Anaesthetic management of a child with Bartter's syndrome

Suresh Kannan MD (Anaesth), Yvette Delph DA, H.S.L. Moseley FRCA

We report the anaesthetic management of an eight-year-old asthmatic boy with Bartter's syndrome who had bilateral orchidopexy with caudal epidural analgesia. Bartter's syndrome is a rare congenital disorder characterized by hypokalaemic hypochloraemic metabolic alkalosis, hyperaldosteronism, hyperreninaemia and hyperplasia of the juxtaglomerular apparatus of the kidneys. Characteristically, although these patients are normotensive they may be hypovolaemic. They may have unstable baroreceptor responses and show marked resistance to vasopressors. Hence, fluid, acid-base and electrolyte imbalances along with haemodynamic instability pose particular problems in their anaesthetic management. Previous case reports have described the management of these patients with general anaesthesia, our patient had his orchidopexy with caudal epidural analgesia using plain bupivacaine 0.5%. The patient was haemodynamically stable throughout surgery and was comfortable with caudal analgesia as the sole anaesthetic. Hypovalaemia, acid-base status and electrolyte imbalance were treated before instituting caudal epidural analgesia. We present this case report which describes the anaesthetic considerations in the light of the pathophysiology of Bartter's syndrome.

Le syndrome de Bartter est une affection congénitale rare caractérisée par une acidose métabolique hypochlohydrique avec hypokaliémie, hyperaldostéronisme, hyperréninémie associées à l'hyperplasie de l'appareil juxtaglomérulaire rénal. Cette observation décrit la gestion anesthésique d'un garçon asthmatique porteur d'un syndrome de Bartter soumis à une orchidopexie bilatérale sous anesthésie caudale. Bien qu'ils soient typiquement normotensifs, parfois ces patients sont en même temps hypovolémiques. Ils présentent des réponses baroréceptrices variables et une résistance marquée aux vasopresseurs. Par conséquent, les désiquilibres hydriques, acidobasiques et électrolytiques sont associés à l'instabilité hémodynamique et, pour cette raison, posent des problèmes particuliers lors de l'anesthésie. Des observations antérieures font état d'une gestion sous anesthésie générale mais dans ce cas-ci, l'orchidopexie a été réalisée sous anesthésie régionale caudale à la bupivacaïne 0,5%. Le patient a été stable sous le plan hémodynamique et confortable avec l'anesthésie caudale seule. L'hypovolémie, l'équilibre acidobasique et le dérangement électrolytique ont été traités avant l'initiation de l'anesthésie caudale. Les auteurs présentent cette observation qui décrit certaines particularités de l'anesthésie propres à la physiopathologie du syndrome de Bartter.

Key words
ANAESTHESIA: paediatric;
ANAESTHETIC TECHNIQUES: epidural, caudal;
COMPLICATIONS: hypokalaemia, metabolic alkalosis;
SYNDROMES: Bartter's syndrome.

From the Department of Anaesthesia and Surgical Intensive Care, Queen Elizabeth Hospital, Barbados, West Indies.
Address correspondence to: Dr. Suresh Kannan, Department of Anaesthesia and Surgical Intensive Care, Queen Elizabeth Hospital, University of West Indies, Barbados.
Accepted for publication 30th April, 1995.

Bartter's syndrome (congenital hypokalaemic alkalosis) is characterized by severe hypokalaemic, hypochloraemic, metabolic alkalosis; extremely high levels of circulating renin and aldosterone; with a paradoxical absence of hypertension.[1-14] The first description of the syndrome was made by Bartter in 1962 when he reported two negro patients aged 5 and 25 yr.[4] Reported ages of diagnosis vary from 10 mo to 46 yr. Clinical features appearing in infancy or childhood include anorexia, failure to thrive, polyuria, polydipsia, constipation and muscle weakness (signs of hypokalaemia are almost always present).[1,5,14] Features that are frequently associated with this syndrome include hypomagnesaemia, hypercalciuria, hyperuricaemia, and increased urinary prostaglandin E_2 excretion.[5] In certain families the disease may be inherited as an autosomal recessive trait.[3] The annual incidence of the syndrome has been estimated at 1.2 per million people.[2] The cause and pathogenesis are unknown. The pathogenesis of the syndrome is thought to be related to sodium reabsorption defects in the proximal or distal renal tubule.[2-5,9] Studies have associated elevated concentrations of prostaglandins with the syndrome and treatment with inhibitors of prostaglandin (e.g., indomethacin) has been advocated.[1-6,8] In addition treatment

with potassium-conserving diuretics (e.g., spironolactone – an aldosterone antagonist) has proved beneficial.[1-5,8] Most patients present in early infancy with severe failure to thrive. Although the prognosis is poor, a few patients seem to have less severe forms of the disease which are compatible with a longer life.[1] This case report describes the anaesthetic implications of Bartter's syndrome in the light of the pathophysiology and the associated fluid, electrolyte and acid-base derangements.

Case report

An eight-year-old boy, weighing 30 kg, a known case of Bartter's syndrome, was scheduled for elective orchidopexy for bilateral undescended testes. In view of his disease, he was admitted to the paediatric ward for investigation, preparation and preanaesthetic evaluation. The preanaesthetic evaluation revealed that, in addition to Bartter's syndrome, he also had asthma. His last attack of asthma was one month before admission. His past history indicated treatment for epilepsy for which therapy had been discontinued about four years previously. The patient was receiving oral indomethacin, spironolactone, potassium chloride, ammonium chloride and sodium chloride for his Bartter's syndrome and beclomethasone and salbutamol inhalers for his asthma.

Initial examination revealed a pleasant, well built, eight-year-old whose physical examination was unremarkable. On admission, investigations showed a hypokalaemic, hypochloraemic, metabolic alkalosis – Na^+134, K^+2.1, Cl^-89, and a HCO_3^- 35 mmol · L^{-1}. His oral supplements of ammonium chloride and potassium chloride were increased and, in addition, intravenous replacement therapy with potassium chloride and saline was commenced. Electrolytes were measured on a six-hourly basis. With the above therapy, at the end of the second day, his electrolytes were as follows: Na^+135, K^+3.8, Cl^-95 and HCO_3^- 28 mmol · L^{-1}. It was decide to proceed with surgery on the following day and his medication was continued through the night. The electrolytes repeated prior to surgery were as follows: Na^+136, K^+3.5, Cl^-95, HCO_3^- 25 mmol · L^{-1}. He received premedication of meperidine 30 mg and promethazine 15 mg, *im*, one hour before surgery. Eutectic mixture of local anaesthetics cream (EMLA) was applied to the sacrococcygeal region to facilitate a caudal epidural analgesia. He had a single dose of beclomethasone and salbutamol inhaler preoperatively.

On transfer to the operating room the ECG, oxygen saturation (SPO_2), end-tidal CO_2 ($PETCO_2$ was measured by a simple modification to the standard twin-nasal cannula) and non-invasive blood pressure (NIBP) monitors were attached. He was placed in the left lateral position and received a caudal epidural analgesia with 12 ml bupivacaine 0.5%, injected into the epidural space after negative aspiration for blood/CSF. There was sensory block to T_8. He was haemodynamically stable throughout surgery and was transferred to the recovery room and then discharged to the ward after an uneventful recovery.

Postoperatively, his oral medication was recommenced and a day later he was discharged to out-patient follow-up.

Discussion

An eight-yr-old asthmatic boy with Bartter's syndrome was posted for elective bilateral orchidopexy. Hypokalaemic hypochloraemic metabolic alkalosis is pathognmonic of the syndrome. However, it is unusual to be able to correct completely the electrolyte abnormalities associated with this syndrome despite treatment. In addition, even though these patients are normotensive, they maybe hypovolaemic. Hence, we hospitalized our patient to evaluate and prepare him for surgery. Although previous case reports have described management for these patients under general anaesthesia (without encountering major problems) we managed our patient with epidural analgesia. Caudal epidural analgesia was our choice of anaesthetic technique, for the surgery he had to undergo. Therefore, an understanding of the pathophysiological basis of Bartter's syndrome is relevant to the anaesthetic management of these patients.

The pathogenesis of Bartter's syndrome is obscure. Experimental patient data support the notion that the failure to conserve potassium is due to an imbalance between tubular secretory and reabsorptive processes.[9,10] Currently, the disorder is best explained as a primary defect in chloride reabsorption in the ascending limb of the loop of Henle. The defect in chloride reabsorption presents an extra load of sodium chloride to the distal tubule, where the sodium is reabsorbed in exchange for potassium, resulting in increased urinary potassium loss.[1-5,8,9] The syndrome is also characterized by signs of severe hyperaldosteronism (hypokalaemic alkalosis) and, in some cases, the hypokalaemia may be further potentiated by a defect *per se* in renal conservation of potassium.[9] Renal tubular function is markedly impaired by potassium depletion. The most obvious abnormality is decreased concentrating ability that may cause polyuria and polydipsia. Juxtaglomerular cell hyperplasia is a prominent feature of the syndrome. The stimulus to hyperplasia is unknown; hypotheses include resistance to angiotensin in blood vessels and subclinical volume depletion due to renal tubular sodium wasting.[8] Hence, depletion of the intravascular fluid volume is an important factor in maintaining metabolic alkalosis. Moderate al-

kalosis is typical of patients with Bartter's syndrome. In addition, hypokalaemia and skeletal muscle weakness are often present when hypovolaemia complicates metabolic alkalosis.[15]

A number of different observations point to overproduction of prostaglandins as one of the major features of the syndrome.[1-13] Overproduction of prostaglandins (PGE_2 and PGI_2) is now recognized to be a secondary phenomenon which occurs in any condition of profound and prolonged potassium depletion. The prostaglandins, in turn, activate the renin-angiotensin-aldosterone system by increasing renin release and by stimulating aldosterone synthesis.[4] Di Pietro *et al.*[11] have sought to explain the contradictory normotension of the syndrome and the associated electrolyte changes on the basis of excess atrial natriuretic peptide concentrations.[11,12]

Review of the implications of the electrolyte and acid-base changes help in the formulation of an appropriate management strategy of a patient with Bartter's syndrome. Hypokalaemia alters the electrical activity of the heart making it more susceptible to dysrhythmias, digitalis and hypoxia.[16-20] Muscle strength may be impaired and neuromuscular relaxants may be potentiated.[17] Hypokalaemia may be associated with ileus and delayed gastric emptying due to smooth muscle weakness and hypoperistalsis, creating the risk of aspiration.[16-18] Acute hypokalaemia has been reported in patients receiving $beta_2$-adrenergic agonists, xanthines and steroids[16-19] (our patient was receiving salbutamol and beclomethasone for his asthma). Potassium deficiency *per se* results in metabolic alkalosis.[4] The increased pH causes a shift of the oxygen dissociation curve to the left with resultant increased oxygen binding to haemoglobin and less oxygen unloading at the tissue level. Also, metabolic alkalosis further potentiates hypokalaemia by causing intracellular shift of potassium.[16,17] In untreated metabolic alkalosis, the other adverse effects are the decrease in ionized calcium concentration, the increased potential for seizures and the compensatory hypoventilation which increases the potential for atelectasis.

In untreated Bartter's syndome, large amounts of potassium chloride may be required to treat hypokalaemia. Potassium replacement alone seldom reverses hypokalaemia and therapy with potassium-sparing diuretics and prostaglandin synthetase inhibitors is often necessary. Metabolic alkalosis is treated by restoring intravascular volume and replacing potassium and chloride deficits. Serum chloride and bicarbonate levels provide indices for assessing correction of the metabolic alkalosis.[21] A combination of oral and intravenous therapy, spread out over two days, with frequent measurements of the electrolyte concentrations renders correction of imbalance, safe.[16,17]

Bartter's syndrome has implications for anaesthesia because of the fluid, acid-base and electrolyte changes.[6,7,10-13] This patient presented with hypokalaemic, hypochloraemic metabolic alkalosis in spite of treatment. This is consistent with the findings of Rudin[2] that treatment rarely resulted in normokalaemia. In our case, we had an added problem of the patient not complying with the oral supplements because of their unpleasant taste. Such patients, especially children, will need hospitalization to prepare them for surgery. Potassium therapy is not benign[16-18] and so we hospitalized our patient to deal with the fluid, electrolyte and metabolic derangements. Higa *et al.*[7] described the management of a patient with Bartter's syndrome with serum potassium concentrations ranging from 1.2 $mmol \cdot L^{-1}$ to 1.7 $mmol \cdot L^{-1}$ in the perioperative period. They anaesthetized him although serum potassium concentration prior to induction was only 1.6 $mmol \cdot L^{-1}$. The pre-anaesthetic serum potassium concentrations in the cases reported by Nishikawa and Dohi and Abston and Priano were 3.1 $mmol \cdot L^{-1}$ and 2.9 $mmol \cdot L^{-1}$ respectively.[6,8] It is now accepted that chronic asymptomatic hypokalaemia is relatively benign and that it does not increase the risk of cardiac dysrhythmias.[16,17,20] However, we thought it prudent to restore potassium to acceptable levels (2.5–3.5 $mmol \cdot L^{-1}$) before surgery.[16-20]

The implications of the fluid, electrolyte and acid-base derangements as outlined above may make general anaesthesia an unattractive option in these patients. However, in the two reported cases of the anaesthetic management of adults with Bartter's syndrome, general anaesthesia was administered without major complications.[6-8,12] Preoperative anxiety may cause a small decrease in serum potassium concentration.[16] Suitable anxiolytic premedication would be expected to prevent such changes. In an anxious patient, however, a combination of hypokalaemia, increased plasma adrenaline concentration and administration of a volatile agent such as halothane might cause arrhythmias during induction of anaesthesia. Acute or chronic hypokalaemia in the maintenance phase of anaesthesia may cause muscle weakness and intermittent positive-pressure ventilation is recommended. If neuromuscular relaxants are used, loading doses of non-depolarizers should be reduced and neuromuscular transmission monitored with a nerve stimulator.[7,16] If hypokalaemia and metabolic alkalosis are present hyperventilation should be avoided and normocapnia maintained.[6,16,17] Abston and Priano[6] managed their patient with Bartter's syndrome with a balanced anaesthetic technique using droperidol, fentanyl, thiopentone, 70% nitrous oxide/30% oxygen and pancuronium. They avoided inhalational anaesthetics because of undesirable cardiac depressant effects and a concern for intraoperative hy-

potension[8,11] on account of the marked resistance to vasopressors, in these patients, attributed to the prostaglandins. Unstable baroreceptor responses, aggravated by halothane and nitrous oxide, have been demonstrated in a patient with Bartter's syndrome. This may be attributable to a number of factors, besides prostaglandins, including hypovolaemia, hypokalaemia and positive-pressure ventilation.[8] This emphasizes the need for haemodynamic stability irrespective of the anaesthetic technique.

Thus, in these patients, regional anaesthesia may be a reasonable alternative. Caudal epidural analgesia with bupivacaine was the anaesthetic planned for the orchidopexy in our patient. The volume of the bupivacaine 0.5% calculated in accordance with the Hain formula was 13 ml for a block up to T_{10} segment. However, the injected volume of 12 ml bupivacaine 0.5% resulted in a sensory block up to T_8. Our patient received 12 ml plain bupivacaine 0.5%, a total dose of 60 mg (bupivacaine 2.0 $mg \cdot kg^{-1}$)[22] to avoid systemic overdosing.[14] We preferred to use a concentration of bupivacaine 0.5% for producing surgical anaesthesia as we intended the caudal epidural to be the sole anaesthetic for the surgical procedure. Caudal epidural analgesia was preferred for a number of reasons. Epidural analgesia with local anaesthetics provides excellent analgesia with haemodynamic stability.[23] Studies by Wolf *et al.*[24] in infants and Murat *et al.* in older children have shown that epidural analgesia suppressed hormonal-metabolic stress responses.[23-25] Several series have suggested that epidural analgesia is particularly suitable for infants and children with respiratory disease[23] (our patient was an asthmatic). Higa *et al.* reported that plasma renin activity, angiotensin II and aldosterone values were highest during surgery in an adult patient with Bartter's syndrome during general anaesthesia.[7] Wolf *et al.* showed that extradural anaesthesia may eliminate the increase in catecholamine concentrations in response to pelvic surgery in adults and that caudal bupivacaine has a similar effect in children undergoing minor urogenital surgery.[24,25] This is important since increase in endogenous catecholamine concentrations may reduce serum potassium. However, Higa *et al.*, reporting the anaesthetic management of an adult with Bartter's syndrome, mentioned that the blood pressures tended to be lower (75/35 to 110/60 mmHg) during surgery. Their patient underwent anterior resection of the rectum with general anaesthesia with 50% nitrous oxide-oxygen, 0.5–0.8% isoflurane, intravenous midazolam, butorphanol and had epidural morphine given postoperatively.[7] For these reasons we preferred an epidural for our patient with Bartter's syndrome.

Abston and Priano reported fluctuation in the serum potassium concentrations between 2.6 and 6.0 $mmol \cdot L^{-1}$, in their report.[6] They also observed changes in central venous pressures between −2 and +7 cm H_2O and mentioned the problem of the brisk continuous diuresis in their patient, which averaged 250–285 $ml \cdot hr^{-1}$. They emphasized the need for careful observation of fluid balance and recommended invasive cardiovascular monitoring in these patients. They recommended a Foley's catheter and arterial line to monitor acid-base and electrolyte status during major surgery (both serum concentrations and urinary excretion with regard to potassium).[6] In addition to the above, we strongly recommend $P_{ET}CO_2$ monitoring in these patients to ensure normocapnia.

In conclusion, Bartter's syndrome should be suspected in any patient, irrespective of age, who manifests hypokalaemic, hypochloraemic metabolic alkalosis not explained by other obvious causes. The anaesthetic management of a patient with Bartter's syndrome must take into account, not only the anaesthetic technique, but also the preoperative preparation and postoperative care of the patient. Formulation of an appropriate management plan for these patients should include considerations of the need for close interaction with the paediatrician for preoperative preparation, the advantages of epidural analgesia and the implications for general anaesthesia.

Acknowledgements

The authors are grateful to Dr. K. Bhavani-Shankar and Professor E.R. Walrond for technical help and for reviewing the manuscript.

References

1 *Lum GM, Todd JK, O'Brien D.* Kidney and urinary tract. *In*: Kempe CH, Silver HK, O'Brien D, Fulginti VA (Eds.). Current Pediatric Diagnosis & Treatment 1987, 9th ed. Norwalk: Appleton & Lange, 1993: 615.

2 *Rudin A.* Bartter's syndrome: a review of 28 patients followed for 10 years. Acta Med Scand 1988; 224: 165–71.

3 *Behrman RE, Kleigman RM, Nelson WE, Vaughan VC III.* Nelson Textbook of Pediatrics, 14th ed. Philadelphia: W.B. Saunders Company, 1992: 1348.

4 *Ledingham JGG.* Disorders of potassium metabolism. *In*: Weatherall DJ, Ledingham JGG, Warrell DA (Eds.). Oxford Textbook of Medicine, vol. 2, 2nd ed. Oxford: Oxford University Press, 1989: 18.31–18.33.

5 *Moxey-Mims M, Stapleton FB.* Renal tubular disorders in the neonate. *In*: Bailie MD (Ed.). Clinics in Perinatology: Renal Function and Disease. Philadelphia: W.B. Saunders Company, 1992: 166–7.

6 *Abston PA, Priano LL.* Bartter's syndrome: anesthetic implications based on pathophysiology and treatment. Anesth Analg 1981; 60: 764–6.

7 *Higa K, Ishino H, Sato S, Dan K.* Anesthetic manage-

ment of a patient with Bartter's syndrome. J Clin Anesth 1993; 5: 321–4.

8 *Nishikawa T, Dohi S.* Baroreflex function in a patient with Bartter's syndrome. Can Anaesth Soc J 1985; 32: 646–50.

9 *Kathpalia S, Coe FL.* Hereditary tubular disorders. *In*: Petersdorf RG, Adams RD, Braunwald E, Isselbacher KJ, Martin JB, Wilson JD (Eds.). Harrison's Principles of Internal Medicine, 10th ed. New York: McGraw-Hill Book Company, 1983: 485, 1668.

10 *Gitelman HJ.* Unresolved issues in the pathogenesis of Bartter's syndrome and its variants. Cur Opin Nephro Hyperten 1994; 3: 471–4.

11 *Di Pietro A, Proverbio MR, Capuano F, Chianese F, Coletta S, Catera P.* Elevated atrial natriuretic peptide (ANP) levels and normotension in Bartter's syndrome in childhood [Italian]. Paediatrica Medica e Chirurgica 1993; 15: 289–90.

12 *Katz J, Steward DJ.* Anesthesia and Uncommon Pediatric Diseases, 2nd ed. Philadelphia: W.B. Saunders Company, 1993: 261–2.

13 *Steward DJ.* Manual of Pediatric Anesthesia, 3rd ed. New York: Churchill Livingston, 1990: 345.

14 *Rasmussen GE, Bell C.* Pediatric syndromes and anesthetic implications. *In*: Bell C, Hughes CW, Oh TH (Eds.). The Pediatric Anesthesia Handbook. St. Louis: Mosby Year Book, 1991: 361.

15 *Stoelting RK, Dierdorf SF.* Handbook for Anesthesia and Co-Existing Disease. New York: Churchill Livingstone, 1993: 218.

16 *Vaughan RS.* Potassium in the perioperative period. Br J Anaesth 1991; 67: 194–200.

17 *Vitez T.* Potassium and the anaesthetist. Can J Anaesth 1987; 34: S30–S31.

18 *Bevan DR.* Acute biochemical disorders. *In*: Vickers MD, Jones RM (Eds.). Medicine for Anaesthetists, 3rd ed. Oxford: Blackwell Scientific Publications, 1989: 362–3.

19 *Eisenkrafi JB.* Electrolyte Disturbances and the ECG. *In*: Thys DM, Kaplan JA (Eds.). The ECG in Anesthesia and Critical Care. New York: Churchill Livingstone, 1987: 167–72.

20 *Wong KC, Sperry R.* What is an acceptable preoperative serum potassium level for surgery? (Letter). Anesthesiology 1994; 81: 269.

21 *Stehling L.* Common Problems in Pediatric Anesthesia, 2nd ed. St. Louis: Mosby Year Book, 1992: 73.

22 *Coad NR, Hain WR.* Caudal anaesthesia for postoperative pain relief in children: a comparative trial of different regimens using plain bupivacaine. Ann R Coll Surg Engl 1989; 71: 245–8.

23 *Berde C.* Epidural analgesia in children (Editorial). Can J Anaesth 1994; 41: 555–60.

24 *Wolf AR, Eyres RL, Laussen PC, et al.* Effect of extradural analgesia on stress responses to abdominal surgery in infants. Br J Anaesth 1993; 70: 654–60.

25 *Nakamura T, Takasaki M.* Metabolic and endocrine responses to surgery during caudal analgesia in children. Can J Anaesth 1991; 38: 969–73.