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The Influence of Targeting Central Venous Pressure (CVP) on Early Graft Function after Living Donor Kidney Transplantation

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Abstract

Introduction: Early graft function is very important and can be achieved with an adequate intraopeartive perfusion characteristics of the graft and urine output. The goal of this study was to examine the influence of targeting CVP on early graft function.

Material and methods: After approval of Ethical committee of the Medical Faculty-Skopje we obtained inform consent of 60 patients ASA 2 - 3 undergoing renal transplantation of living-related person in the Clinic of Urology-Skopje. A prospective clinical study which was performed in the period of 2 years. They were divided in 2 groups of thirty patients: group A receiving normal saline intraoperativly targeting for CVP 15 mmHg until vascular clamps were off and group B receiving normal saline 10 ml/kg/h. We recorded onset of diuresis and total urine output from unclamping the renal vessels to the end of the surgery in both groups and postoperative serum, urine creatinin and FENa % in 3 times (3,12,36 hours).

Results: The onset of diuresis in seconds was insignificantly longer in group B $p > 0.05$ ($p = 0.31$) we didn't find any statistical differences in postoperative serum creatinin in both groups.

Conclusion: Our study didn't show any benefit from targeting CVP to 15 mmHg. We couldn't find any significant differences on onset of diuresis and urine output after the unclamping the vessels.

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Introduction

Kidney transplantation is the best choice for patients in end-stage renal disease (ERSD). It becomes a routine intervention nowadays. Early graft function is very important and it's always a good predictor of the survival of the graft in the new environment and it can be achieved with adequate intraoperative perfusion. Early graft malfunction has been associated with decreased graft survival and increased recipient complication[1-5]. A lot of studies have examined specific value of the perioperative central venous pressure (CVP) that may reduce the risk of postoperative graft failure[7-10]. Intra-operative volume expansion is associated with increased renal blood flow and an improvement in immediate graft function[12,13]. Immediate function is associated with increased graft survival and lower patient mortality[13-16]. It is well known that the most important measure to improve immediate graft function is to maintain an adequate intravascular volume.

To our knowledge, no published studies have validated the relationship between time course of volume expansion and the period of renal ischemia and beside the recommendation for CVP values, we still don't have an answer for exact recommended value of CVP. Recommendations for the intraopertive hydration are not clear[8,13,16]. Although this recommendations have wide range of CVP between 7 - 17 mmHg and mean arterial pressure of 80 - 90 mmHg[8,16,17]. Volume expansion is associated with better graft flow and early graft function[16-19]. Previous studies have examined specific values of perioperative central

venous (CVP) that may reduce the risk of postoperative graft failure. In the postoperative period the biochemical parameters are still most important measurement for evaluation of recovery of the graft in new environment. This led for need of protocols regarding intraoperative management and hydration during the intraoperative. The goal of this study was to examine the influence of targeting CVP of 15 mmHg on onset of duresis and biochemical parameters in early postoperative period.

Methods

After approval of Ethical committee of the Medical Faculty-Skopje we obtained inform consent of 60 patients undergoing renal transplantation of living-related person in the Clinic of Urology-Skopje. A prospective clinical study which was performed in the period of 2 years. They were divided in 2 groups: group A receiving normal saline intraoperativly targeting for CVP 15 mmHg until vascular clamps were off and group B receiving normal saline 10 ml/kg/h. The exclusion criteria were: severe left ventricular impairment, cardiomiopathy with ejection fraction bellow 50%, problem with coagulation, excessive bleeding during the operation, resistant graft arterial spasm or any other surgical difficulty.

All transplantations in this study were performed by the same surgical team. All patients underwent full medical and surgical history, and routine laboratory investigations (i.e., blood Hb, plasma proteins, coagulation status, serum electrolytes, blood glucose, lactate, arterial blood gases, chest radiograph, and echocardiography). All patients underwent preoperative hemodialysis 24 hours before renal transplant surgery.

Protocol for anesthesia

Standard monitoring ECG in 5 leads, noninvasive blood pressure and pulse oximetry before the induction were recorded. Before the induction the epidural catheter was inserted on level L2-L3 or L3-L4 and it was given a test dose of bupivacain 10 mg. We didn't use the epidural catheter until the end of surgery. At the end of the intervention we gave 100 mcg fentanyl and 20 mg of bupivacain in volume of 10 ml to avoid any interference with intraoperative hemodynamics. For induction we used remifentanyl in dose 0.5 mcg/kg and propofol 2 mg/kg and the intubation is facilitated with dose of atrcurium 0.5 mg/kg and maintaining of anesthesia was with remifentanyl 0.25 mcg/kg and propofol 0.5 - 1 mg/kg depending on depth of anesthesia which was recorded with entropy electrodes. Patients were ventilated with mixed oxygen/air 50 - 50% with tidal volume of 7 - 9 ml/kg and end-tidal CO_2 between 35 - 40 mmHg (Datex-Ohmeda Avance S-5). After the induction central venous catheter aseptically was placed in the internal jugular vein and pressure was transdused and recorded. For measuring invasive arterial pressure an arterial catheter was placed in a radial is and it was recorded. We noted the time of urine onset (sec) and the total amount of diuresis in ml until end of the surgery. In postoperative period we measured the total urine output (ml), the level of plasma and urine creatinine (mmol/L) and fraction excretion of sodium in 3 times -3.12 and 36 hours after the surgery.

Statistical analysis

Statistical analysis was performed with SPSS (version 9.0 for Windows, SPSS, Chicago, IL). Continuous data are described as mean ± SD and categorical variables are given as percentages. All data were tested for normality using the method of Kolmogorov-Smirnov. Intergroup differences in demographic, perioperative hemodynamic values, and laboratory values were compared using unpaired Student *t*-test. Mann-Whitney *U*- test was used for unpaired nonparametric data, including the volume of crystalloid infused, urine output, and the onset of diuresis. Percentages were compared by X^2 contingency analysis. $P < 0.05$ was considered to be significant. Mean group differences and their 95% confidence intervals were calculated to determine which of the specific variables differed between groups. If the 95% confidence interval includes 0, it indicates no significant difference between groups.

Results

All the patients underwent for hemodialysis 24 hours before surgery except 4 patients in group A who had not required hemodialysis and 2 patients in group B. Mean arterial preoperative blood Hb and serum creatinine were similar in both groups. Average Hb in group A was 116.73 ± 19.07 and for group B was 112.93 ± 17.19. Average creatinine for group A was 632.63 ± 187.00 and for group B 556.52 ± 164.14. The demographic and operative data are shown in table 1.

Table 1: Demographic and operative data of both groups.

	Group A	Group B
Age(years)	37.87 ± 9.32	41.47 ± 10.25
Sex F/M	15/15	17/13
Body weight kg	74.17 ± 10.92	70.83 ± 11.83
Duration of surgery(min)	236.67 ± 40.33	250.83 ± 61.65
Cold ischemia(min)	210.10 ± 33.98	221.43 ± 35.62
Warm ischemia(sec)	170.30 ± 39.34	184.20 ± 38.13
Months on hemodialysis	12.17 ± 13.32	17.95 ± 31.71
Comorbidites		
1. None	11	16
2. hipertension	16	11
3. Hypertension and diabetes melitus	3	3

Values are mean ± sd; group A is CVP 15 target group, group B constant infusion group

The onset of diuresis and urine output at the end of the surgery showed no statistical differences between the groups but in 5 patients in control group we didn't achieve urine output at the end of the surgery (Table 2)

Table 2: The onset of diuresis and urine output at the end of the surgery.

Parameter	Rank Sum Group A	Rank Sum Group B	U	Z	p-level	Valid N Group A	Valid N Group B
Urine output	829.50	710.50	364.50	-0.18	0.86	30	25
Onset of diuresis (sec)	780.00	760.00	315.00	-1.01	0.31	30	25

The creatinine levels in serum (mmol/L) in postoperative period for both groups in 3.12 and 36 hours are showed in (the Table 3). Between average values of serum creatinin in relation between 3.12 and 36 hours for $p > 0.05$ we didn't find any statistical differences

Table 3: Serum cretinin (mmol/L) in 3.12 and 36 hours after the surgery.

	group	R1	{1} 454.69	{2} 352.84	{3} 220.64	{4} 456.87	{5} 352.88	[6} 238.68
1.	A	Creatinin/3h		0.000	0.000	0.97	0.009	0.000
2.	A	Creatinin /12h	0.000		0.000	0.008	0.99	0.004
3.	A	Creatin /36h	0.000	0.000		0.000	0.000	0.77
4.	B	Creatinin/3h	0.97	0.008	0.000		0.000	0.000
5.	B	Creatinin /12h	0.009	0.99	0.0009	0.000		0.000
6.	B	Creatin /36h	0.000	0.004	0.77	0.000	0.000	

The creatinine levels in urine (mmol/L) in postoperative period for both groups in 3.12 and 36 hours are showed in (the Table 4). Between average values of urine creatinin in relation between 3.12 and 36 hours for $p > 0.05$ we didn't find any statistical differences.

Table 4: urine cretinin (mmol/L) in 3.12 and 36 hours after the surgery.

	group	R1	{1} 18.14	{2} 17.92	{3} 24.82	{4} 9.29	{5} 15.46	[6} 18.48
1.	A	Creat/3h/urine		0.96	0.14	0.17	0.61	0.95
2.	A	Creat /12h/urine	0.96		0.13	0.10	0.70	0.92
3.	A	Creat /36h/urine	0.14	0.13		0.003	0.08	0.33
4.	B	Creat/3h/urine	0.17	0.10	0.003		0.17	0.04
5.	B	Creat /12h/urine	0.61	0.70	0.08	0.17		0.50
6.	B	Creat /36h/urine	0.95	0.92	0.33	0.04	0.50	

The fraction extraction of sodium in percentage (FENa %) in postoperative period for both groups in 3.12 and 36 hours are showed in (the Table 5). Between average values of FENa % in relation between 3.12 and 36 hours for $p > 0.05$ we didn't find any statistical differences.

Table 5: urine cretinin (mmol/L) in 3.12 and 36 hours after the surgery.

	group	R1	{1}	{2}	{3}	{4}	{5}	[6}
1.	A	FENa %/3h		0.004	0.000	0.85	0.003	0.000
2.	A	FENa %/12h	0.004		0.10	0.06	0.56	0.059
3.	A	FENa %/36h	0.000	0.10		0.002	0.66	0.63
4.	B	FENa %/3h	0.85	0.06	0.002		0.0004	0.0000
5.	B	FENa %/12h	0.003	0.56	0.66	0.0004		0.15
6.	B	FENa %/36h	0.000	0.06	0.63	0.000	0.15	

Discussion

Many studies suggest that during kidney transplantation the systolic and diastolic should be higher than 120/85 mmHg. They also suggest that the MAP should be higher than 95 mmHg and CVP above 10 mmHg[10-16]. These values are favorable to ensure maximal filling pressure of the graft and its fast recovery. Prolonged arterial hypotension can led to graft hypoperfusion and after that to prolonged time for graft recovery and delay graft function[17-19]. In both groups we didn't had any episode of hypotension and there was no need for vasopresors. Intraoperative volume expansion is associated with increased renal blood flow and better immediate graft function[15,16]. Early graft malfunction has been associated with decreased graft survival and increased recipient complication[12]. Earlier at al showed that maximal hydration during anesthesia up to 100 ml/kg and 30 ml/kg/h and CVP 10 - 17 were associated with improved early graft function[8].

Many of the clinical trials showed that that regimen targeting CVP before cross-clamp of the donor kidney provides a more favorable outcome[10,15,17]. They showed that high hydration regime provides more turgid graft and faster onset of diuresis. The time of surgery, cold ischemia and warm ischemia were similar in both groups. Our study didn't show any benefit from targeting CVP to 15 mmHg. We couldn't find any significant differences on onset of diuresis and urine output after the unclamping the vessels. In 5 patients in control group we didn't achieved a urine output at the end of the surgery. Decreased value of serum creatinine in postoperative period is good sign of fast recovery of the graft. In our study 36hours after the transplantation 9 patients in group A had normal values of serum cratinine and 6 patients in group B. The average values of serum cratinine for group A was 220.64 ± 158.10 and 238.68 ± 131.50 for group B In postoperative biochemical parameters we had no statistical

difference between the average values of cratinine in serum and in urine. After renal transplantation low urinary sodium concentration (UNa) has been used to diagnose acute rejection (AR), for the early phase of AR is often associated with reduced renal perfusion. Early postoperative graft failure without low UN favors the diagnosis of ischemic tubular damage (ATN). With fraction extraction of the sodium we can make a distinction between prerenal and renal failure of the kidney in new environment. In our study in both groups in time 3 hours after surgery only 3.33% of the patients had prerenal failure. In 12 hours after surgery in group A we had only 1 patient but in group B 4 patients (13.33%) with prerenal failure. In the postoperative period the hydration regime is based in iso balance administration of normal saline. This opens a dilemma regarding the intraoperative hydration regime and how it can influence the postoperative recovery of the kidney. Drops in FENa % should be interpreted in conjunction with state of fluid balance, particularly in the early diuretic phase.

Conclusion

This study shows that there isn't any statistical difference between the groups however in group B we had 5 patients with no diuresis at the end of the surgery. Our study didn't show any benefit of targeting CVP. This study has limitations. We only evaluated onset of the diuresis and have not considered whether there are long-term benefits. There is need for larger study to confirm if there is true benefit (improved long-term outcomes).

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