

Case Reports

Medications for Improving Urine Output and Renal Insufficiency Following Surgery for Congenital Heart Disease: A Case Study

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Abstract

We report the effects of various agents for treatment of renal insufficiency in the immediate post-operative period in a case of Fontan surgery. Because of the failing atriopulmonary Fontan, the patient underwent a total cavopulmonary connection, atrial septectomy, homograft patch angioplasty of the left pulmonary artery, modified MAZE procedure, and placement of a permanent pacemaker. Diuretics, dopamine and low-dose intravenous Fenoldopam were used for renal insufficiency intra- and postoperatively. The cardiovascular effects and renal function were documented during the use of these agents. Apart from transient hypotension, oliguria and impairment of renal function following cardiopulmonary bypass, there was no deleterious haemodynamic effect. Fenoldopam is a benzazepine derivative with selective dopamine-1 receptor agonist properties. At low doses, it has also been proposed that fenoldopam exerts effects on renal blood flow similar to that of dopamine. The availability of a new agent for postoperative use is attractive but further studies are warranted to explore its potential use in children following congenital heart surgery who are likely to have reduced renal function.

Key words

Congenital heart surgery; Fenoldopam; Renal insufficiency

Acute renal failure after cardiac surgery is associated with renal ischaemia and reduced renal functional reserve.^{1,2} Preoperative congestive cardiac failure, cardiopulmonary bypass and perioperative reduced cardiac output all

contribute to reduction in renal blood flow and glomerular filtrate rate³⁻⁶ Ryckwaert and co-investigators report a 20% increase in plasma creatinine after cardiac surgery with a significant deleterious effect on postoperative outcome.⁷ They also found that the renal risk is increased by preoperative reduced reserve or perioperative renal ischaemia. In addition, patients with cyanotic congenital heart disease have a significantly greater risk of perioperative acute renal failure.⁸

Acute renal failure in children undergoing cardiopulmonary bypass is common but acute renal failure requiring dialysis is uncommon.⁹ Current evidence-based strategies in preventing and treating acute renal failure in the post-operative period have been lacking. Low cardiac output appeared to be a significant risk factor for developing acute renal injury or failure.⁹ Sirivella et al suggested that infusion of solution of mannitol, furosemide, and dopamine promoted diuresis in patients with acute postoperative renal failure complicating cardiac surgery and decreased the need for dialysis when compared with patients given intermittent doses of diuretics and fluids alone.¹⁰ Various agents with dopamine-1 receptor activity have been used in attempt to

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enhance renal blood flow in critically ill patients. Fenoldopam¹¹ is a benzazepine derivative with selective dopamine-1 receptor agonist properties which is primarily used in the management of severe hypertension, particularly in patients with renal impairment. Clinical studies have reviewed its efficacy and safety profiles for the treatment of hypertension.¹¹ At low doses, it has also been proposed that fenoldopam exerts effects on renal blood flow similar to that of dopamine. Compared with dopamine, in the setting of liver transplantation, fenoldopam was associated with better creatinine and blood urea nitrogen values in a randomised, controlled trial.¹² To our knowledge, there has been scanty literature regarding the combined effects of various diuretics, dopamine and fenoldopam in congenital heart surgery. We report the use of furosemide, dopamine together with fenoldopam in the immediate post-operative period in a case of Fontan surgery and renal insufficiency and discuss the effects of these agents.

Case Report

The patient is a 34-year-old woman (47 kg) who had a Blalock-Taussig shunt for tricuspid atresia and hypoplastic right ventricle as an infant, Pott's shunt at age 3 years, and an atriopulmonary Fontan procedure at age 16 years. She developed ascites 7 years ago and a liver biopsy 5 years ago showed mild hepatic cirrhosis. She was found to have an elevated creatinine of 1.9 mg/dl (168 $\mu\text{mol/l}$) five months prior to presentation. Glomerular filtration rate (GFR) study indicated she had 54% renal function and subsequent magnetic resonance imaging/angiography demonstrated poor perfusion to her kidneys. Two weeks prior to hospitalisation, her urine output became reduced to approximately 250 ml per day and she developed symptoms of upper back pain, increasing abdominal distension and a weight gain of 6 kg. She was given a course of acyclovir for suspected diagnosis of shingles and Rofecoxib (a nonsteroidal anti-inflammatory drug) for her back pain. Two peritoneal taps were performed with removal of 3 and 5 litres of clear peritoneal fluids, respectively. The maximum BUN and creatinine were 51 (18.2 mmol/l) and 3.7 mg/dl (327 $\mu\text{mol/l}$), respectively. There was no history of dysuria, frequency, haematuria, proteinuria, urinary tract infection or hypertension. Past history also includes transient stroke and hypothyroidism (following amiodarone use) of three years duration, atrial flutter, right ear hearing deficit, possible hepatitis C infection. There was no significant family history of cardiac or renal disease. Her medications

prior to admission include levothyroxine, coumadin, and amiodarone for atrial flutter. Her coumadin was discontinued, and intravenous heparin and furosemide started two days prior to surgery.

Clinically, she had evidence of heart failure with heart rate between 50-70 beats/min, respiratory rate 16-18 breaths/min, and blood pressure of 91/55 mmHg. There was some peripheral oedema, but marked ascites and liver edge 3 cm below the right costal margin (liver span of 10 cm). There was no focal neurologic deficit. Laboratory results prior to her surgery were as follows: haemoglobin, 10.9 g/dl; white blood count, $2.2 \times 10^9/\text{ul}$, and platelet count, $109 \times 10^9/\text{ul}$. Serum sodium was 134 mmol/l, potassium was 4.2 mmol/l, and glucose was 106 mg/dl. Creatinine was 1.1 mg/dl (or 97 $\mu\text{mol/l}$), blood urea nitrogen was 18 mg/dl (or 6.4 mmol/l); aspartate aminotransferase was 41 U/L and alanine aminotransferase was 27 U/L; prothrombin time was 15.1 secs, APTT was 48.5 secs; and albumin 3.3 gm/dl (or 33 gm/l). HIV antibodies were negative.

Because of the failing atriopulmonary Fontan, she underwent a total cavopulmonary connection, atrial septectomy, homograft patch angioplasty of the left pulmonary artery, modified MAZE procedure, and placement of a permanent pacemaker. The MAZE procedure consists of creating a number of incisions in the atrium that disrupt the re-entrant circuits. The incisions are sewn together again but the electrical impulse cannot cross the incisions. There is only one path that the electrical impulse can take from the sinoatrial node to the atrioventricular node. The atrium can no longer fibrillate, and sinus rhythm is restored. Intraoperatively, a left radial arterial line was placed for blood pressure monitoring and a right internal jugular line was placed for pulmonary artery pressure monitoring. Fenoldopam, epinephrine and dopamine were started. Fenoldopam (as a 0.1 mg/mL solution in 5% dextrose water) was initiated at 0.05 mcg/kg/h without a bolus dose and titrated to 0.025 mcg/kg/h to maintain a steady state systolic blood pressure of 80 mmHg and diastolic blood pressure of 40 mmHg. The low doses were used for its presumptive agonist effect on renal perfusion in an attempt to avoid systemic hypotension. Postoperatively, the fenoldopam was maintained at 0.05 mcg/kg/min. The renal function and urine output were followed (Table 1). Epinephrine (maximal at 0.03 mcg/kg/min) was weaned off on post-op day two and dopamine (maximal at 10 mcg/kg/min) by post-op day seven. Because of reduced urine output on post-op day two to day four, regular furosemide plus boluses of furosemide and

Table 1 Summary of clinical evolution of the patient

Days	Pre-op	OR	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Fenoldopam	+	+	+	+	+	+	+	+	off										
Dopamine	+	+	+	+	+	+	+	+	off										
Epinephrine	+	+	+	off															
Cefazolin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	off				
Ventilation	+	+	+	+	off														
24h Urine (ml)	1780	160/8h	639	596	488	529	739	972	973	915	190+	1500	1250	1620	855	1665	2100	850	
Urine (ml/h)	74	20	27	25	20	22	30	40	40	38	?	63	52	68	36	69	8888	35	
BUN (mmol/l)	6.4	4.6	5.7	8.6	10.4	14.3	16.4	18.6	19.3	16.8	-	-	9.6	7.1	6.8			5.7	
Cr (mmol/l)	97	88	115	133	115	133	124	124	106	88	-	-	80	88	80			80	
Sodium (mmol/l)	134	139	137	143	141	136	129	128											
SBP mmHg	80-100	85-100	80-115	95-120	95-115	95-115	90-115	90-105	78-79	81-88	65-83	82-87	80-107	76-85	81-104	81-96	80-95	84-106	91-106
DBP mmHg	50-60	40-55	45-55	45-60	50-65	40-65	45-70	40-55	50-58	51-53	40-60	54-63	65-52	50-59	43-66	50-60	50-55	48-52	49-69
BP mean		55-65	55-75	70-85	65-75	55-80	60-90	55-65											
CVP mmHg		2-6	11-17	12-18	12-26	7-24	7-32	9-20											
median		4	14	15	19	15	19	14											
LAP mmHg		13-19	3-10	2-6	3-10	1-10	2-17	1-3											
Remarks		OR	ICU	ICU	ICU	ICU	ICU	ICU	Ward	Ward	Ward	Ward	Ward	Ward	Ward	Ward	Ward	Ward	Home

Note: blood pressure measured with intra-arterial line in post-op day 1 to 6; see dosages of fenoldopam and inotropes in report OR, operating room; CVP, central venous pressure; LAP, left atrial pressure; ICU, intensive care unit; BUN, blood urea nitrogen; Cr, creatinine; SBP, systolic blood pressure

ethacrynic acid were given. The maximum scheduled furosemide requirement was 60 mg q8h intravenously on post-op day five. She was subsequently weaned to oral furosemide (20 mg q12h) and spironolactone (25 mg q12h). The daily fluid intake was restricted to 1.2 litres. She developed a left pleural effusion and required chest drainage. Her SaO₂ remained in the 80's. The creatinine clearance was 17.9 ml/min/1.73 m² (reference range 90-150 ml/min/1.73 m²) on postoperative day 5. The fenoldopam was maintained at 0.05 mcg/kg/min to assist renal perfusion. The urine output began to improve and the serum creatinine decreased from postoperative day 5. Before the transfer of the patient out of the ICU on day 7, the dopamine infusion was weaned off and fenoldopam discontinued.

Discussion

This report documents the use of diuretics, dopamine and fenoldopam in combination in a patient with renal insufficiency and surgery for congenital heart disease. We did not appreciate a dramatic immediate beneficial effect on the urine output and plasma creatinine, and even a transient reduction in urine output and an elevation in serum creatinine were observed during the immediate post-operative period. The haemodynamic and renal effects of cardiopulmonary bypass had probable confounding effects on the patient's renal function. The creatinine clearance was reduced on postoperative day 5, and we did not have creatinine clearance data at other time points. By day 5, however, both the urine output and plasma creatinine levels began to improve. The renal protective effect of fenoldopam was not dramatic in this patient who was at great risk for developing postoperative renal failure. Halpenny and colleagues have demonstrated a renal protective effect of fenoldopam in adults undergoing coronary bypass grafting with the use of cardiopulmonary bypass.¹³ In order to minimise haemodynamic instability from fenoldopam, low doses¹⁴ were used throughout the treatment period. Intraoperatively, the fenoldopam was started at 0.05 mcg/kg/min but was momentarily reduced to 0.025 mcg/kg/min for transient hypotension. It was difficult to delineate if the transient hypotension was due to the fenoldopam or rather the effect of cardiopulmonary bypass. Postoperatively, the dosage was maintained at 0.05 mcg/kg/min. The fenoldopam did not seem to exert any significant or lasting hypotensive effect on this patient. The dosages of epinephrine and dopamine were not considered to be

excessively high. Epinephrine was discontinued on postoperative day 2. The patient's blood pressure remained in the low range (systolic 85-100, diastolic 52-60) throughout the recovery period. For this reason, the dose of fenoldopam was never increased.

Fenoldopam is a dopamine D1-like receptor agonist formulated as a solution to be diluted for intravenous infusion. Its pharmacology has been extensively reviewed.^{11,15} It has no significant affinity for D2-like receptors, alpha1 and beta adrenoceptors, 5HT1 and 5HT2 receptors, or muscarinic receptors.¹⁵⁻¹⁸ It is also a rapid-acting vasodilator. In animals, fenoldopam has vasodilating effects in coronary, renal, mesenteric and peripheral arteries. All vascular beds, however, do not respond uniformly to fenoldopam. Vasodilating effects have been demonstrated in renal efferent and afferent arterioles. In human controlled clinical trials, increases in renal blood flow were demonstrated in hypertensive¹⁷⁻²⁰ and normal subjects¹⁴ treated with intravenous fenoldopam. In patients with renal failure, Fenoldopam 0.1-0.2 mcg/kg/min has been found to be effective in restoring both renal plasma flow and glomerular filtration rate.^{14,18,21,22} Clearance of fenoldopam is not altered in patients with end-stage renal disease on continuous ambulatory peritoneal dialysis and is not affected in severe hepatic failure. In radiolabelled studies in rats, no more than 0.005% of fenoldopam crossed the blood-brain barrier.¹⁶ There have been no formal drug-drug interaction studies using intravenous fenoldopam. There is limited experience with concomitant ACE inhibitors and diuretics.

No deleterious haemodynamic effects were observed in the use of fenoldopam during the post-operative period in this patient with renal insufficiency. It is uncertain if fenoldopam may have contributed to the rapid renal recovery of this patient who was at high risk for postoperative renal failure. This case report also documents the potential safe use of fenoldopam in adult congenital heart disease patients undergoing surgery. Since congenital heart surgery mainly involves children who are likely to have reduced renal function relative to their adult counterpart, the benefit of fenoldopam in this group of patients is potentially substantial. The major limitation of this case report of a single patient is that there are many confounders such as the effect of cardiopulmonary bypass on renal function and the concomitant use of dopamine (also a DA-1 receptor agonist) and epinephrine. In addition, oliguria and biochemical evidence of renal impairment were evident following surgery. Further studies are warranted to assess if fenoldopam use would alter the incidence of renal

failure in at risk patient groups before it can be recommended for routine use in the congenital heart surgery patients postoperatively.

In conclusion, renal insufficiency can be a significant cause of morbidity following congenital heart surgery. Meticulous peri-operative care together with the combination of fenoldopam, dopamine and diuretics can be safely given and is potentially beneficial for the optimal renal outcome. Our understanding and evaluation of new therapies is hindered by a lack of consensus on diagnostic criteria of renal dysfunction and acute renal failure.⁹ Much effort is required to explore this challenging but difficult area of postoperative management of critically ill children undergoing cardiac surgery.

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