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Effect of Low Dose Dopamine on Hemodynamic and Renal Function in Children

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ABSTRACT. The purpose of the study was to investigate the effect of low doses of dopamine in children. Fourteen cases were studied after open heart surgery. Cardiac output and renal parameters were determined under baseline conditions and under continuous infusion of dopamine 2.5 and 5 μg/kg/min. During the control period cardiac index was 2.62 ± 0.19 L/min/m^2, renal plasma flow was decreased at 269 ± 41 mL/min/1.73 m^2, GFR was 86.6 ± 9.2 mL/min/1.73 m^2, and filtration fraction was elevated at 37.1 ± 1.9%. Plasma concentration of aldosterone correlated with the filtration fraction. At 5 μg/kg/min dopamine increased significantly cardiac output, renal plasma flow, and to a lesser extent GFR, thus decreasing the filtration fraction. At 2.5 μg/kg/min dopamine, increased renal plasma flow only in patients older than 5 y and had no effect on the other parameters. The increase of cardiac output in response to dopamine was abolished by propanolol pretreatment. By contrast, the hemodynamic renal response to dopamine was not altered by β-blockade. These results indicate that 5 μg/kg/min of dopamine could prevent renal failure after open heart surgery in children by increasing renal blood flow and attenuating renal compensatory mechanisms. (*Pediatr Res* 26:200–203, 1989)

Abbreviation

PAH, para-aminohippurate

In the presence of reduced cardiac output, dopamine is frequently used for both its positive cardiac inotropic and its renal vasodilatory effects. A considerable amount of data supports its use in adults (1–5) but hemodynamic and renal effect of dopamine have not yet been assessed in children. Some animal (6–8) and clinical studies (9) suggest that differences in response to dopamine exist between adults and pediatric patients.

After open heart surgery, cardiac output and systemic pressure are often depressed. Renal failure develops in 3 to 20% of patients depending on the criteria used and the patient population. It markedly influences the ultimate prognosis (10–15).

Our study was designed to test the effect of a continuous infusion of dopamine, 2.5 and 5.0 μg/kg/min, on hemodynamic and renal function in children after open heart surgery.

PATIENTS AND METHODS

Patients. A total of 14 children were randomly selected from patients who underwent open heart surgery and had normal renal function before the operation. The group consisted of eight girls and six boys aged 18 mo to 15 y. The clinical characteristics and the preoperative plasma creatinine concentrations are given in Table I. All the patients had normal urinalysis with negative or trace proteinuria. Before the operation, six children with tetralogy of Fallot were treated with 1 to 4 mg/kg/day of propranolol to prevent hypoxic spells; the drug was stopped 8 h before the beginning of the operation. The surgery was performed with cardiopulmonary bypass, deep hypothermia (18 to 24°C), and moderate hemodilution (20 to 30%).

Cold chemical cardioplegia was used to obtain asystole. When cardiopulmonary bypass was discontinued, blood was infused until the left atrial pressure reached 9.5 to 12.5 mm Hg, and a single dose of furosemide (1 mg/kg) was given.

Method. After the operation, a Swan-Ganz catheter (5 Fr) was placed into the pulmonary artery. During the study, a solution containing 5% glucose and NaCl and KCl (2 mEq/kg/24 h) was infused at a rate of 750 mL/m^2/24 h. The patient was ventilated with a volume controlled ventilator to maintain arterial carbon dioxide tension between 4.5 and 5.5 kPa and sedated with a continuous infusion of morphine sulfate (0.1 mg/kg/h). Cold solution of 5% glucose was injected through the proximal port of a Swan-Ganz catheter (American Edwards Laboratories, Santa Ana, CA). Patients weighing <20 kg received 3.5 mL, those more than 20 kg 5 mL. Cardiac output was determined with a Kimray 3500E thermodilution computer (K.M.A. Inc., Oklahoma City, OK), by averaging three consecutive measurements. Simultaneously, heart rate, systemic arterial pressure, central venous pressure, and left atrial pressure were measured through lines placed at surgery. Vascular pressures were measured with Hewlett-Packard pressure modules 78353B, (Hewlett-Packard Co., Palo Alto, CA), zero level positioned at mixthorax.

GFR and effective renal plasma flow were determined by the clearances of inulin (Laevosan AG, Zürich, Switzerland) and para-aminohippurate (PAH) (BAG, Hessen). A priming dose of PAH (8 mg/kg) and inulin (50 mg/kg) was followed by a continuous infusion in order to achieve plasma concentration of 20 mg/L for PAH and 200 mg/L for inulin. After an equilibration period of 1 h, six 30-min urine collections were performed through an intravesical Foley catheter. Blood samples were obtained at the beginning and end of each collection period. PAH and inulin were analyzed by colorimetric techniques (16, 17). The clearance of PAH was corrected assuming a PAH extraction of 0.9 (18). Renal blood flow was calculated by dividing PAH clearance by 1-hematocrit. The renal fraction of total cardiac output was calculated by dividing the renal blood flow per m^2 of body surface area by cardiac index. Fractional excretion of sodium and filtration fraction were calculated using standard formula. Aldosterone plasma concentrations were measured by RIA (Diagnostic Prod. Co., Los Angeles, CA; kit TKAL).

The study started 3 to 4 h after the end of anesthesia; the patient was in stable condition. A first set of measurements was made without dopamine infusion and served as a control. Do-

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pamine was then infused at 2.5 and 5.0 μg/kg/min, the doses being randomly alternated. Each of the three periods lasted 1 h; the results of the two 30 min clearances within each period were averaged and hemodynamic measurement were performed 45 min after the beginning of the period. During the study, the patients did not receive any other medication. The study protocol was approved by the ethics committee of the pediatric department.

Statistical analysis. Two-way ANOVA was used to test the effect of dopamine at various dose levels. When the F values were significant, the effect of each dose *versus* control was evaluated using the Newman-Keuls test. Correlations between two variables were analyzed by the nonparametric Spearman test and by linear least square regression. Values with and without preoperative propranolol treatment were compared by Student's *t* test.

RESULTS

Control period. During the control period, renal plasma flow was 269 ± 41 mL/min/1.73 m^2, compared to normal values for the age [1–3 y: 537 ± 122 mL/min/m^2; 3–8 y: 659 ± 115; 8–14 y: 631 ± 98 (19)]. Cardiac index was comparatively preserved at 2.62 ± 0.19 L/min/m^2, so the fraction of the cardiac output delivered to the kidney, 10.0 ± 1.2%, was markedly decreased. GFR was 86.6 ± 9.2 mL/min/1.73 m^2, resulting in a high filtration fraction of 37.1 ± 2.9% (Table 2). Renal blood flow was strongly related to mean systemic blood pressure ($p < 0.01$) (Fig. 1) but did not correlate with cardiac output. GFR showed a statistically significant correlation with the renal fraction of cardiac output ($p < 0.05$) (Fig. 2). Eleven of the 14 subjects had plasma aldosterone concentrations higher than the upper confidence limit for the age (20). The mean value was 3.62 ± 1.27 mmol/L. These circulating aldosterone levels correlated significantly with the filtration fraction ($p < 0.005$) (Fig. 3).

Effect of dopamine. At 2.5 μg/kg/min, dopamine did not increase the cardiac index, GFR, the renal fraction, or the urinary sodium excretion. The filtration fraction decreased to 32.8 ± 3.0 ($p < 0.05$). The heart rate, mean systemic pressure, and left atrial pressure also remained unchanged (Table 2). The renal plasma flow increased slightly in the group as a whole; however, the rise was significant only in the subgroup of seven patients older than 5 y ($p < 0.05$).

For the whole group, at 5.0 μg/kg/min, dopamine increased the cardiac output, the renal plasma flow, the GFR, and the urinary sodium excretion, whereas it decreased the filtration fraction. The heart rate and the mean systemic pressure remained unchanged. Left atrial pressure decreased compared to the control period (Table 2). Figure 4 describes the percent change of the hemodynamic and renal parameters in response to 2.5 and 5.0 μg/kg/min of dopamine. Dopamine treatment did not modify significantly plasma aldosterone levels that averaged 3.30 ± 1.11 and 3.77 ± 1.26 mmol/L with 2.5 and 5.0 μg/kg/min of dopamine, respectively.

Preoperative treatment with propranolol. During the control period cardiac index was similar in two subgroups of patients, one treated preoperatively with propranolol and the other not (2.76 ± 0.27 *versus* 2.52 ± 0.28 L/min/m^2). The effect of 5.0 μg/kg/min of dopamine was abolished by propranolol pretreatment: the increase of the cardiac index after dopamine was 1.5% in the propranolol-treated group and 26.4% in the untreated group ($p < 0.02$). Figure 5 compares the effect of 5.0 μg/kg/min of dopamine on the cardiac index, renal plasma flow, and urinary

Table 1. *Clinical characteristics and preoperative plasma creatinine concentrations**

Age (y mo)	Diagnosis	Operation	Plasma creatinine (mmol/L)
$1^{6/12}$	T-F	ccs	54
$1^{10/12}$	T-F	ccs	58
$2^{2/12}$	VSD	Patch	31
$2^{3/12}$	T-F	ccs	42
$3^{4/12}$	T-F	ccs	48
$3^{5/12}$	T-F	ccs	48
$3^{10/12}$	T-F	ccs	52
$7^{4/12}$	T-F	ccs	56
$9^{2/12}$	Aortic stenosis	Aortotomy	43
$10^{6/12}$	Mitral insufficiency	Valvuloplasty	50
$12^{2/12}$	Mitral insufficiency	Valvuloplasty	46
$12^{5/12}$	Partial atrioventricular defect	Dacron patch	50
$14^{5/12}$	Mitral sufficiency	Valvuloplasty	49
15	T-F	ccs	59

* T-F, tetralogy of Fallot; VSD, ventricular septal defect, ccs, complete corrective surgery: patch for VSD and infundibular enlargement.

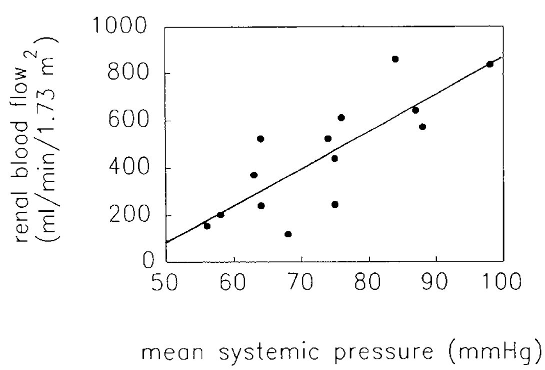

Fig. 1. Correlation between mean systemic pressure and renal blood flow ($r = 0.81$, $p < 0.001$).

Table 2. *Hemodynamic and renal parameters after open heart surgery (mean ± SEM)*

Parameter	Dopamine (μg/kg/min) 0	2.5	5
GFR (mL/min/1.73 m^2)	86.6 ± 9.2	89.0 ± 12.4	103.4 ± 7.0*$^{a+}$
Renal plasma flow (mL/min/1.73 m^2)	269.2 ± 41	320.0 ± 55.7	406.3 ± 61.0*$^{c+}$
Filtration fraction (%)	37.1 ± 2.9	32.8 ± 3.0*^{a}	29.8 ± 2.5*^{c}
Urinary sodium excretion (mmol/kg/h)	0.18 ± 0.04	0.23 ± 0.06	0.33 ± 0.08*$^{b+}$
Cardiac index (L/min/m^2)	2.62 ± 0.19	2.75 ± 0.19	2.96 ± 0.17*$^{c+}$
Renal fraction (%)	10.0 ± 1.2	11.1 ± 1.5	13.0 ± 1.3*$^{b+}$
Heart rate (beats/min)	106 ± 6	107 ± 6	109 ± 6
Mean systemic pressure (mm Hg)	73.6 ± 3.3	65.3 ± 4.8	73.8 ± 2.5
Left atrial pressure (mm Hg)	11.7 ± 0.9	10.1 ± 0.9	9.9 ± 1.0*^{a}

* p compared to control period, ^{a} <0.05; ^{b} <0.01; ^{c} <0.001.
$^{+}$ $p \leq 0.05$ for values compared to dopamine 2.5 μg/kg/min.

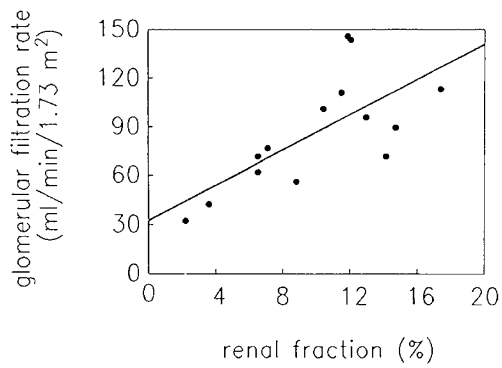

Fig. 2. Correlation between the renal fraction of cardiac output and GFR ($r = 0.69$, $p < 0.01$).

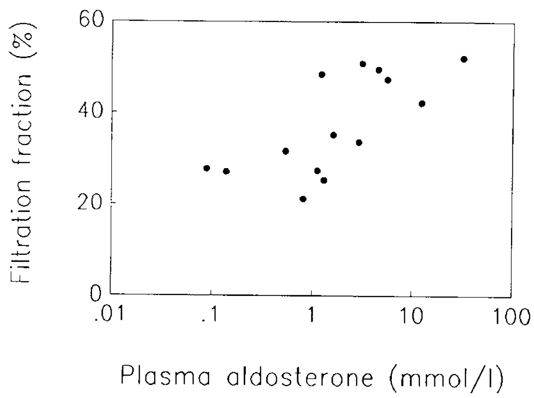

Fig. 3. Correlation between the logarithm of plasma aldosterone concentrations and filtration fraction ($r = 0.70$, $p < 0.005$).

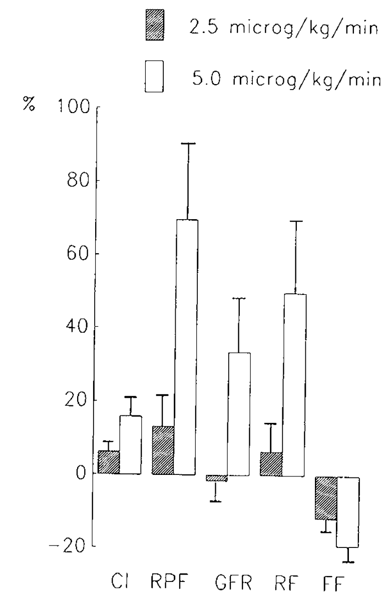

Fig. 4. Effect of 2.5 and 5.0 μg/kg/min of dopamine on hemodynamic and renal parameters. Values are expressed as percent changes ± SEM compared to control period. *CI*, cardiac index; *RPF*, renal plasma flow; *RF*, renal fraction of cardiac output; *FF*, filtration fraction.

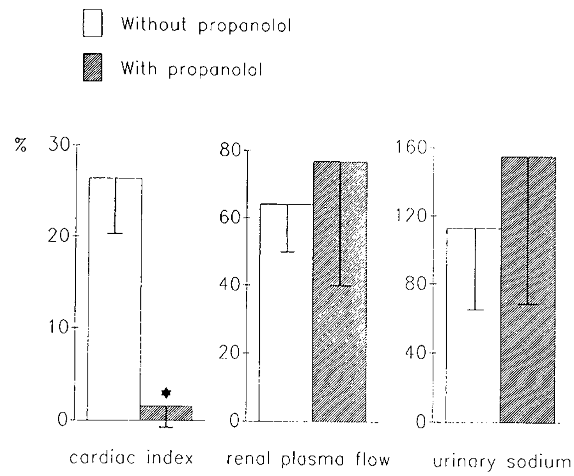

Fig. 5. Effect of 5.0 μg/kg/min of dopamine between patients treated preoperatively with propanolol and those untreated. Values are expressed as percent changes compared to control period *p < 0.02.

sodium excretion in the group of patients treated preoperatively with propranolol and in the untreated group. The effect of dopamine on renal plasma flow and urinary sodium excretion was not altered by propranolol pretreatment.

DISCUSSION

The results of our study demonstrate that compensatory mechanisms are involved to maintain normal renal function in the presence of borderline cardiac output after open heart surgery in children. Dopamine, as a 5.0 μg/kg/min continuous infusion, improves renal blood flow and GFR. This reduces the filtration fraction and thus restores some degree of "functional renal reserve."

The striking feature in our patients, 3 to 4 h after completion of cardiopulmonary bypass, was their reduced renal blood flow as assessed by the PAH clearance method. PAH is an accurate measure of renal plasma flow providing that the extraction ratio of PAH is stable and reproducible under the experimental conditions. PAH extraction has been found to average 90.4% ± 1.7 in children over a wide age range (18). Previous studies have shown that PAH extraction decreases during the hypothermic period of open heart surgery but returns to preoperative values immediately after surgery, as soon as the patient's temperature is normal (21).

The reduction in renal plasma flow in our patients, with only a moderate decrease in cardiac output, indicates renal vasoconstriction. GFR is preserved at the expense of a high filtration fraction, induced by postglomerular vasoconstriction. This compensatory mechanism allows maximum GFR for the available renal blood flow and correlates in an animal model with high endogenous levels of angiotensin II (22). We measured high levels of circulating aldosterone, which were positively correlated to the filtration fraction. This is further evidence of the importance of the angiotensin-aldosterone system in the preservation of GFR, when renal blood flow is decreased. Renal blood flow did not correlate with cardiac index, whereas it did with systemic arterial pressure; the GFR also correlated with the renal fraction of cardiac output. This underlines the critical importance of blood pressure over blood flow to maintain adequate renal blood flow in the immediate postoperative period and stresses the importance of the renal resistance in maintaining adequate renal function.

Dopamine at 5.0 μg/kg/min has cardiac and renal effects. Cardiac output increases and left atrial pressure decreases, whereas heart rate and systemic vascular resistance are unchanged, indicating a true inotropic action of dopamine at this dosage. At the same time, renal blood flow, GFR, and urinary sodium excretion are significantly enhanced along with a reduction in filtration fraction. This suggests more pronounced pre-compared to postglomerular vasodilation and indicates that compensatory mechanisms are attenuated. Inhibitory modulation of aldosterone release by dopamine has been recently suggested.

Metoclopramide induced secretion of aldosterone in man is reduced by concomitant infusion of dopamine (23, 24). However, as in our study, infusion of dopamine alone did not significantly affect aldosterone concentrations (23).

The renal effects of dopamine were identical in children who received propranolol preoperatively and those who did not. By contrast, the increase in cardiac output was abolished in those patients receiving propranolol preoperatively. This confirms the participation of the β-adrenergic receptors in this cardiac action of dopamine. Although the $t_{1/2}$ of propranolol is 4 h, its effect on the receptors has been found to be more prolonged (25). This underlines also that the renal effects of dopamine are not secondary to the improvement in cardiac function and are most likely mediated by the activation of the δ-receptors previously described (26, 27).

Analyzing the results of the whole group of children, dopamine at 2.5 μg/kg/min had no effect on cardiac functions and only a moderate effect on renal functions (slight reduction of filtration fraction). The lack of effects of dopamine at this dosage in children after cardiac surgery contrasts with report on adults (3, 4). Interestingly, the renal response to low-dose dopamine is age dependent in animals. This is interpreted as a maturation process of renal dopamine receptors (6–8). However, premature neonates with respiratory distress syndrome receiving 2 μg/kg/min of dopamine increased their natriuresis compared to a matched control group not treated by dopamine (28). In our study, some age dependency of the response to dopamine at 2.5 μg/kg/min is suggested by a significantly greater increase in renal plasma flow in children older than 5 y.

In conclusion, continuous infusion of dopamine at 5.0 μg/kg/min might prove helpful in preventing renal failure after cardiopulmonary bypass in children by increasing renal functional reserve.

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