Br J clin Pharmac 1994; **37**: 261–263

The acute effects of a single dopamine infusion in elderly patients with congestive cardiac failure

THOMPSON ROBINSON, SALAH GARIBALLA, GRAHAM FANCOURT, JOHN POTTER & MARK CASTLEDEN
University Division of Medicine for the Elderly, Leicester General Hospital, Gwendolen Road, Leicester LE5 4PW

1 Dopamine (DA) at low doses (2.5 μg kg^{-1} min^{-1}) produces a measurable increase in glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) in young healthy subjects and has a therapeutic effect in younger patients with congestive cardiac failure (CCF). In elderly healthy subjects, DA increases ERPF but does not increase GFR in all subjects.

2 To determine the potential therapeutic use of DA in elderly subjects with CCF, we studied 17 patients (5 male) aged 79.9 years (range 68 to 93 years) admitted to hospital for inpatient treatment of CCF resistant to diuretic and angiotensin converting enzyme inhibitor therapy. The effects of a single infusion DA at 2.5 μg kg^{-1} min^{-1} on GFR and ERPF were assessed in a double-blind, placebo controlled prospective study.

3 There were no significant differences in GFR or ERPF between control and DA. A reduction in GFR was seen in some patients.

4 DA at low dosage was not shown to benefit elderly patients with resistant CCF, and in some patients was detrimental. Higher doses or a combination with other inotropes may be necessary for a renal effect in elderly patients.

Keywords ageing congestive cardiac failure dopamine effective renal plasma flow glomerular filtration rate

Introduction

Dopamine (DA) affects renal perfusion by a number of dose related mechanisms including specific renal vasodilatation and indirectly by its positive inotropic effect on the heart. It produces a measurable increase in glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) in young subjects [1, 2], in whom DA administration is used as a technique to assess renal functional reserve capacity (RFRC).

There is a reduction of 50% in GFR and ERPF by the age of 80 [3], but until recently the effects of DA on these parameters in the elderly was unknown. Fancourt *et al.* [4] showed that a low dose DA infusion significantly increased ERPF with no overall change in GFR. Individual results identified two groups: those in whom there was no RFRC, and those in whom there was reserve capacity.

In congestive cardiac failure (CCF), DA selectively increases renal blood flow and GFR at low doses producing a marked naturesis. This has prompted its therapeutic use in young patients with intractable CCF [5, 6, 7]; in addition to its acute benefit, one study showed a sustained benefit for up to 28 months [6]. Since the effects of DA in CCF in the elderly had not been previously studied, we investigated the acute response to a DA infusion in such patients.

Methods

We studied 17 patients (five male) mean age 79.9 years (range 68 to 93) who had been admitted for inpatient management of symptomatic CCF resistant to standard therapy. Patients were in sinus rhythm or controlled atrial fibrillation (rate <100) and had a serum creatinine of <200 μmol l^{-1} on admission. Patients with valvular heart disease, unstable angina, recent myocardial infarction, hypertension, peripheral vascular disease, or a history of ventricular dysrhythmias were excluded.

Patients received 1000 ml fluid day^{-1}, and a controlled protein (1 g kg^{-1} body weight day^{-1}) and sodium (no added salt) diet for at least 3 days prior to

Correspondence: Dr T. G. Robinson, University Division of Medicine for the Elderly, Leicester General Hospital, Leicester LE5 4PW

intervention. Their weight was recorded daily and their usual medication continued throughout the study.

There followed a randomised, double-blind, placebo-controlled study, performed on successive days at the same time of day. Patients rested for 30 min, and venous blood was taken for the measurement of full blood count and biochemistry, and a 24 h urine collection started. ERPF was measured using bolus injection of [^{125}I]-labelled hippuran (5 MBq), and GFR using [^{51}Cr]-labelled EDTA (5 MBq) [8]. Patients received an infusion over 4 h of 5% dextrose with or without added DA at a rate of 2.5 μg kg^{-1} min^{-1}. There was continuous electrocardiographic monitoring, and blood pressure and heart rate were recorded at 15 min intervals using a DINAMAP semi-automatic recorder. The infusion was terminated if there was a significant tachycardia, hypotension or hypertension; or palpitations, arhythmia, vomiting or angina. (One subject developed fast atrial fibrillation.) ERPF analysis in five patients and GFR in one patient were not technically possible.

Statistical analysis using Student's paired *t*-test was performed comparing data during DA with that during control infusion.

All patients gave their informed written consent, and the study was approved by the Leicestershire Health Authority Ethics Committee.

Results

Mean (s.e. mean) values of measurements are given in Table 1. There was no significant difference in weight change between hospital admission, control and DA infusion days. Similarly the DA infusion had no effect on serum creatinine, 24 h urine sodium excretion and volume, and there was no significant increase in systolic blood pressure (Table 1). There was no increase in mean GFR (Table 1), and although GFR increased in six patients, no concomitant increase in ERPF was seen in all these patients (Figure 1). There was no significant change in mean ERPF (Table 1), an increase being shown in only 50% of patients (Figure 1).

Discussion

We found no increase in ERPF in response to low dose DA infusion in elderly patients with CCF. However, baseline ERPF was low compared with that reported for normal elderly subjects [4], and may reflect renal hypoperfusion secondary to poor cardiac output. CCF is associated with low tissue perfusion pressure and reduced oxygen saturation of tissues, causing increased sympathetic activity with increased noradrenaline and DA concentrations [9, 10]. It is possible that, in the presence of high endogenous DA concentrations, further intravenous infusion will not be beneficial. It is known that downregulation of β-adrenoceptors occurs in CCF [10] and with ageing [11]. Changes in DA receptor number and/or properties could also occur, though there has been little convincing evidence to suggest an alteration in DA receptors [10], or endogenous renal DA formation in CCF [12]. Though studies in young patients with CCF

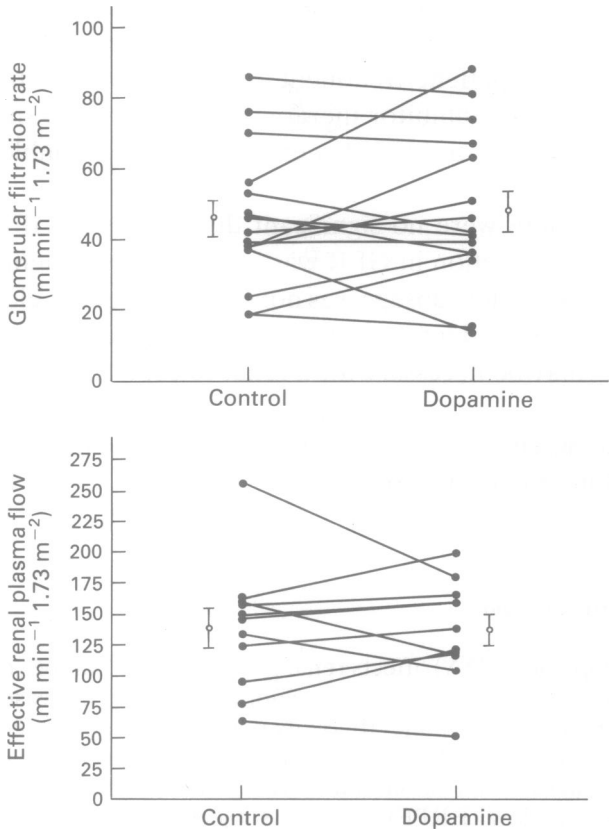

Figure 1 Glomerular filtration rate (ml min^{-1} 1.73 m^{-2}) and effective renal plasma flow (ml min^{-1} 1.73 m^{-2}) in elderly patients with intractable cardiac failure. Effects of dopamine.

Table 1 Means (± s.e. mean) for control and dopamine infusion days

	n	*Control*	*Dopamine*	P *value*
Pulse (beats min^{-1})	16	80 ± 3.3	79 ± 4.2	0.74
SBP (mm Hg)	16	114 ± 4.6	120 ± 3.9	0.20
DBP (mm Hg)	16	69 ± 12.3	72 ± 13.4	0.03
Creatinine (μmol l^{-1})	16	160 ± 18.8	166 ± 20.7	0.66
Weight change (kg)	16	−0.4 ± 0.51	−0.5 ± 0.55	0.81
GFR (ml min^{-1} 1.73 m^{-2})	15	46 ± 5.1	48 ± 5.7	0.52
ERPF (ml min^{-1} 1.73 m^{-2})	11	139 ± 15.7	138 ± 12.5	0.92
Urine NA (mmol 24 h^{-1})	11	54 ± 14	46 ± 15.4	0.45
Urine volume (ml 24 h^{-1})	11	1098 ± 161.0	1001 ± 191	0.50

did show a significant increase in ERPF with renal dose DA, these studies used higher but sub-inotropic doses of DA [5, 7] or dobutamine [6]. This may explain improvements seen in other studies but not in the present study. As neither cardiac output nor peripheral vascular resistance were measured in this study, we are unable to say whether the dose of DA used had an inotropic effect though there was no significant change in SBP. It is possible that higher doses of DA are required in elderly patients with CCF, and that this study should be repeated using such concentrations.

There was no significant change in GFR with a DA infusion, and more disturbingly a decrease in about 50% of patients. GFR has also been noted to fall with DA in some normal elderly subjects, and an inverse correlation between baseline GFR and % change in GFR with DA was observed [4]. The implication is that patients with higher GFR are already approaching their maximal filtration capacity and cannot increase this further. No significant inverse correlation was seen in our study. Beukhof *et al.* [1] found that when GFR was below 73 ml min^{-1} 1.73 m^{-2} RFRC was exhausted. All but two of our patients had GFRs below this level. Ter Wee *et al.* [2] found that RFRC could only reliably be established by combined DA and amino acid infusion which was not performed in the present study or the study of Beukhof [1].

We have shown that in elderly patients with CCF, low dose DA infusion reduces GFR and urine sodium excretion in some patients, and appears of equivocal benefit in the management of CCF. Further studies are still needed to define the role of DA in this group of patients, and the potential benefits of higher dose DA infusion.

References

1 Beukhof H, ter Wee P, Sluiter W, Donker A. Effect of low-dose dopamine on effective renal plasma flow and glomerular filtration rate in 32 patients with IgA glomerulopathy. *Am J Nephrol* 1985; **5**: 267–270.

2 ter Wee P, Rosman J, van der Geest S, Sluiter W, Donker A. Renal hemodynamics during separate and combined infusion of amino acids and dopamine. *Kidney Intern* 1986; **29**: 870–874.

3 Davies D, Shock N. Age changes in glomerular filtration rate, effective renal plasma flow, and tubular excretory capacity in adult males. *J clin Invest* 1950; **29**: 496–507.

4 Fancourt G, Asokan V, Bennett S, Walls J, Castleden C. The effects of dopamine and a low protein diet on glomerular filtration rate and renal plasma flow in the aged kidney. *Eur J clin Pharmac* 1992; **42**: 375–378.

5 McDonald R, Goldberg L, McNay J, Tuttle E. Effects of dopamine in man: augmentation of sodium excretion, glomerular filtration rate, and renal plasma flow. *J clin Invest* 1964; **43**: 1116–1124.

6 Applefeld M, Newman K, Sutton F, *et al.* Outpatient dobutamine and dopamine infusions in the management of chronic heart failure: Clinical experience in 21 patients. *Am Heart J* 1987; **114**: 589–595.

7 Kubota J, Kubo S, Nishimura H, *et al.* Cardiorenal effects of an orally active dopamine prodrug (TA-870) in patients with congestive heart failure. *J cardiovasc Pharmac* 1989; **14**: 53–57.

8 Britton K, Maisey M. Renal radionuclide studies. In *Clinical nuclear medicine*, ed. Maisey M, Britton K, Gilday D. Chapman and Hall, London, 1983.

9 Viquerat C, Daly P, Swedberg K, *et al.* Endogenous catecholamine levels in chronic heart failure. *Am J Med* 1985; **78**: 455–460.

10 Thomas P, Sheridan D. Pathophysiology of autonomic dysregulation in heart failure. In *Autonomic failure. A textbook of clinical disorders of the autonomic nervous system*, ed. Bannister R. Oxford Medical Publications, Oxford, UK, 1988.

11 Vestal R, Wood A, Shand D. Reduced beta-adrenoceptor sensitivity in the elderly. *Clin Pharmac Ther* 1979; **26**: 181–186.

12 Lee M. Dopamine and the kidney: 10 years on. *Clin Sci* 1993; **84**: 357–375.

(Received 22 June 1993, accepted 27 October 1993)