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Early postoperative renal function following renal transplantation surgery: effect of anesthetic technique

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Abstract
Purpose. The use of continuous epidural anesthesia in patients with chronic renal failure is rare and controversial. In this study, we compared the effects of epidural versus general anesthesia on early postoperative renal function in patients who underwent renal transplantation surgery.
Methods. Sixty-eight adult patients were prospectively randomized to two groups. Group 1 (*n-37*) received epidural anesthesia with bupivacaine and fentanyl, and group 2 (*n-31*) received general anesthesia with nitrous oxide and isoflurane. The patients' renal function was compared both with qualitative scintigraphic analysis (kidney perfusion, concentration, and excretion capabilities) and biochemically [serum sodium, potassium, creatinine, and blood urea nitrogen) (BUN)] within the first postoperative week.
Results. Patient demographics were similar in the two groups, and the scintigraphic and biochemical evaluations were also comparable. The time of the first appearance of Tc-99m diethylene triamine pentaacetic acid (DTPA) was within normal limits in 75.7% of patients in group 1 and 61.3% of those in group 2. The number of patients with normal peak/background activity and 20 min/peak activity were 15 (40.5%) and 19 (51.4%), respectively, in group 1, and 12 (38.7%) and 15 (48.4%) in group 2 ($P > 0.05$ for both). The levels of serum creatinine and urea in both groups decreased within days postsurgery compared with preoperative levels ($P < 0.05$), but the changes were similar in the two groups ($P > 0.05$). A similar number of patients in both groups were treated for acute rejection ($P > 0.05$).
Conclusion. Our results demonstrate the safe use of both anesthetic techniques in renal transplantation surgery.

Key words Renal transplantation · Anesthetic technique · Postoperative renal function.

Introduction

Patients undergoing renal transplantion present many challenges for the anesthesiologists [1]. Appropriate anesthesia for this procedure has minimal toxicity for the patient and the graft, in addition to providing sufficient pain relief and maintaining renal functions [2]. The use of continuous epidural anesthesia in patients with chronic renal failure is controversial. The method has been used, though rarely, since 1990. After having applied general anesthesia for more than 900 transplantations at our institution since 1985, in the past 3 years we have adopted, and now prefer to use, continuous epidural anesthesia for these procedures [3]. In this prospective study, we compared general and epidural anesthesia with respect to early postoperative renal function in renal transplant recipients randomly assigned to either treatment.

Methods

After approval of the ethics committee and informed consent of the patients had been obtained, adult patients (ASA 3) scheduled for renal transplantation surgery were randomly allocated to two groups. Patients in group 1 had epidural anesthesia and those in group 2 (control group) underwent general anesthesia. All patients had normal prothrombin times, and all had undergone unheparinized hemodialysis in their last several sessions. Prior to surgery, patients in the two groups were given oral diazepam (10 mg) and famotidine (40 mg) for premedication. Intraoperative monitoring was performed by ECG, measurement of heart rate, noninvasive measurement of blood pressure, and pulse oximetry. Central venous pressure was not monitored. Patients were administered 0.9% saline solution at a rate of 5–7 $mg \cdot kg^{-1} \cdot h^{-1}$ for maintenance and dopamine infusion at a rate of 2 $\mu g \cdot kg^{-1} \cdot min$ (renal

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dose) throughout surgery. In both groups, patients were given intravenous methylprednisolone and antibiotics at induction of anesthesia, and all received intravenous mannitol ($0.5\,g\cdot kg^{-1}$) and furosemide ($1\,mg\cdot kg^{-1}$) during vascular anastomoses. In group 1 (epidural, $n = 37$), standard epidural anesthesia was performed in all patients with the use of a 16G Tuohy needle from the L1–2 or T12–L1 interspace, and they were given 0.5% bupivacaine 20 ml with fentanyl 50 μg. At 2 hs after the first epidural injection, a 10-ml bolus of 0.5% bupivacaine was routinely added, and a $7\,ml\cdot h^{-1}$ infusion of 0.25% bupivacaine was continued until the end of surgery. Intraoperatively, all patients were sedated to a level of "eyes closed, responding to verbal stimulus" with intravenous midazolam as needed. The patients were monitored for neurologic signs related to bleeding or hematoma during the postoperative period. The catheter was removed on postoperative day 3, at latest. In group 2 (control, $n = 31$), anesthesia was induced with thiopenthal $5–8\,mg\cdot kg^{-1}$, and fentanyl $1–2\,\mu g\cdot kg^{-1}$. The trachea was intubated with vecuronium $0.1\,mg\cdot kg^{-1}$, and anesthesia was maintained with isoflurane 0.7%–1% in oxygen and nitrous oxide (50%). Postoperative pain control was provided with patient control epidural analgesia (PCEA) by morphine in group 1 and with intramuscular injection of meperidine in group 2. All patients received a standard immunosupressive protocol postoperatively, starting with initial doses of cyclosporine A ($8\,mg\cdot kg^{-1}$), prednisolone ($1.5\,mg\cdot kg^{-1}$) and azothioprine ($2–3\,mg\cdot kg^{-1}$) and followed by appropriate dose adjustments.

Postoperative renal function in the two groups was compared based on the qualitative scintigraphic analysis performed on the postoperative fifth day and the biochemical findings obtained during the postoperative first 5 days. For scintigraphic evaluation, a large-field-of-view gamma camera with a low-energy, all-purpose collimator was used. Radionuclide imaging included evaluation of both the perfusion and the parenchymal phases. After bolus intravenous injection of 340 MBq Tc-99m diethylene triamine pentaacetic acid (DTPA), images were acquired in 1-s frames for 1 min. Time–activity curves were generated from the region of interest, which included the renal cortex and part of the iliac artery. Kidney perfusion was evaluated visually by determining the time the activity first appeared in the kidney and iliac artery (normal value <5 s). For the parenchymal phase, data were acquired in 30-s frames for 20 min. Time–activity curves were generated from the equal-sized regions of interest, which included the whole kidney and background. The concentration of the kidney was measured by the ratio of peak kidney activity to background activity (normal >3), and the excretion was measured by the percentage of peak kidney activity retained at 20 min (R_{20}, normal 60%). Recipients were scored qualitatively as "good" for normal values and "altered" for below-normal values.

The biochemical assessment was based on the levels of serum sodium, potassium, creatinine (Cr), blood urea nitrogen (BUN), and urine volume measured at six time intervals: preoperatively, and on days 1 to 5 postoperatively. We also recorded the number of patients in each group who were treated for acute rejection.

The results are expressed as means ± SD. Data were analyzed using the independent Student's *t*-test, Mann-Whitney U test, and chi-square test between groups and the dependent *t*-test for studies of measurements within groups. We accepted $P < 0.05$ as indicating statistical significance.

Results

The recipients' demographic characteristics are shown in Table 1. In the group receiving epidural anesthesia, the average dose of midazolam used for intraoperative sedation was 7.77 ± 4.56 mg. There were no significant changes in hemodynamic variables either within groups or between groups. The total mean intraoperative systolic blood pressure was 120 ± 22 mmHg in group 1 and 142 ± 13 mmHg in group 2. There were no hypotensive episodes or requirements for vasoactive drugs to control blood pressure in either group, and there were no pharmacological, technical, or neurological complications.

Scintigraphic evaluation showed no significant differences between the groups with regard to the time of first appearance of Tc-99m DTPA, ratio of peak to background activity, and ratio of 20-min to peak activity (Fig. 1). A full of 75.7% of patients in group 1 and 61.3% in group 2 had normal values for the first appearance of Tc-99m DTPA on postoperative day 5 ($P = 0.549$, $P > 0.05$). The ratio of peak to background activity was good in 51.4% and 48.4% of patients in the groups 1 and 2 ($P = 0.752$, $P > 0.05$), respectively, and

Table 1. Patient demographics in the two groups[a]

Characteristic	Group 1 (epidural)	Group 2 (general)
N	37	31
Age (yr)	29.3 ± 1.6	31.5 ± 2.4
Sex (M/F)	26/11	23/8
Weight (kg)	59.5 ± 1.6	59.9 ± 2.3
Duration of CRF (mo)	30.6 ± 4.2	29.6 ± 4.6
Duration of HD (mo)	19.9 ± 3.2	16.1 ± 2.3
Source of organs (cadaveric/living-related)	14/23	11/20

[a] Plus-minus values are means ± SD. CRF, Chronic renal failure; HD, hemodialysis. $P > 0.05$ for all characteristics

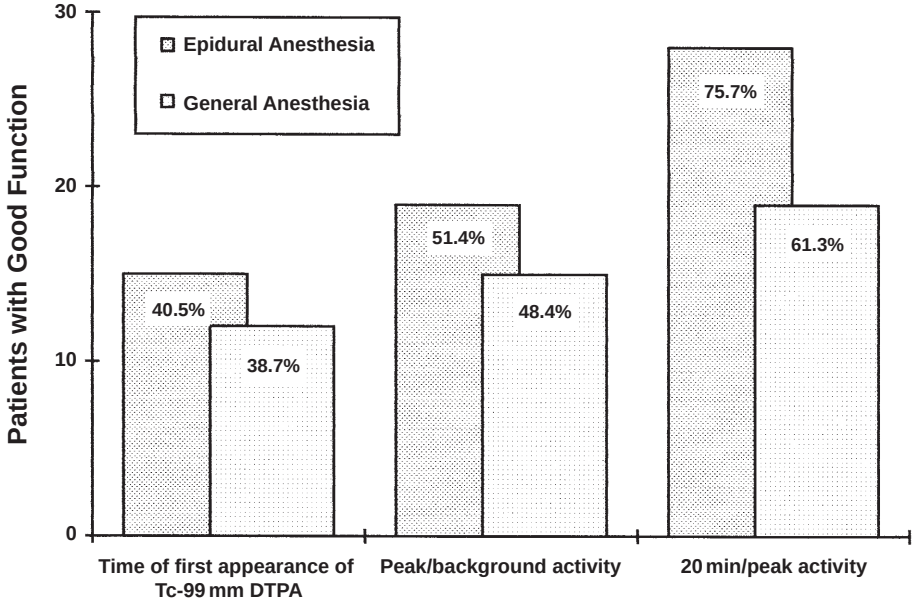

Fig. 1. Scintigraphic evaluation of the patients with good renal function in the two groups on the fifth day posttransplantation ($P > 0.05$)

Table 2. Biochemical evaluation of the renal function in the two groups (mean ± SD)

Measurement	Anesthesia	Preoperative	Day 1	Day 2	Day 3	Day 4	Day 5
Urine output (ml)	Epidural		5006 ± 3600	3436 ± 2719	3772 ± 2655	3751 ± 2438	3344 ± 1718
	General		5460 ± 3026	4354 ± 2895	4088 ± 2331	4247 ± 2309	4198 ± 2237
Specific gravity	Epidural		1006 ± 2	1006 ± 3	1007 ± 3	1007 ± 3	1007 ± 3
	General		1006 ± 2	1007 ± 2	1006 ± 2	1006 ± 2	1006 ± 2
Sodium ($mEq \cdot l^{-1}$)	Epidural	137.9 ± 0.6	135.9 ± 0.8	133.4 ± 0.8	134.1 ± 0.9	133.5 ± 0.9	133.9 ± 0.8
	General	138.5 ± 0.7	135.4 ± 0.7	135.5 ± 0.9	135.7 ± 0.9	134.6 ± 0.8	134.1 ± 1.1
Potassium ($mEq \cdot l^{-1}$)	Epidural	5.2 ± 0.1	4.5 ± 0.1	4.3 ± 0.1	4.3 ± 0.2	4.5 ± 0.2	4.6 ± 0.1
	General	5.0 ± 0.1	4.3 ± 0.2	4.1 ± 0.1	4.3 ± 0.1	4.3 ± 0.1	5.0 ± 0.1
Blood urea nitrogen (BUN) ($mg \cdot dl^{-1}$)	Epidural	59.2 ± 3.1	47.1 ± 2.9	47.7 ± 3.6	48.3 ± 3.9	50.6 ± 4.1	53.1 ± 4.9
	General	61.9 ± 3.1	41.9 ± 3.4	43.5 ± 4.1	45.6 ± 4.7	45.6 ± 4.8	45.8 ± 4.9
Creatinine ($mg \cdot dl^{-1}$)	Epidural	7.7 ± 0.5	5.1 ± 0.4*	4.2 ± 0.4*	3.9 ± 0.5*	3.6 ± 0.4*	3.4 ± 0.5*
	General	7.7 ± 0.4	4.1 ± 0.5*	3.9 ± 0.5*	3.6 ± 0.5*	3.3 ± 0.5*	3.1 ± 0.5*

* $P < 0.05$ compared with both preoperative and previous measurements

the ratio of 20-min to peak activity was good in 40.5% and 38.7%, respectively ($P = 0.767$, $P > 0.05$). Serum sodium, potassium, and BUN levels remained similar over time and did not differ between the groups. Serum creatinine levels decreased with time in both groups ($P < 0.05$), but the difference between the groups was not significant (Table 2). Six patients in each group (19% of group 1 and 16% of group 2) were treated for acute allograft rejection.

Discussion

In this study we wanted to compare the early postoperative renal effects of epidural versus general anesthesia used for renal transplantation. It is well documented that anesthesia affects renal function indirectly as well as directly [4,5]. Indirectly, the effects on hemodynamics, sympathetic activity, and humoral regulation can hamper renal function via mechanisms of lowered blood pressure and cardiac output, increased sympathetic outflow (renal nerve stimulation and increased plasma catecholamines), and increased release of renin, angiotensin, and vasopressin. Although we did not measure the hormonal status of our patients while they were under surgical stress, and there were no differences in respect to intraoperative hemodynamic variables, the knowledge that regional anesthesia attenuates stress response better than general anesthesia initiated our focus on the use of epidural anesthesia.

Patients with renal disease who are subjected to anesthesia and surgery are at risk of further deterioration in

renal function and of developing acute tubular necrosis. Optimal fluid loading and careful selection of anesthetic techniques and agents, appropriate monitoring, and the use of mannitol and dopamine assist in the maintenance of renal blood flow and help preserve renal function in these patients. In our study we did not monitor patients' central venous pressure and volume status, but we routinely used mannitol and steroids intraoperatively. We observed urine output postoperatively as an indicator of renal function, intravascular volume status, and fluid balance. Perioperatively we encountered no requirements for vasoactive drugs to control blood pressure, and postoperatively the urine volume did not differ between the two groups.

The use of continuous epidural anesthesia in renal transplant recipients increased during the 1990s but is still rare. One barrier to widespread use was the belief that the tendency to uremic bleeding combined with the residual effects of the heparin given during dialysis might lead to hemorrhagic complications [1]. However, reports have shown that these techniques may be safely used in patients with various forms of coagulopathy who would most certainly benefit from regional anesthetic and/or analgesic techniques [6]. All patients in our study underwent thorough system analysis. None had shown preoperative laboratory abnormalities that might indicate bleeding diathesis, apart from high BUN levels. Prothrombin times were normal in all cases, and all patients had undergone nonheparinized hemodialysis in their last several sessions. In each patient, well-trained anesthetists performed atraumatic placement of epidural catheters. We followed the patients clinically in the postoperative period with daily neurological examinations and found no complications related to bleeding tendency.

The literature search produced very few studies related to epidural anesthesia for renal transplantation surgery. We did not compare the postoperative complications related to anesthetic technique. However, there is nothing intrinsic to renal transplantation surgery to indicate that regional anesthesia causes fewer complications and less morbidity than general anesthesia. Murakami et al. [7] showed that epidural analgesia better inhibited cardiovascular fluctuations during surgical stress. Hammouda et al. [8] used bupivacaine in renal transplant recipients and found no higher plasma concentrations. Solonynko et al. [2] found that continuous epidural anesthesia was the preferable method because of its lower toxicity and significantly lower number of postoperative complications.

We found no significant differences between patients with epidural anesthesia and controls in respect to the scintigraphic evaluation of renal function on the fifth day post-transplantation. Functional capabilities were shown to be similar between groups. Scintigraphically demonstrated function of the kidneys was not expected to fully recover at the fifth day after surgery. This was expected to be the normal trend, since these capabilities improve at later stages following renal transplantation. Further, this adaptation and recovery period is longer for cadaveric grafts. The proportion of cadaveric to live donor grafts as organ sources was similar between groups, which may explain why the percentage of "altered" functioning kidneys in both groups was similar, as well. The scintigraphic findings mostly reflect the glomerular function in the graft, whereas the specific gravity of urine and the concentration capability are functions of tubular activity. The only study investigating the effects of anesthesia on scintigraphic evaluation was an experimental study that demonstrated the distinct influence of general anesthetics on reference values [9]. However, to date, no one has assessed the effects of regional anesthesia on renal scintigraphic evaluation in renal transplantation cases.

Serum biochemistry followed for 5 days postoperatively revealed no significant differences between the groups. Serum sodium, potassium, and BUN levels were always within normal limits. The high serum creatinine levels measured preoperatively in both groups decreased significantly as the days passed, due to the good function of the transplanted kidney.

The 1-, 3-, and 5-year patient and graft survival rates in renal transplantation surgery done under general anesthesia in our center have already been reported [10,11]. However we do not yet have adequate data to accurately calculate mortality rates and incidences of acute or chronic rejection associated with renal transplantation surgery performed under epidural anesthesia, nor can we accurately compare such figures for the anesthetic techniques. The reasons that accurate figures are not yet available are that not all patients in the epidural anesthesia group have reached their 1-year postoperative mark, and that our total numbers are currently insufficient.

In conclusion, comparing epidural and general anesthesia in renal transplantation surgery, we found that the two techniques were similar with respect to good and/or early graft function in the postoperative period. Our preliminary results are encouraging with regard to safe and more frequent use of epidural anesthesia in renal transplantation surgery.

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