RENAL FUNCTION AFTER CARDIOPULMONARY BYPASS IN CHILDREN: COMPARISON OF DOPAMINE WITH DOBUTAMINE

R. WENSTONE, J. M. CAMPBELL, P. D. BOOKER AND R. MCKAY

SUMMARY
We have compared low dose dopamine with dobutamine in conserving renal function in 142 children younger than 10 yr undergoing cardiopulmonary bypass (CPB). Patients were allocated randomly to receive a continuous infusion of either dopamine 2.5 μg kg⁻¹ min⁻¹ (group 1) or dobutamine 2.5 μg kg⁻¹ min⁻¹ (group 2) from the time of induction of anaesthesia. Administration of inotropes and diuretics was controlled strictly to agreed regimens. There was no clinical or statistically significant difference between the two groups in postoperative urine output, serum concentration of creatinine, fractional sodium excretion or need for diuretic therapy. This was true also of the subgroup of patients who received no other inotropic support. However, the subgroup of patients in group 1 who underwent periods of CPB in excess of 2 h (n = 17) had persistently greater postoperative serum concentrations of creatinine. Low dose dopamine did not appear to be superior to dobutamine for protection of renal function in these patients.

KEY WORDS

Acute renal failure has long been recognized as one of the more serious complications of cardiac surgery and cardiopulmonary bypass (CPB) in both adults [1] and children [2]. Dopamine has been used to improve and maintain renal function in several circumstances including the period of CPB in adults [3, 4]. This effect is thought to be a result of selective action on renal D₁ receptors [5, 6], enhancement of cyclic AMP activity [6] and suppression of aldosterone secretion [7]. It is thought to increase renal blood flow [5, 8, 9], glomerular filtration rate (GFR) [8], sodium excretion [8] and urine output [10].

In adults, at equal systemic arterial pressure and flow, dopamine produces a greater diuresis and natriuresis than does dobutamine with similar GFR and effective renal plasma flow [3]. It also produces a greater reduction in renal vascular resistance and a greater increase in the renal blood flow:cardiac output ratio [4]. However, one small study of 14 children [11] was unable to demonstrate any benefit of low dose dopamine after CPB. Although both dobutamine and dopamine are useful inotropes after cardiac surgery [12, 13], there has been no study to determine their relative effect upon renal function in children.

We have compared the effects of continuous infusions of low dose dopamine and dobutamine on renal function in the perioperative period in children undergoing CPB.

PATIENTS AND METHODS
We studied 147 children aged 5 weeks to 9 yr undergoing elective open-heart surgery with cardiopulmonary bypass (CPB). Approval was obtained from the Ethics Committee of the Royal Liverpool Childrens Hospital (Alder Hey) and informed signed consent was obtained from one or both parents of each child.

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Patients were allocated randomly to one of two groups using opaque sealed envelopes: group 1 received “low dose” dopamine (2.5 µg kg⁻¹ min⁻¹) and group 2 the same dose of dobutamine. The “trial” drug was started immediately after induction of anaesthesia and insertion of central venous cannulae and given continuously throughout CPB.

All patients received our standard premedication, induction and intraoperative management of CPB (Appendix).

If inotropic support was required before or after CPB, patients in group 1 received dobutamine as needed up to 10 µg kg⁻¹ min⁻¹; patients in group 2 received dopamine as needed up to 10 µg kg⁻¹ min⁻¹. If greater inotropic support was required, adrenaline was used in place of dobutamine or dopamine, respectively, maintaining a constant dose of the trial drug throughout. Isoprenaline or vasodilators (glyceryl trinitrate or epoprostenol) were used where indicated for bradycardia or afterload reduction.

Postoperative fluid therapy was managed as follows: a total fluid intake of 500 ml m⁻² on the first day after operation, 750 ml m⁻² on the second and 1000 ml m⁻² on the third. Further diuretic therapy was given if urine output decreased to less than 2 ml kg⁻¹ h⁻¹ (averaged over 2 h): mannitol 20% was given first at the rate of 1 ml kg⁻¹ h⁻¹ for 5 h and if there was no response after 1 h, frusemide 1 mg kg⁻¹ was given. The dose of frusemide was doubled every 30 min thereafter until a urine output of 2 ml kg⁻¹ h⁻¹ was obtained (up to a maximum dose of 4 mg kg⁻¹). Mannitol infusion was repeated at intervals of 12 h for the same criteria of urine output.

Blood and urine samples were obtained after induction of anaesthesia, before commencement of the trial drug, 30 min after cessation of CPB and thereafter at 6-h intervals for 48 h or until arterial and urinary catheters were removed, whichever occurred sooner. These samples were used to measure urine and serum concentrations of sodium and creatinine, blood-gas tensions and acid–base state. Fractional sodium excretion ($F_{E_Na}$) was calculated from the formula:

$$F_{E_Na} = 100 \times \frac{Cu_{Na}}{Cs_{Na}} \times \frac{Cs_{Cr}}{Cu_{Cr}}$$

where $Cu$ and $Cs$ are the urine and serum concentrations respectively of sodium (Na) or creatinine (Cr).

Data were analysed graphically to determine whether or not they were distributed normally. An unpaired Student’s t test was used where data were found to be normally distributed. The Mann–Whitney U test was used for other data. Data are expressed as mean (SEM) except where stated otherwise.

**RESULTS**

Of the 147 children entered into the study, one child died in theatre and one soon after leaving theatre. The data on three patients were missing.
TABI: Urine output and diuretic administration (mean (sd) [range])

<table>
<thead>
<tr>
<th></th>
<th>Whole group (n = 74)</th>
<th>Single inotrope (n = 37)</th>
<th>CPB &gt; 2 h (n = 9)</th>
<th>Whole group (n = 68)</th>
<th>Single inotrope (n = 38)</th>
<th>CPB &gt; 2 h (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine output</td>
<td>3.1 (1.1)</td>
<td>3.1 (0.9)</td>
<td>2.4 (1.1)</td>
<td>3.3 (1.6)</td>
<td>3.4 (1.3)</td>
<td>2.3 (1.2)</td>
</tr>
<tr>
<td>(ml kg⁻¹ h⁻¹)</td>
<td>[0-5.7]</td>
<td>[1.8-5.7]</td>
<td>[1.3-3.7]</td>
<td>[0.1-9.5]</td>
<td>[1.9-6.9]</td>
<td>[0.1-4.4]</td>
</tr>
<tr>
<td>Total frusemide</td>
<td>99 (149)</td>
<td>47 (62)</td>
<td>255 (350)</td>
<td>96 (89)</td>
<td>65 (62)</td>
<td>151 (109)</td>
</tr>
<tr>
<td>(µg kg⁻¹ h⁻¹)</td>
<td>[0-1128]</td>
<td>[0-300]</td>
<td>[0-1128]</td>
<td>[0-358]</td>
<td>[0-166]</td>
<td>[0-306]</td>
</tr>
<tr>
<td>Mannitol</td>
<td>0.9 (0.7)</td>
<td>0.6 (0.5)</td>
<td>1.3 (0.7)</td>
<td>0.8 (0.8)</td>
<td>0.5 (0.6)</td>
<td>1.1 (1.1)</td>
</tr>
<tr>
<td>(g kg⁻¹/48 h)</td>
<td>[0-3]</td>
<td>[0-2]</td>
<td>[0-2]</td>
<td>[0-4]</td>
<td>[0-2]</td>
<td>[0-3]</td>
</tr>
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Fig. 1. Comparison of the mean serum concentrations of creatinine for four patient subgroups: low dose dopamine only (+); low dose dobutamine only (○); group 1 patients, CPB > 2 h (×); group 2 patients, CPB > 2 h (●).

DISCUSSION

We have been unable to show any advantage of low dose dopamine (2.5 µg kg⁻¹ min⁻¹) in comparison with a similar dose of dobutamine given without any other inotropic therapy. This would appear to be contrary to the findings in adults undergoing CPB [3, 4] or aortic cross-clamping [14], but accords with the findings of Girardin and colleagues [11]. A study in piglets [15] showed a more beneficial effect of dobutamine than dopamine on renal function. This may have been a result of a maturation process of dopamine receptors in the kidney [16]. However, we were unable to demonstrate any differences in our results throughout the age range of the patients in this study, and other workers have claimed that there is functional maturity of dopaminergic receptors, even in preterm infants [17].

These results question the value of an infusion analysis; eight of these died (three in group 1; five in group 2).

More detailed analyses of the results to evaluate the effect of other variables (age (< 1 yr, 1-3 yr, > 3 yr), sex, bypass, aortic cross-clamp, low flow times and inotropic therapy) also showed no clinically or statistically significant differences. Assessment of the patients who received the trial drug in isolation and required no other inotropic agents (table II) also revealed no differences between groups.

Patients with prolonged CPB (> 2 h) (n = 18), aortic cross-clamp (> 1 h) (n = 22) or low flow times (> 20 min) (n = 18) showed greater impairment of renal function, but the numbers were too small to demonstrate any significant differences between the trial drugs (fig. 1).
of low dose dopamine as a method of protecting renal function compared with dobutamine infused at the same rate.

Although the numbers of patients in the groups at greater risk of impaired postoperative renal function were too small to demonstrate statistically significant differences, there appeared to be a trend towards poorer renal function in the patients who received the low dose dopamine infusion. The reasons for this are not clear, because of the large number of variables in these patients, but the possibility remains that the patients who received the low dose dobutamine infusion benefited from the high dose of dopamine that they received for inotropic support or, conversely, that the larger doses of dobutamine received by the low-dose dopamine patients were more detrimental to renal function.

APPENDIX

MANAGEMENT OF CPB PATIENTS

Premedication. Trimeprazine 1.5 mg kg\(^{-1}\) orally 3 h before operation; morphine 0.25 mg kg\(^{-1}\) and atropine 20 \(\mu\)g kg\(^{-1}\) i.m. 1 h before operation. Children younger than 6 months received atropine only; those between 6 months and 1 yr received atropine and morphine only.

Induction of anaesthesia. Thiopentone 4 mg kg\(^{-1}\) with vecuronium 0.15 mg kg\(^{-1}\).

Maintenance. Midazolam 120 \(\mu\)g kg\(^{-1}\) h\(^{-1}\) with diamorphine 12 \(\mu\)g kg\(^{-1}\) h\(^{-1}\).

Intraoperative fluids. Glucose 5% in 0.45% saline 1 ml kg\(^{-1}\) h\(^{-1}\), except for children weighing less than 10 kg who received 10% glucose in 0.45% saline at the same rate.

Before CPB all patients received potassium canrenoate 5 mg kg\(^{-1}\). This dose was repeated at the end of CPB, together with frusemide 0.25 mg kg\(^{-1}\).

Oxygenator. Either a bubble or a membrane oxygenator, the latter being used in the more complex cases.

Prime. A mixed blood and crystalloid prime was used to produce a final PCV of 0.25.

Cardioplegia. Blood cardioplegia was used for all cases.

Bypass. Full flow on CPB was calculated as either 100 ml kg\(^{-1}\) min\(^{-1}\) where body weight was less than 10 kg or 2.4 litre m\(^{-2}\) min\(^{-1}\) if greater than 10 kg.

None of the oxygenator fluid volume was re-infused after bypass.

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REFERENCES