Supraventricular tachycardia associated with continuous furosemide infusion

Nigel J Wilson MBChB MRCP, Robert J. Adderley MD FRCPC, Julie A. McEniery MBBS FRACP

Three cases of supraventricular tachycardia (SVT) associated with the use of furosemide infusion (FI) in children following cardiac surgery are reported. The SVT occurred three to seven hours after starting an infusion at 1.0 mg·kg^{-1}·hr^{-1}. All three patients had a diuresis of 8–10 ml·kg^{-1}·hr^{-1} compared with a mean average of 2.5 ml·kg^{-1}·hr^{-1} in 22 other patients who had received a similar infusion. A rapid fluid shift was the most likely mechanism of the tachycardia. Sotalol was effective in controlling the tachycardia in the two patients in whom it was tried. We now recommend a starting dose of 0.3 mg·kg^{-1}·hr^{-1} in using furosemide as a continuous infusion, with hourly increments of 0.1 mg·kg^{-1}·hr^{-1} until the desired diuresis is obtained.

Trois cas de tachycardie supraventriculaire (SVT) associée à l'utilisation de perfusion de furosémide postchirurgie cardiaque (FI) chez les enfants sont rapportés. Les SVT sont survenus trois à sept heures après le début de la perfusion à 1,0 mg·kg^{-1}·hre^{-1}. Tous les trois patients avaient une diurèse de 8–10 ml·kg^{-1}·hre^{-1} comparé une moyenne de 2,5 ml·kg^{-1}·hre^{-1} chez 22 autres patients qui ont reçu une perfusion identique. Une translocation rapide des liquides fut le mécanisme le plus probable de la tachycardie. Le sotalol fut efficace pour contrôler la tachycardie chez les deux patients à qui il fut administré. On recommande actuellement une dose initiale de 0,3 mg·kg^{-1}·hre^{-1} lorsqu'on utilise le furosémide en perfusion continue avec une augmentation horaire de 0,1 mg·kg^{-1}·hre^{-1} jusqu'à ce que la diurèse désirée soit obtenue.

Key words

HEART: arrhythmia, supraventricular tachycardia;
KIDNEY: diuretics, furosemide;
SURGERY: cardiac, complications;
SYMPATHETIC NERVOUS SYSTEM: beta-adrenergic antagonists, sotalol.

From the Department of Pediatrics, The University of British Columbia.

Address correspondence: Dr. R.J. Adderley, Intensive Care Unit, British Columbia's Children's Hospital, 4480 Oak Street, Vancouver, B.C. V6H 3V4 Canada.

Accepted for publication 14th January, 1991.

Following repair of congenital heart malformations using cardiopulmonary bypass (CPB), it is common for extracellular fluid to accumulate leading to oedema which may be resistant to conventional diuretic and supportive treatment. Furosemide by continuous infusion may result in a more effective diuresis, with consequent reduction of oedema, and improvement in cardiopulmonary function.[1,2] The regimen used in our institution had been 1.0 mg·kg^{-1}·hr^{-1} reducing incrementally every two hours, once a urine output of 2–3 ml·kg^{-1}·hr^{-1} was achieved.

We report three cases of SVT with onset associated with furosemide infusion. Rechallenging with furosemide infusion on two occasions provoked the arrhythmia.

Case Reports

Case 1

A 2.9 kg full-term female infant underwent complete repair of a type C interrupted aortic arch, ventricular septal defect and subaortic stenosis under cardiopulmonary bypass at 15 days of age. Her postoperative course was complicated by severe low output syndrome, requiring substantial inotropic and colloid support. Oedema developed and treatment with intermittent furosemide at 4 mg·kg^{-1}·day^{-1} was initiated, but by the seventh postoperative day, she weighed 3.9 kg with a central venous pressure (CVP) of 11 mmHg. She was started on 1.0 mg·kg^{-1}·hr^{-1} of FI. Concomitant medications were adrenalin 0.3 μg·kg^{-1}·min^{-1}, dopamine 17 μg·kg^{-1}·min^{-1}, isoprenaline 0.1 μg·kg^{-1}·min^{-1}, and pancuronium. Urine output pre-FI, with bolus furosemide averaged 5.5 ml·kg^{-1}·hr^{-1}. The serum K^+ was 2.5 mmol·L^{-1}, sodium 139 mmol·L^{-1} and calcium 2.6 mmol·L^{-1}.

After two hours the FI was reduced to 0.75 mg·kg^{-1}·hr^{-1} as the urine output had increased to 12 ml·kg^{-1}·hr^{-1}. Seven hours after the start of FI her cardiac rhythm changed from sinus tachycardia at 150·min^{-1} to a tachycardia with atrioventricular dissociation at 250·min^{-1}, compatible with the diagnosis of SVT (Figure). Despite cessation of the FI there were frequent runs of SVT over the next few hours. The urine output for the nine hours after commencement of FI was 10 ml·kg^{-1}·hr^{-1};

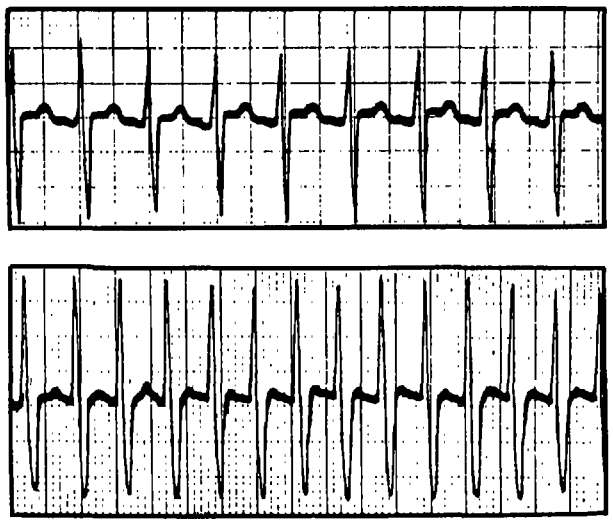

FIGURE ECG lead I. Baseline sinus tachycardia before furosemide infusion (above). Supraventricular tachycardia with furosemide infusion (below).

serum K^+ was 2.8 mmol·L^{-1}, Na^+ and Ca^{++} were unchanged, and the CVP decreased to 10 mmHg. The FI at 1.0 mg·kg^{-1}·hr^{-1} was restarted the following day, after correction of serum K^+, and after nine hours there were frequent nonsustained bouts of SVT. Urine output measured 8 ml·kg^{-1}·hr^{-1} and FI was discontinued. The child went on to develop multi-organ system failure and after a protracted course died eight weeks following her cardiac surgery.

Case 2

A 5.8-kg male with pulmonary atresia with intact ventricular septum and right modified Blalock-Taussig shunt underwent right ventricular outflow tract enlargement under cardiopulmonary bypass at four months of age. The early postoperative course was complicated by low cardiac output, and left lung segmental atelectasis. On the seventh day, he remained oedematous, 0.25 kg over his preoperative weight with a mean left atrial pressure (LAP) of 14 mmHg, was unresponsive to the administration of furosemide 4 mg·kg^{-1}·day^{-1}, and remained ventilator-dependent. A furosemide infusion was commenced at 1.0 mg·kg^{-1}·hr^{-1}. Chloral hydrate and spironolactone were the only other medications. The cardiac rhythm was sinus at 120·min^{-1}. Urine output averaged 2 ml·kg^{-1}·hr^{-1}. Serum Na^+ 139 mmol·L^{-1}, K^+ 3.6 mmol·L^{-1}, and Ca^+ 2.25 mmol·L^{-1}.

After three hours he developed a narrow complex tachycardia at 300·min^{-1} which lasted 20 min without cardiac decompensation. The FI had been reduced to 0.75 mg·kg^{-1}·hr^{-1} after 80 min because of a profound diuresis. Just before the onset of SVT, the urine output had been 8.9 ml·kg^{-1}·hr^{-1} for three hours, serum K^+ was 2.9 mmol·L^{-1}, and the LAP had decreased to 12 mmHg. The infusion was stopped. Serum K^+ was now 2.9 mmol·L^{-1}, despite receiving 3 meq·kg^{-1}·day^{-1} of K^+ as KCl, Na^+ and Ca^{++} were unchanged. Several further episodes of SVT lasting one to five minutes occurred despite cessation of the FI and correction of serum K^+. Digoxin was ineffective in controlling the arrhythmia but two days later during a prolonged burst of SVT in which the child became haemodynamically unstable, with commencement of 1 mg·kg^{-1} of sotalol (2 mg·kg^{-1}·day^{-1}), the rhythm converted to and persisted in sinus. Diuresis was continued with ethacrynic acid. Bolus *iv* furosemide was introduced four days later without recurrence of arrhythmia, and his trachea was extubated fifteen days after surgery.

Case 3

A 17 month, 9.6-kg female with trisomy 21 underwent repair of an atrioventricular septal defect and pulmonary artery debanding under cardiopulmonary bypass. Following surgery, atrioventricular sequential pacing was required for three days to treat a slow nodal rhythm. By day eight she was 0.35 kg over her preoperative weight with a CVP of 17 mmHg, and was receiving chloral hydrate, digoxin, and furosemide by bolus at 4 mg·kg^{-1}·day^{-1}. Extubation had not been possible due to fluid retention. She was in sinus rhythm at 150·min^{-1} with right bundle branch block. Serum K^+ was 4.4 mmol·L^{-1}, Na^+ 127 mmol·L^{-1}, and Ca^{++} 2.11 mmol·L^{-1}, with a urine output of 1.3 ml·kg^{-1}·day^{-1}.

She was started on FI at 1.0 mg·kg^{-1}·hr^{-1}. Three hours later her heart rate increased to 210·min^{-1}, without change in QRS morphology, which was consistent with SVT. The arrhythmia lasted 15 min and was associated with moderate hypotension. Urine output was 8.8 ml·kg^{-1}·hr^{-1} and serum K^+ had decreased to 3.6 mmol·L^{-1}. Urinary K^+ was 75 mmol·L^{-1}. The FI had been reduced to 0.5 ml·kg^{-1}·hr^{-1} because of the diuresis, and was now stopped. After additional supplementation of K^+, and an hour of sinus rhythm at 130·min^{-1}, with decreasing urine output, the FI was restarted at 0.4 mg·kg^{-1}·hr^{-1}, but 20 minutes later SVT recurred at 220·min^{-1}. The FI was discontinued. The plasma digoxin level was 1.79 mmol·L^{-1} and the serum K^+ was 4.8 mmol·L^{-1}. There were recurrent bouts of SVT over the next 12 hr, but 15 min after starting sotalol 1 mg·kg^{-1} (2 mg·kg^{-1}·day^{-1}) orally, the rhythm converted to and stayed sinus. She was discharged to the ward 15 days after surgery.

The charts of 24 additional children who received furosemide by infusion in our intensive care unit were then reviewed. Two cases with pre-existing tachyarrhythmia were excluded from analysis. All 22 children had

been started on a furosemide infusion at 1 $mg \cdot kg^{-1} \cdot hr^{-1}$ with incremental decreases in infusion rate following the onset of diuresis. The mean urine output was 2.5 $ml \cdot kg^{-1} \cdot hr^{-1}$ with a mean infusion rate of 0.6 $mg \cdot kg^{-1} \cdot hr^{-1}$ of furosemide.

Discussion

Furosemide, a potent loop diuretic, is frequently prescribed following cardiac surgery for both adult and paediatric patients, to promote diuresis. The most common causes of clinical toxicity are abnormalities of fluid and electrolyte balance. Side-effects are related to the primary action of the drug which acts by inhibiting active chloride transport at the loop of Henle with resultant loss of sodium, chloride, potassium, and water. Bolus therapy may produce an acute decrease in cardiac output and increase in systemic vascular resistance. As the drug has neither intrinsic vasodilator, nor myocardial depressant properties, this effect is likely due to decreased plasma volume.[5–11] Rapid changes in intravascular volume in the face of limited myocardial reserve, with or without concomitant vasodilator therapy, may cause haemodynamic instability. Furosemide by infusion may provide a more controlled and physiological diuresis in patients, who, following cardiopulmonary bypass, develop oedema resistant to diuresis by conventional bolus therapy, and may in certain patients convert oliguric renal failure to nonoliguric renal failure and obviate or delay dialysis.[2,3] Furosemide is not an ideal infusion drug because it has a half-life of 50 min (range 30–70 min), and a duration of up to six hours.[12] Therefore, changes in infusion rates are not reflected quickly in changes in urine output, which may occur much later.

Our previous protocol of starting the furosemide infusion at the maximal dose of 1 $mg \cdot kg^{-1} \cdot hr^{-1}$ and decreasing by 0.25 $mg \cdot kg^{-1} \cdot hr^{-1}$ every two hours once a urine output of 2–3 $ml \cdot kg^{-1} \cdot hr^{-1}$ was established, was designed to promote a diuresis as rapidly as possible in the oliguric patient. Dose reponse curves have not been established for furosemide infusions. In our 22 "control" patients without supraventricular tachycardia, the effective infusion rate ranged from 0.4–1.0 $mg \cdot kg^{-1} \cdot hr^{-1}$. Even at maximal dose, the onset of diuresis in the responsive patient took as long as one to two hours. However, because of the long duration of effect, an excessive diuresis in the sensitive patient may persist before the furosemide infusion has been reduced to the desired response level, suggesting that a more conservative approach may be safer. Our current protocol is to start the furosemide infusion at 0.3 $mg \cdot kg^{-1} \cdot hr^{-1}$ and increase hourly by 0.1 $mg \cdot kg^{-1} \cdot hr^{-1}$ to a maximum infusion rate of 1 $mg \cdot kg^{-1} \cdot hr^{-1}$. Using this modified regimen, we have not encountered diuresis of the magnitude experienced in these three patients, nor have we seen persistent or recurrent SVT.

Following cardiac surgery in adults, furosemide infusion has been used at 0.05–0.75 $mg \cdot kg^{-1} \cdot hr^{-1}$ without producing important side-effects.[1,2] However, there have been reports[13–17] of both sudden death (4) and non-fatal arrhythmia (1) following a singular *im* or *iv* injection of furosemide. The arrhythmias reported have been complete atrioventricular block and ventricular fibrillation, but not supraventricular tachycardia.

A causal relationship between the furosemide infusion and the supraventricular tachycardia seen in our three patients seems likely in that five distinct episodes (twice each for case #1 and case #3) occurred within hours of commencing the infusion. At the onset of arrhythmia urine output averaged 9.0 $ml \cdot kg^{-1} \cdot hr^{-1}$ (range 8–10 $ml \cdot kg^{-1} \cdot hr^{-1}$), in contrast with a mean urine output of 2.5 $ml \cdot kg^{-1} \cdot hr^{-1}$ of the 22 "control" cases who did not develop SVT. In two cases the bursts of SVT arrhythmia persisted despite aggressive correction of potassium and patient rehydration. Although it appears most likely that the SVT was secondary to excessive diuresis with intercompartmental shifts of electrolytes and water, the reemergence of arrhythmia within 20 min of rechallenging (case #3) might suggest an additional direct effect.

Other causes of arrhythmia following cardiac surgery were considered. Mechanical or other effects of cardiopulmonary bypass seemed unlikely, as in each case seven days had elapsed since surgery. Atrial distension as a mechanism was unlikely as the diuresis had resulted in a moderate decrease in central venous pressure. A drug interaction could not be ruled out; all three of the children were receiving concomitant medications, although none of the three received the same combination of medications.

Two patients with persistent supraventricular tachycardia responded favourably to sotalol at 2 $mg \cdot kg^{-1} \cdot day^{-1}$, a class III antiarrhythmic with beta blocking properties, effective in treating supraventricular tachycardias.[18] Sotalol is recommended rather than propranolol as sotalol is less likely to exert a negative inotropic effect. Unfortunately the drug is only available in oral form.

We believe that furosemide infusion is a useful technique in promoting diuresis in selected postcardiac surgical patients but emphasize caution, with an awareness of the potential complications of excessive diuresis and with a recommendation that emergence of SVT while on furosemide infusion is an absolute indication for withdrawal of the furosemide infusion.

References

1 *Copeland JG, Campbell DW, Plachetka JP, Salomon NW, Larson DF.* Diuresis with continuous infusion of frusemide after cardiac surgery. Am J Surg 1983; 146: 796–9.

2 *Krasna MJ, Scott GE, Scholz, Spotznitz AJ, MacKenzie JW, Penn F.* Postoperative enhancement of urinary output in patients with acute renal failure using continuous furosemide infusion. Chest 1986; 89: 294–5.

3 *Gray JMB, Henry DA, Lawson DH, Tilstone WJ.* Continuous infusion of frusemide in refractory oedema. Br J Clin Pharm 1978; 6: 461P.

4 *Lant A.* Diuretics, clinical pharmacology and therapeutic use (Part 1). Drugs 1985; 29: 57–87.

5 *Poulton TJ, Burnett PS.* Immediate hemodynamic effects of high-dose furosemide in normovolemic and hypovolemic dogs. Crit Care Med 1985; 13: 420–2.

6 *Ikram H, Chan W, Espiner EA, Nicholls MG.* Haemodynamic and hormone response to acute and chronic furosemide therapy in congestive cardiac failure. Clin Sci 1980; 58: 443–9.

7 *Roztocil K, Oliva I, Prerovsky I, Stribrna J.* Hemodynamic effects of intravenous furosemide on peripheral circulation in humans. Vasa 1978; 7: 86–9.

8 *Koob R, Prasad K.* Acute effects of furosemide on blood electrolytes and hemodynamics in dogs. Angiology 1978; 29: 463–72.

9 *Mierzwiak DS.* Acute effects of furosemide on left ventricular contractility in dogs. Arch Int Pharmacodyn 1975; 213: 180–5.

10 *Lacrochelle P, Miulic E, Ogilvie RI.* Effects of isoproterenol, diazoxide, ethacrynic acid, and furosemide on skeletal muscle vascular resistance. Can J Physiol Pharmacol 1973; 51: 183–9.

11 *Lal S, Murtagh JG, Pollock AM, Fletcher E, Binnion PF.* Acute haemodynamic effects of furosemide in patients with normal and raised left atrial pressure. Br Heart J 1969; 31: 711–7.

12 *Gilman AG, Goodman LS.* The Pharmacologic Basis of Therapeutics. New York: MacMillan Publishing Co Inc. 1980.

13 *Massari P, Moore N, Bonmarchand G, Moirot E, Droy JM, Leroy J.* Complete atrioventricular block after furosemide. Intensive Care Med 1986; 12: 54–5.

14 *Dagli AJ, Moos JS.* Sudden death following injection of furosemide. Indian J Med Sci 1983; 37: 49–50.

15 *David DS, Hitzig P.* Diuretics and ototoxicity. N Engl J Med 1971; 284: 1328.

16 *Machtey I.* Sudden death after intramuscular frusemide Lancet 1968; 2: 1301.

17 *Rance CP.* Cardiac arrest after intravenous frusemide Lancet 1969; 1: 1265–6.

18 *Bowman E, Paes BA, Way RC.* Oral sotalol in neonatal supraventricular tachycardia. Acta Paediatr Scand 1988; 77: 171.