; **14**: 807-816.
11. Sinclair JC, Engel K, Silverman WA. Early correction of hypoxemia and acidemia in infants of low birth weight. A controlled trial of oxygen breathing, rapid alkali infusion and assisted ventilation. *Pediatrics.* 1968; **42**: 565-589.
12. Hobel CJ, Oh W, Hyvarinen MA, Emmanouilides GC, Erenberg A. Early vs late treatment of neonatal acidosis in low-birth-weight infants. Relation to respiratory distress syndrome. *J Pediatr.* 1972; **81**: 1178-1187.
13. Corbett AJ, Adams JM, Kenny JD, Kennedy J, Rudolph AJ. Controlled trial of bicarbonate therapy in high-risk premature newborn infants. *J Pediatr.* 1977; **91**: 771-776.
14. Usher R. Comparison of rapid versus gradual correction of acidosis in RDS of prematurity. *Pediatr Res.* 1967; **3**: 221-
15. Simmons MA, Adcock EW, Bard H et al. Hyponatremia and intracranial hemorrhage in neonates. *N Eng J Med.* 1974; **291**: 6-10.
16. Papile L, Burstein J, Burstein R et al. Relationship of intravenous sodium bicarbonate administration and cerebral intraventricular hemorrhage. *J Pediatr.* 1978; **93**: 834-836.
17. Kalhoff H, Manz F, Diekmann L, Kunz C, Stock GJ, Weisser F. Decreased growth rate of low-birth-weight infants with prolonged maximal renal acid stimulation. *Acta Paediatr.* 1993; **82**: 522-527.
18. Peters O, Ryan S, Matthew L, Cheng K, Lunn J. Randomised controlled trial of acetate in preterm neonates receiving parenteral nutrition. *Arch Dis Child Fetal Neonatal Ed.* 1997; **77**: F12-15.

