Klin Wochenschr (1982) 60:193–197

Klinische Wochenschrift

Dopamine Treatment of Human Cadaver Kidney Graft Recipients: A Prospectively Randomized Trial

R. Grundmann, J. Kindler, G. Meider, H. Stöwe, H.G. Sieberth, and H. Pichlmaier

Chirurgische Klinik (Direktor: Prof. Dr. Dr. H. Pichlmaier)
und Medizinische Klinik (Direktor: Prof. Dr. R. Gross) der Universität Köln
und Medizinische Klinik I, Köln-Merheim (Direktor: Prof. Dr. E. Renner)

Summary. In a prospectively randomized trial, 50 human cadaver kidney graft recipients were tested for the effect of dopamine infusion on kidney function after transplantation. The kidneys were taken from beating-heart donors under optimal conditions. The dopamine infusion did not affect the dialysis frequency in the 1st week after transplantation, in the dopamine group only slightly better creatinine clearances could be detected. However, the diuresis increased significantly when dopamine was given and this resulted in the fact that in the dopamine group 47.4% of the patients were dialyzed although the diuresis amounted to more than 11/day as compared to 15.7% of such patients in the nondopamine group. These findings correspond to experimental data, which showed that the dopamine infusion of the recipient mainly ameliorated renal function in those cases where kidneys were taken after hypotensive injury of the donor.

Key words: Kidney transplantation – Dopamine infusion – Dialysis frequency

Dopamininfusion bei Nierentransplantatempfängern. Eine prospektive randomisierte Studie

Zusammenfassung. In einer prospektiven randomisierten Studie wurde an 50 Patienten überprüft, ob die Gabe von Dopamin nach Nierentransplantation die Funktion des Transplantates verbessern könne. Die Nieren waren hirntoten Spendern unter optimalen Kreislaufverhältnissen entnommen worden. Es zeigte sich, daß die Dialysefrequenz in der ersten Woche pOp von der Dopamingabe nicht beeinflußt wurde, nach Dopamingabe wurden nur geringgradig bessere Kreatininclearance-Werte gefunden. Hingegen ließ sich die Wasserausscheidung durch Dopamin deutlich steigern, entsprechend wurden in der Dopamingruppe 47,4% der Patienten mit einer Diurese von mehr als 11/Tag dialysiert, verglichen mit 15,7% solcher Patienten, in der Gruppe, die kein Dopamin erhielt. Diese Befunde entsprechen experimentellen Ergebnissen, die gezeigt hatten, daß Dopamin die Nierenfunktion hauptsächlich dann verbesserte, wenn die Niere nach hypotensiver Vorschädigung konserviert und transplantiert wurde.

Schlüsselwörter: Nierentransplantation – Dopamininfusion – Dialyserate

Kidneys that are removed for use in transplantation may widely vary in their functional condition on removal. The removal may take place after a shorter or longer warm ischemic time or after a short period of hypotension, or may be under optimum blood-circulation conditions in the case of brain trauma. Under an organ exchange system such as Euro-Transplant, in principle, only kidneys which have been removed under favorable conditions will be sent. Nevertheless, the functional state of the kidney after transplantation is often unsatisfactory: 65% of our own patients have to be dialyzed in the 1st week after transplantation [4]. This is certainly mainly attributable to the length of the preservation period (=damage due to long cold ischemic time) but the question should also be asked whether other factors, such as hypotension and warm ischemic time on kidney removal are responsible.

If hypotension in the donor is responsible for restricted function of the kidney in the recipient after transplantation, then it should in theory be possible to improve renal function by infusing dopamine. Dopamine causes, independently of α- und β-receptor stimulation, a marked increase (depending on dosage) in blood circulation through the kidneys, the visceral nervous system and the coronary vessels [10]. Patients with acute renal failure usually have lowered total re-

Offprint requests to: PD Dr. R. Grundmann (address see page 197)

nal blood circulation with considerably restricted cortical perfusion. The vasodilatory effect of dopamine can be used to influence this humoral or reflex vasoconstriction to increase blood circulation in the whole kidney and in the renal cortex [1]. In the experimental models [6–8] to date, these effects have led to a well-established reduction of retention of urea and creatinine and an increase in the glomerular filtration rate.

For the present investigation we thus administered dopamine to the graft recipients. We then investigated whether the dopamine could improve the function of the grafted kidney even in cases where the graft recipient's blood circulation appears fully normal and he exhibits no signs of hypotension. The situation in this study is thus basically different from situations in which dopamine has previously been administered. While the effect of dopamine on the kidneys of patients suffering from shock has been reliably established and dopamine is, therefore, given routinely to kidney donors on nephrectomy [3, 9], the present study is concerned with investigating whether dopamine administered to the recipient posttransplantation can improve kidney function.

Materials and Method

This investigation covered 50 patients who received kidney grafts from cadaver donors in the period 1 October 1979 to 31 December 1980. The kidneys were provided through the Euro-Transplant organ exchange system. All the kidneys were preserved by Collins' method [2]. The selection criteria used were a preservation time not exceeding 30 h, warm ischemia time on kidney removal not exceeding 10 min, and a serum creatinine level in the donor of not more than 2.5 mg%. To investigate whether kidney function after transplantation could be improved by infusing dopamine, 25 patients were purely selected in a random fashion from among the 50 and dopamine was administered to these 25 patients at a dosage of 2.0 µg/kg body weight/min. The administration of the dopamine was commenced immediately posttransplantation and was continued for 4 days. The following were measured postoperation: blood pressure, pulse rate, urine excretion, serum creatinine level, creatinine clearance, and dialysis rate. Factors which could have adversely affected kidney function (such as warm ischemia time on removal, preservation time, length of anastomosis time, age, blood circulation condition, and kidney function of donor) were also analyzed.

Results

The two groups (with/without dopamine) showed no differences as regards condition of the donor (Table 1) or condition of the recipient (Table 2). Both groups also did not differ in preoperative risks since patients with increased pulmonary or cardiac risk were refused transplantation in principle. The administration of dopamine had no influence on the frequency of dialysis: in each of the groups 19 patients (76%) required dialysis in the first postoperative week. Urine production was higher in the group receiving dopamine, but

Table 1. Condition of the kidney donor (mean values and standard deviation)

	With dopamine ($n=25$)	Without dopamine ($n=25$)
Donor age (years)	25 ± 10.6	27 ± 11.3
Systolic blood pressure last hour before removal (mm Hg)	110 ± 18.0	126 ± 20.0
Warm ischemia time before removal (min)	2.0 ± 2.3	2.0 ± 2.2
Diuresis in last hour (ml)	330 ± 230	300 ± 268
Serum creatinine (mg/dl)	1.25 ± 0.5	1.20 ± 0.5
Dopamine administered on removal	$n=22$	$n=18$
Anastomosis time (min)	29 ± 6.0	28 ± 4.0
Preservation time (h)	21.3 ± 3.3	21.3 ± 2.9

Table 2. Condition of the transplant recipient (mean values and standard deviation)

	With dopamine ($n=25$)	Without dopamine ($n=25$)
Age (years)	35 ± 11.1	35 ± 12.4
Men: women	3:2	1.9:1
Those receiving antihypertensive medication before transplantation	$n=13$	$n=13$
Those receiving digitalis before transplantation	$n=9$	$n=11$
β-blockers before transplantation	$n=4$	$n=2$
Hemoglobin concentration (g/100 ml) before transplantation	9.3 ± 2.2	8.8 ± 2.5

the creatinine clearance remained unaffected by the administration of dopamine (Fig. 1). As a consequence of the high urine production, 9 of 19 patients (47.4%) receiving dopamine who required dialysis in the 1st week had diuresis of more than 1,000 ml/day. In the group without dopamine this number was lower: 3 of 19 patients (15.7%) requiring dialysis had urine production exceeding 1,000 ml/day. The dialysis frequency in the 2nd and 3rd week after transplantation was also nearly the same in both groups (Table 3).

The effect of dopamine on the blood circulation was small. The number of patients receiving antihypertensive medication in the 1st postoperative week was roughly the same in each group: 48% in the group with dopamine and 44% in the group without dopamine. The incidence of tachycardia (pulse rate >100) was however markedly higher in the group with dopamine (Fig. 2). In 3 of 25 patients the tachycardia was so pronounced that at a pulse rate of 120–168/min the dopamine had to be prematurely dis-

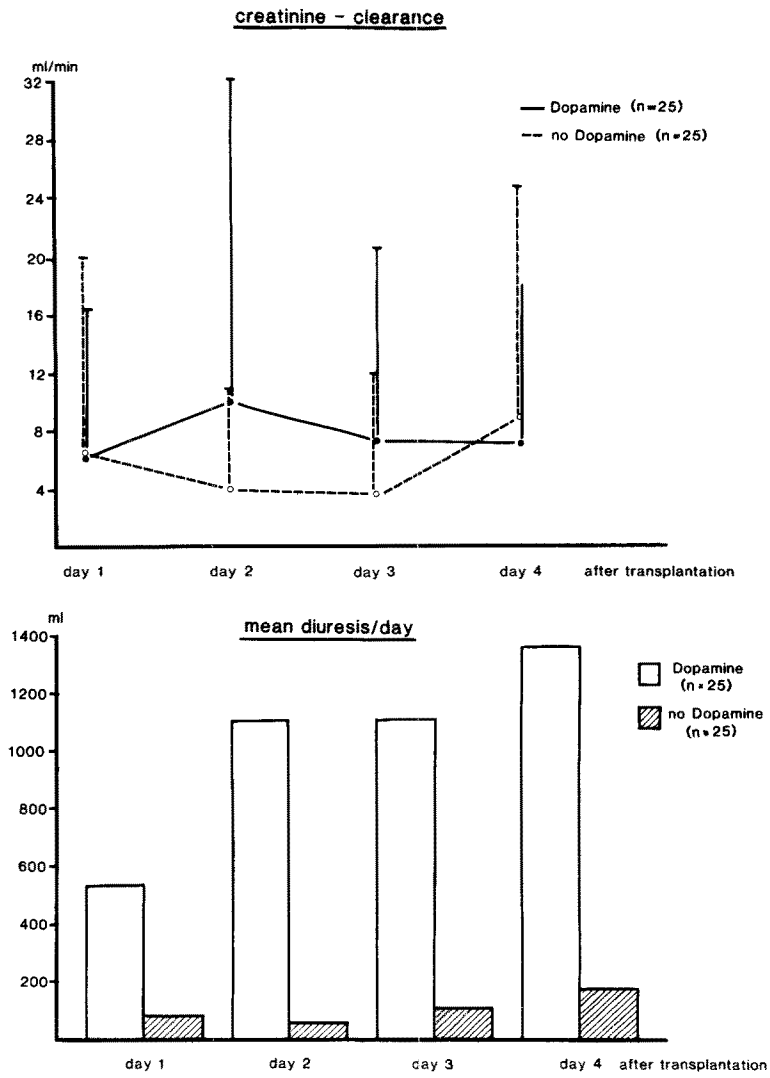

Fig. 1. Mean creatinine-clearance and diuresis/day after transplantation in patients either receiving or not receiving dopamine (mean value and standard deviation)

continued since it was not tolerated by the patient. According to this the number of patients receiving β-blockers was higher in the group with dopamine.

Kidney graft recipients receiving dopamine infusion showed a significantly higher rate of acute rejection episodes in the 1st week after transplantation ($p < 0.05$). Three weeks after transplantation, however, the number of patients who underwent a rejection crisis was nearly identical in both groups (Table 3).

Discussion

The purpose of the present study was to investigate whether or not it is appropriate to administer dopamine after transplantation. The results showed that the incidence of dialysis in the group of patients who received dopamine posttransplantation was no less than in the control group who did not receive dopamine. The same incidence of acute renal failure (76%

Table 3. Results (mean values and standard deviation)

	With dopamine ($n=25$)	Without dopamine ($n=25$)	
Those receiving antihypertensive medication 1st week after transplantation	$n=13$	$n=12$	n.s.
Those receiving β-blockers 1st week after transplantation	$n=8$	$n=4$	n.s.
Rejection episode in the 1st week after transplantation	$n=18$	$n=10$	$p<0.05$ χ^2 test
Rejection episode in the first 3 weeks after transplantation	$n=20$	$n=22$	n.s.
Patients dialyzed			
end of week 1	$n=19$	$n=19$	n.s.
end of week 2	$n=11$	$n=13$	n.s.
end of week 3	$n=6$	$n=8$	n.s.

(n.s. = not significant)

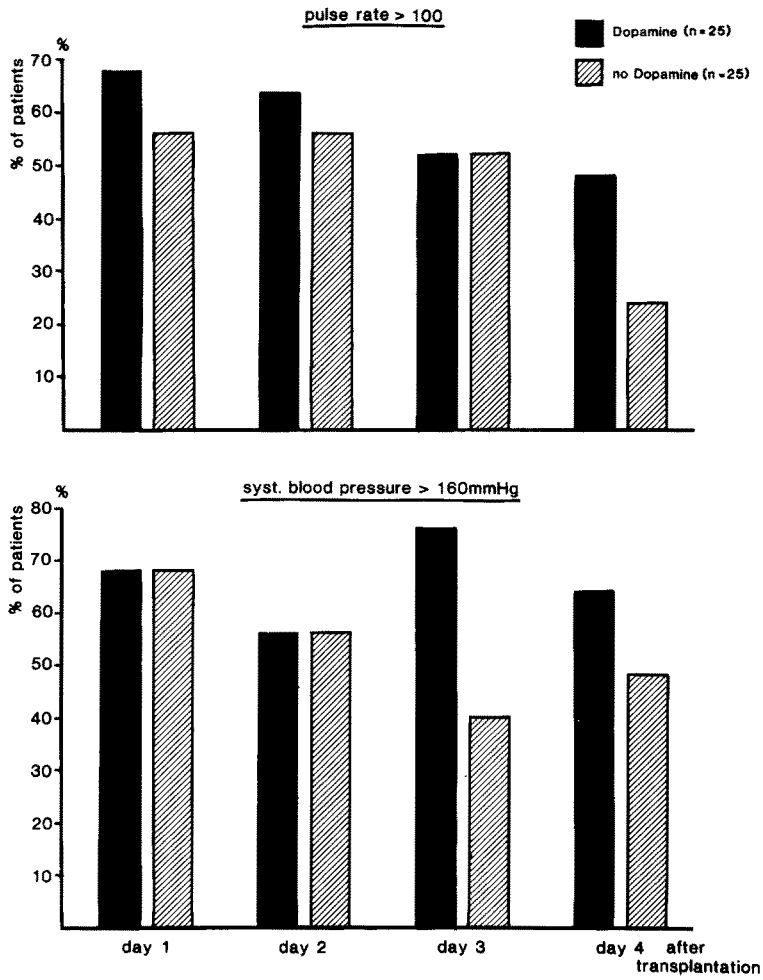

Fig. 2. Pulse rate > 100 and systolic blood pressure > 160 mm Hg after transplantation in patients either receiving or not receiving dopamine

of all patients) was found in both groups. Nevertheless a certain benefit from the dopamine was demonstrable: patients given dopamine produced on average more urine, i.e., dopamine is capable of stimulating the excretion of water. The excretion of the substances required to be excreted in the urine was however not increased, and the ability of the kidney to concentrate the urine was not affected by the increased diuresis. Thus the administration of dopamine did not reduce the rate of postoperative dialysis required.

In this context it should be mentioned that in the present investigation the indication for dialysis only depended on the blood urea concentration which should not amount to more than 200 mg/100 ml. Hyperhydration or an extremely high increase of the serum potassium concentration could be avoided in all cases and, therefore, represented no indication for dialysis.

The question is whether dopamine infusions should be given after transplantation or not. On the basis of the present investigation, no general recommendation to administer dopamine posttransplantation can be made. In experiments on dogs, however, clear indications of improved kidney function on administration of dopamine posttransplantation were found: if a kidney was taken from a hypotensive donor and then preserved, its function after transplantation was significantly improved by the administration of dopamine to the recipient [5]. On the assumption that in the present study the preponderant majority of the kidneys used were taken from brain-dead donors with adequate blood circulation, then these previous findings would lead one to expect the effect of dopamine to be small; dopamine cannot affect the reduction in kidney function after storage and transplantation caused by ischemia damage.

The dosage of dopamine infusion given in this study was also based on these former experiments in which it was demonstrated that renal function after transplantation did not differ whether 2 μg or 5 μg dopamine/kg body weight/min were given. Nevertheless, the dosage level should have been increased in human kidney graft recipients. This was not tried, however, since the side effects of dopamine at the dosage level used were already obvious. Thus a rise of the pulse rate to an intolerable level was observed

in three patients and the number of patients receiving β-blockers was also clearly higher in the dopamine group.The question remains whether dopamine should have been given for longer periods than 4 days after transplantation. This was not done for two reasons: on the one hand, the dopamine infusion did not alter the dialysis frequency. Therefore, a long-term infusion therapy for patients with high risk of infections who otherwise can eat and drink normally and do not need a venous blood catheter was not justified. On the other hand, it could be assumed that the majority of these kidneys that showed a low immediate function after transplantation would start to function in the 2nd or 3rd week after transplantation, at least in the cases where no rejection episode occurred. Therefore the demand for an improvement of diuresis was higher in the 1st than in the 2nd or 3rd week after transplantation (see also Table 3, dialysis frequency).

In this analysis it was surprisingly found that patients receiving dopamine showed a significantly higher rate of acute rejection episodes in the 1st week after transplantation, although the number of rejection episodes occuring in the first 3 weeks after transplantation was nearly identical in the two groups. The reasons for this are not quite clear, however, the results of Sampson [11] could give a possible explanation: he found kidneys functioning well immediately after transplantation were rejected sooner than those that did not function immediately. If one starts with the concept that dopamine increased the blood circulation through the kidneys, these findings would mean that the commencement of the rejection episode depended on the amount of renal blood flow.

In the present study urine production in the group receiving dopamine was increased. This can be advantageous since it is psychologically reassuring to the patient if urine production commences directly after transplantation and his daily fluid intake need not be restricted. Furthermore, this effect of dopamine treatment may be of advantage to all those patients that have to be infused for longer periods where there is reduced renal function, since fluid and drug application becomes easier with better diuresis.

Conclusions

If kidneys for transplantation are removed under optimum conditions from brain-dead donors, preserved, and then transplanted, then the improvement in function produced by infusing dopamine is only very slight. The improvement is represented by increased, isosthenuric diuresis, but the postoperative dialysis rate is not reduced.

These findings are consistent with the findings from animal experiments in which the main improvement in renal function was where the kidney was preserved and transplanted after previous hypotensive damage.

References

1. Augustin HJ, Huland H, Novak D, Kürschner HD (1975) Der Einfluß von Dopamin auf die renale und intrarenale Hämodynamik. In: Schröder R (ed) Dopamin, Arbeitstagung über die klinische Anwendung. Schattauer, Stuttgart pp 171–185
2. Collins GM, Bravo-Shugarman M, Terasaki PI (1969) Kidney preservation for transportation. Initial perfusion and 30 hours' ice storage. Lancet 2: 1219–1222
3. Dhabuwala CB, Bird M, Salaman JR (1979) Relative importance of warm ischaemia, hypotension, and hypercarbia in producing renal vasospasm. Transplantation 27:238–241
4. Grundmann R, Kindler J, Sieberth G, Finke K, Meider G, Pichlmaier H (1981) Ergebnisse der Nierentransplantation 1968–1979. Dtsch Med Wochenschr 106:106–110
5. Grundmann R, Kämmerer B, Franke E, Pichlmaier H (1981) The effect of hypotension on the results of kidney storage and the use of dopamine under these conditions. Transplantation 32:184–187
6. Held E, Edmaier MA (1979) Therapie des akuten Nierenversagens: Pathophysiologische und klinische Aspekte. In: Sieberth HG (ed) Akutes Nierenversagen, Intensivmedizin, Notfallmedizin, Anasthesiologie (INA). Thieme, Stuttgart, pp 119–133
7. Iaina A, Salomon S, Gavendo S, Eliahon HE (1977) Reduction in severity of acute renal failure in rats by dopamine. Biomedicine 27:137–141
8. Lindner A, Cutler RE, Forrey A (1976) Modification of uranyl nitrate induced acute renal failure by Dopamine and Furosemide in the dog. Kidney Int 10:561
9. Raftery AT, Johnson RWG (1979) Dopamine pretreatment in unstable kidney donors. Br Med J 87:522–523
10. Rosenblum R, Tai AR, Lawson D (1970) Cardiac and renal hemodynamic effects of dopamine in man. Clin Res 18:326
11. Sampson D, Kauffman HM, Walczak P (1978) Flow and function in machine-preserved kidneys. Br J Surg 65:37–40

Received May 19, 1981
Accepted October 28, 1981

PD Dr. R. Grundmann
Chirurgische Universitäts-Klinik
Joseph-Stelzmann-Str. 9
D-5000 Köln 41
Federal Republic of Germany