Bilateral nephrectomy simultaneously with renal allografting does not alleviate hypertension 3 months following living-donor transplantation

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Abstract Severe hypertension prior to renal transplantation has traditionally been an indication for bilateral nephrectomy. The reasons for hypertension after successful renal transplantation are however many, and the impact of simultaneous bilateral nephrectomy (BN) in this setting has not been well documented. We retrospectively evaluated 158 living-donor renal graft recipients. BN had been performed in 76 patients at the time of the transplantation and 82 were not nephrectomized (controls). All received a triple immunosuppressive drug regimen. Before transplantation, patients in the BN group used 1.8 ± 0.9 (mean ± SD) antihypertensive drugs/day, significantly more than in the control group (1.3 ± 0.8; P < 0.05). Three months after renal transplantation no difference was found (0.9 ± 1.0 drugs/day in the BN group vs 1.0 ± 0.8 drugs/day in the control group). No difference was found with respect to serum creatinine, whole blood cyclosporin A (CsA) concentration or blood pressure between the groups. The number of blood transfusions during the first week after transplantation was significantly increased in the BN group (66 SAG units vs 4 SAG units). The median hospitalization length was also longer in the BN group (21 days vs 16 days). In order to circumscribe the pre-transplant difference in use of antihypertensive medication we studied a subgroup of 62 hypertensive recipients (BN/control = 31/31) matched for number of antihypertensive drugs at the time of transplantation (2.3 ± 0.5 drugs/day in the BN group, 2.1 ± 0.3 drugs/day in the control group). Three months after transplantation the use of antihypertensive drugs remained the same in the two groups (2.3 ± 0.6 drugs/day in the control group). Three months after transplantation the use of antihypertensive drugs remained the same in the two groups (2.3 ± 0.5 drugs/day in the BN group, 2.1 ± 0.3 drugs/day in the control group). At 3 months no difference was found between the two hypertensive subgroups regarding serum creatinine, whole blood CsA and haemoglobin concentration or systolic blood pressure. However, the BN patients were younger than the control group (38 ± 10 years vs 49 ± 11 years, P < 0.05) and this may explain the marginally lower diastolic blood pressure observed in the BN group (82 ± 10 mmHg vs 87 ± 7 mmHg, P < 0.05). It is concluded that, in recipients of living-donor grafts, bilateral nephrectomy performed at the time of transplantation did not influence the number of antihypertensive drugs used 3 months after a successful transplantation. Bilateral nephrectomy did however increase the need of blood transfusions during the first week after transplantation and also the hospitalization length.

Key words: bilateral nephrectomy; post-transplant hypertension

Introduction

Undisputed indications for bilateral nephrectomy (BN) prior to renal transplantation are chronic pyelonephritis with recurrent infections and polycystic kidney disease with haemorrhage or excessive physical size. Severe hypertension refractory to medical therapy (or volume reduction by haemodialysis) may also be an indication for bilateral nephrectomy [1].

Hypertension in end-stage renal disease (ESRD) patients often persists after transplantation [2]. The reported incidence of hypertension following renal transplantation after the introduction of cyclosporin A (CsA) is 50–80% [3–6]. Hypersecretion of renin or increased afferent sympathetic nerve traffic by native kidneys may be causes of hypertension in this setting [7–9] and are abolished by BN [10,11]. The impact of BN on the prevalence of hypertension after successful renal transplantation has, however, not been well documented. At our centre 70–80 living-donor transplantations are performed yearly and simultaneous BN is performed in 30–40 of these. Therefore, a large number of nephrectomized patients could be retrospectively evaluated to assess the impact of nephrectomy on post-transplant hypertension. To circumscribe the selection bias in favour of nephrectomy among the hypertensive patients, we also evaluated a subgroup of hypertensive non-nephrectomized patients and compared them to a randomly selected group of BN patients matched for

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donor age and antihypertensive treatment at the time of transplantation.

BN implies an extended operative trauma. We evaluated the number of blood transfusions and post-operative haemoglobin values in all patients, and also compared the length of hospitalization in the two groups.

Subjects and methods

Patient population

From January 1992 to December 1994 a total of 574 renal transplantations were performed at our centre. Living donors were used in 228 of the cases. The study population was retrospectively reviewed. Seventy renal recipients were not included in the study due to various reasons (19 were under 18 years of age at transplantation, 17 had non-functioning graft at 3 months and 34 had either been nephrectomized earlier, died or were followed up by other centres so that adequate data could not be obtained). This leaves a total of 158 living-donor recipients over 18 years of age with functioning graft eligible for the study. Seventy-six patients had undergone BN at the time of transplantation. The indication for BN was hypertension alone in 33 patients, polycystic kidney disease in 13 patients, recurrent urinary tract infections in 11 patients and a combination of reasons/other in 19 patients. In 82 patients BN was not performed (controls).

Immunosuppressive protocol

All patients were treated with a triple immunosuppressive regimen consisting of cyclosporin A (CsA), azathioprin and prednisolone. Prednisolone (30 mg/day) and CsA (15 mg/kg/day) were started 2 days before the transplantation. On the day of transplantation all patients received 500 mg methylprednisolone i.v. After transplantation the initial daily oral dose of prednisolone was 80 mg tapered by 10 mg each day until 20 mg/day was reached. A prednisolone dose of 20 mg/day was used for the remainder of the first month and was then gradually tapered to 10 mg/day which was normally reached after 60–90 days. CsA dosage was adjusted in order to obtain early whole blood CsA trough levels of about 300–400 ng/ml, with a reduction to 125–200 ng/ml at 3 months. Initial azathioprin dosage was 2 mg/kg/day for 1 week, and the maintenance dose was 1 mg/kg/day. All patients received co-trimoxazole 80–400 mg daily as prophylaxis against Pneumocystis carinii.

Study design

All patients. In the retrospective evaluation of 76 BN and 82 control transplant patients, we compared the following baseline parameters: donor age, recipient age, haemoglobin concentration and the number of antihypertensive drugs/day at the time of transplantation (excluding diuretics). Following transplantation we evaluated the need for blood transfusions during the first week, recorded the haemoglobin value at day 7 and assessed the total length of hospitalization. Blood pressure (mean of three measurements in a sitting position at three subsequent visits), serum creatinine and whole blood CsA concentration were evaluated in a stable phase 3 months post-transplantation. The number of antihypertensive drugs/day was also evaluated after 3 months when changes in antihypertensive medication as a rule no longer occurred.

The number of patients in the entire group requiring more than one antihypertensive drug 3 months after transplantation was registered. No patients received recombinant erythropoetin following renal transplantation.

Hypertensive patients. In order to evaluate the effect of BN in hypertensive patients we evaluated a subgroup of patients. Thirty-one patients were treated with two or more antihypertensive drugs before transplantation and were still not selected for nephrectomy (probably because of the indication for BN not being well defined at our centre). This control group was compared to a randomly selected group of 31 BN patients matched for number of antihypertensive drugs at the time of transplantation. In this subpopulation the following baseline parameters were recorded: donor age, recipient age, haemoglobin values and the number of antihypertensive drugs/day at the time of transplantation. The number of antihypertensives was again evaluated in a stable phase 3 months post-transplantation, together with blood pressure, serum creatinine and whole blood CsA concentration.

Statistics

All results are given as means ±SD. The Mann–Whitney test is applied in all analyses. P values are two-tailed.

Results

All patients

As shown in Table 1, the recipients in the BN group were significantly younger at transplantation than the control group (P<0.05). The age of donors was similar in the two groups. Three months after transplantation serum creatinine, whole blood CsA concentration and systolic and diastolic blood pressure were similar in the two groups. As shown in Fig. 1, the number of antihypertensive drugs used prior to transplantation was (as would be expected) significantly higher in the BN group than in the control group, i.e. 1.8±1.1 drugs/day in the BN group vs 1.3±0.8 drugs/day in the control group (P<0.05). Three months after transpl-

Table 1. All living-donor recipients

<table>
<thead>
<tr>
<th></th>
<th>BN (n=76)</th>
<th>Control (n=82)</th>
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<tbody>
<tr>
<td>Baseline demographics</td>
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<td></td>
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<tr>
<td>Recipient age (years)</td>
<td>40±13*</td>
<td>44±15</td>
</tr>
<tr>
<td>Donor age (years)</td>
<td>49±13</td>
<td>48±11</td>
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<tr>
<td>Data at 3 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum creatinine (µmol/l)</td>
<td>144±54</td>
<td>148±43</td>
</tr>
<tr>
<td>CsA concentration (ng/ml)</td>
<td>175±52</td>
<td>181±57</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>135±16</td>
<td>137±13</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>84±8</td>
<td>86±7</td>
</tr>
</tbody>
</table>

Data given as means ±SD.

BN = bilateral nephrectomy.

* P<0.05 compared to control group.
Bilateral nephrectomy and post-transplant hypertension

Fig. 1. Number of antihypertensive drugs used per group before transplantation (baseline) and in a stable phase 3 months after transplantation. Data are given as means ± SD. BN = bilateral nephrectomy. * Significantly different from baseline (P < 0.05); § Significantly different from baseline in BN group (P < 0.05); NS = not significantly different from baseline or BN group after 3 months.

Table 1. Antihypertensive medication 3 months after transplantation

<table>
<thead>
<tr>
<th>Number of antihypertensive drugs</th>
<th>BN (n = 76)</th>
<th>Control (n = 82)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Double therapy</td>
<td>15</td>
<td>19</td>
</tr>
<tr>
<td>Three or more</td>
<td>6</td>
<td>3</td>
</tr>
</tbody>
</table>

BN = bilateral nephrectomy.

As shown in Table 3, there was no statistical difference in donor age between the BN group and the control group. The patients in the BN group were, however, on average 11 years younger than the control patients. Three months after transplantation serum creatinine, whole blood haemoglobin, whole blood CsA concentration and systolic blood pressure were not different between the two groups. The diastolic blood pressure was, however, somewhat lower in the BN group.

The hypertensive subgroups of patients were matched for use of antihypertensive medication prior to transplantation, as shown in Fig. 2. The BN group used 2.3 ± 0.5 antihypertensive drugs/day, not different from 2.1 ± 0.3 drugs/day in the control patients. Three

Table 2. Hypertensive subgroup

<table>
<thead>
<tr>
<th></th>
<th>BN (n = 31)</th>
<th>Control (n = 31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline demographics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recipient age (years)</td>
<td>38 ± 10*</td>
<td>49 ± 11</td>
</tr>
<tr>
<td>Donor age (years)</td>
<td>50 ± 13</td>
<td>47 ± 10</td>
</tr>
<tr>
<td>Data at 3 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum creatinine (µmol/l)</td>
<td>148 ± 57</td>
<td>158 ± 41</td>
</tr>
<tr>
<td>CsA concentration (ng/ml)</td>
<td>170 ± 52</td>
<td>183 ± 40</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>134 ± 18</td>
<td>139 ± 13</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>82 ± 10*</td>
<td>87 ± 7</td>
</tr>
</tbody>
</table>

Data given as means ± SD. BN = bilateral nephrectomy.
P < 0.05 compared to control group.

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Table 2 shows the number of patients using more than one antihypertensive drug 3 months after transplantation. No difference was found between BN and control patients. Only one of these 43 hypertensive patients was without antihypertensive medication prior to transplantation.

Plantation there was no longer a difference in the use of antihypertensive drugs between the two groups, i.e. 0.9 ± 1.0 drugs/day in the BN group vs 1.1 ± 0.8 drugs/day in the control group. The reduction in number of antihypertensive drugs following transplantation was significant in the BN group (P < 0.05) but not in the control group.

The number of red blood cell transfusions (SAG) was significantly higher in the BN group, comprising 66 SAG units in 17 out of 76 patients vs four SAG units in two out of 82 patients in the control group (P < 0.05). Also the haemoglobin values fell significantly more during the first week following transplantation in the BN group, from 11.0 ± 1.4 (mean ± SD) to 9.1 ± 1.3 g/dl, compared to a fall from 11.3 ± 1.4 to 9.6 ± 1.3 g/dl in the control group. No patient death could be ascribed to BN.

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months after transplantation the number of antihypertensive drugs was the same in the two groups, i.e. 1.3 ± 1.0 drugs/day in the BN group vs 1.3 ± 0.9 in the control group. The reduction in absolute number of antihypertensive drugs following transplantation was not statistically different between the BN and control group.

Discussion

The present study has shown that BN performed at the time of a successful renal transplantation does not reduce the number of antihypertensive drugs used 3 months later when compared to a control group who did not undergo nephrectomy. To our knowledge this is the largest series ever published on the effect on hypertension of BN performed simultaneously with renal transplantation after the introduction of CsA. Due to selection bias for BN in hypertensive patients, the groups were not comparable regarding the blood pressure-lowering effect of BN. We found the same results, however, in a subgroup of hypertensive patients matched for number of antihypertensive drugs prior to transplantation. One may discuss whether a selection bias still exists between the BN and the selected control group. In the subgroup analysis we selected hypertensive patients who did not undergo nephrectomy. They were compared with BN patients with similar hypertensive treatment at the time of transplantation. Why were only half of them selected for BN in the first place? There are two main reasons for not performing BN in a hypertensive patient. One is the age and the general condition of the patient at the time of transplantation: with increased age and high cardiovascular risk one would be reluctant to perform a major surgical procedure such as BN. This is likely to be the reason for the control group being significantly older than the BN group. Another reason is that hypertension has not been difficult to control, however no accurate data are available concerning this difficulty in this retrospective study. The fact that both groups used a comparable antihypertensive drug regimen at the time of transplantation does, however, indicate no difference between the groups in this respect.

The degree of hypertension was assessed by the number of antihypertensive drugs used. An alternative would be to assess both dosage and number of different antihypertensive drugs. However, the efficacy of a particular dose may differ considerably in ESRD patients due to differences in renal function and drug metabolism. We therefore agree with previous authors on using the number of antihypertensive drugs needed as an indicator of the severeness of hypertension [2,12]. This method implies equal blood pressure control between the groups. Blood pressure control cannot be optimally evaluated in a clinical setting by casual blood pressure recordings at the clinical visits, as done in this retrospective study. We used the mean of three blood pressure measurements in a sitting position at three different visits. This may be the best method available for retrospective analysis. Optimal blood pressure recordings would imply 24-hour blood pressure measurements, unfortunately not performed in our patients. By using the mean of three measurements we did however find a somewhat lower diastolic (but not systolic) blood pressure in the BN group 3 months after transplantation. The importance of this difference cannot be elucidated due to the method used. To evaluate the effect of BN on post-transplant hypertension, confounding factors such as graft dysfunction and inappropriate effects of CsA would also need to be evaluated. There was however no difference between the groups regarding serum creatinine and whole blood CsA concentration 3 months after transplantation.

It is well known that blood pressure is volume dependent in most patients with ESRD. In addition, increased renin secretion by native kidneys may promote hypertension both before and after renal transplantation [2,10]. For this reason BN is often recommended and performed in patients with severe hypertension prior to renal transplantation. Hypertension following renal transplantation is however often a low-renin hypertension, indicating that secretion of renin from native kidneys is of minor importance in this setting [12-15]. Our study supports these findings since we found no effect of BN on the need for antihypertensive treatment 3 months after transplantation. By contrast, some studies have demonstrated hypertension to be more frequent when native kidneys are left in situ, indicating a contribution of renin secretion from native kidneys also after renal transplantation [10,11,16]. The number of patients included in these studies was small. It may well be that native BN after transplantation may in some cases lower plasma renin activity and alleviate hypertension [10,11]. Such selected cases may not have been prevalent enough in our patient population to reach significance in the overall results.

In renal transplant patients treated with CsA, hypertension is characterized by sodium retention, renal vasoconstriction and lower plasma renin levels than in azathioprine-treated patients [13]. However, high renin output from native kidneys may still be responsible for persisting hypertension in a small percentage of patients despite successful transplantation. This can usually be controlled with antihypertensive therapy. The diagnosis may be confirmed by a high native kidney to transplant vein renin ratio. If severe, bilateral native kidney nephrectomy [10,11] or ablation by embolization [17] may be effective in selected patients.

BN implies an extended operative trauma. To avoid sequential operations our centre when indicated usually performs BN simultaneously with living-donor transplantation. No patient death that could be related to BN has ever occurred at our centre. Complications have previously been reported to be higher, probably reflecting general improvement of performance of modern surgery in recent years [18,19]. However, our results clearly demonstrate an increase in the need for post-operative blood transfusions in the BN group caused by surgical bleeding. BN patients are also in...
Bilateral nephrectomy and post-transplant hypertension need of a significantly longer hospitalization after transplantation.

We conclude that BN performed at the time of renal transplantation did not have a significant influence on the need for antihypertensive therapy following renal transplantation. Considering the higher complication rate, extra use of resources and the inconvenience for the patient, BN should only be performed on selected hypertensive patients, preferably in a randomized prospective protocol.

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References

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