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Role of Intraoperative Hemodynamic Factors with Respect to Graft Functioning in Renal Transplant Recipients and Current Trends in Perioperative Hemodynamic Management

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Abstract

Introduction

Chronic Kidney Disease (CKD) was ranked 18th commonest causes of mortality worldwide in 2010. Renal transplantation as Renal Replacement gives better quality of life, cost effective and possibly prolonged survival .Optimized perioperative hemodynamic management leads to prevention of delayed graft function, this retrospective study was aimed to observe the various intraoperative hemodynamic characteristics with respect to graft functional outcome.

Material and Methods: *This retrospective study contained 50 consecutive patients who underwent live Renal transplantation in a tertiary Institute. patients were divided into two groups for purpose of analysis based on a CVP and MAP values at time of declamping of vessels. Both these were analyzed with respect to the fall in creatinine trend was analyzed in the first 7 postoperative days.*

Results: *On comparing the trends in fall of creatinine levels upto 7th post-operative day, was found to be stastically insignificant when compared to CVP & MAP groups respectively.*

Conclusion: *Traditional CVP & MAP guided management although continues to be still relevant and commonly practiced in evolving centres but in light of improved understanding of this subject and indivisualized needs , a more evidence based approach catering to patient's physiological needs and assessment of responsiveness would be constructive.*

Abbreviations: *CKD – Chronic Kidney Disease , DGF - Delayed graft function , CVP -Central Venous Pressure , MAP - mean arterial pressure , PEEP - Positive end-expiratory pressure , POD – Post operative Day , ATN – Acute Tubular Necrosis , PCA - pulse contour analysis.*

Keywords: *Renal Transplantation, Graft function, Central venous pressure, Mean arterial pressure, serum creatinine, hemodynamic management*

1. INTRODUCTION

According the 2010 Global Burden of Disease study, Chronic Kidney Disease (CKD)was the 18th most common cause of mortality worldwide affecting 10% of population and approximately 10 million people are dialysis dependant.[1,2] Of this only around 10 % of population gets access to Renal Replacement modalities like Dialysis, transplantation.[3]

Renal transplantation as Renal Replacement gives a better quality of life, cost effective and possibly prolonged survival. [4]. A Delayed graft function (DGF) has been related to decreased graft survival, poor long term function and also high chance of acute rejection. The need of the hour is proper preoperative hemodynamic management leading to prevention of complications like graft rejection. These factors prompted us to study the early graft function characteristics with respect to intraopertive hemodynamics considering these being an important preoperative means to improve early graft function, by preserving an adequate intravascular volume [5, 6]

Breakthrough of better Preoperative management techniques, Medically composite patients like geriatric patients and having multiple co-morbidities are being taken up for

renal transplantation. The intra-operative Central Venous Pressure (CVP) should be maintained between 10 to 15 mmHg which is being invariably recommended Anaesthesiological management. [5, 6] This results in increased renal blood flow and improved graft perfusion & function. [7] However, some writers did argue this traditional practise. [8] Therefore, this retrospective study was aimed to observe the various intraoperative hemodynamic characteristics namely CVP and mean arterial pressure (MAP) and its relation to graft functional outcome.

2. Material And Methods

This was a retrospective study done at J.S.S. Medical college and Hospital, Mysore from January 2016 to January 2019 wherein 50 consecutive patients who underwent live related donors renal transplant were evaluated. All transplants were done by a team of experienced urologists comprising two surgeons with similar experience and one senior urologist & same team of anesthesiologists supervised by a senior Anaesthesist. The study was done after informed consent and Hospital Ethical committee approval.

The data was collected from the Medical records of the hospital which includes the demographics, indications of renal transplant, blood parameters like Complete blood count, renal function tests. All other information was obtained from medical & anesthesia charts, including intra-operative monitoring chart. As a protocol transplant recipients underwent hemodialysis 24-48 hours before surgery. Intra-operative cardiac monitoring, vitals, CVP, urine output, core temperature, pulse oxymetry and were observed and documented. Invasive arterial blood pressure monitoring was done in all the patients.

Anesthesia was administered using a standard protocol in all patients comprising of injection Propofol 2mg/kg, fentanyl 2 µg/kg, muscle relaxation was achieved with atracurium 0.5 mg/kg and maintaining with oxygen/ air/ isoflurane @ at minimum alveolar concentration of 1.2. Patient's ventilation was controlled by ventilator keeping the PEEP near to 5 mmHg. Core body temperature was maintained to around 36°C. Central Venous line was placed and fluid administration was done according to CVP which was recorded periodically stressing the time of arterial declamping.

Once the vessels were declamped, it is practiced to maintain CVP between 12-15 mmHg & MAP is usually kept above 65 mmHg. . Both CVP and MAP were documented at the time of decalmping. In the postoperative period strict input output monitoring was done and fluid balance was regulated. All the patients underwent daily serum creatinine levels, serum electrolytes, hemogram and input-output charting. The data collected up to 7th Post operative day.

We divided patients into two groups for purpose of analysis based on a CVP (baseline 12mmHg) and MAP values (100 mmHg) at time of declamping of vessels. Both these were analyzed with respect to the fall in creatinine trend was analyzed in the first 7 postoperative days.

2.1. Statistical Analysis

We evaluated data using version 21.0 of SPSS, USA. Correlation analysis and analysis of variance test (ANOVA) technique was used for statistical computation. Multivariate analysis was used to compare various variables.

3. Results

Table1. *Baseline characteristics of the study*

	Mean ± SD	Minimum	Maximum
Age in yrs.	40.22 ± 11.08	23	62
Weight in kgs.	58.92 ± 12.33	40	86
Hb (gm/dl)	8.84 ± 1.52	6	12.1
Haematocrit (vol %)	25.30 ± 4.55	18.2	34.9
Urea (mg/dl)	33.63 ± 16.44	18	88
Pre-op Creatinine (mg/dl)	4.20 ± 1.33	2.3	7.6
CVP (mmHg)	12.30 ± 1.98	8	16
SBP (mmHg)	154.11 ± 14.67	120	171
DBP (mmHg)	87.41 ± 10.90	70	112
MAP (mmHg)	109.67 ± 10.86	87	129
Male : Female ratio	7:2 (39 were male and 11 female)		

We evaluated 50 consecutive patients who underwent related live donor transplantation in our Institute between Jan 2016 and Jan 2019. of the 50 Transplant recipients, 11 females and 39 males. The mother donating Kidney to son comprised most common form of Transplantation pair in this study (19 recepients). The age of the renal transplant recipients in our study varied between 62 maximum to 23 years minimum with mean being 40.22 years. The Mean Haemoglobulin concentration was low at 8.84 gm/dl in our study. The Mean Pre operative levels of Blood Urea and Serum Creatinine was 33.63 and 4.20 respectively .The mean CVP and MAP at declamping were 12.30 $\pm$ 1.98 and 109.67 $\pm$ 10.86 respectively. The mean core body temperature was 36.08°C. The mean EtCO2 was 31.46 mmHg.The dry weights being 58.92 $\pm$ 12.33 Kgs.

The value of serum creatinine lowered gradually as day post surgery progressed, On comparing the trends in fall of Renal functions, we found a statistically significant fall in serum creatinine on POD1 & POD2 ($p<0.05$) on rest days upto 7 days post-surgery but the Creatinine levels drop was not seen to be stastically significant. [Table2].

Table2. *Trends in fall in serum creatinine in first seven PODs*

Allotted pair	POD	Computation of Differences					P value
					95% CI of the Difference		
		Mean	SD	SEM	Lower	Upper	
Pair 1	Creatinine 1 - Creatinine2	0.60	0.55	0.105	0.382	0.81	0.000
Pair 2	Creatinine 2- Creatinine 3	0.12	0.33	0.064	-0.002	0.26	0.054
Pair 3	Creatinine 3 - Creatinine 4	0.13	0.52	0.100	-0.073	0.34	0.196
Pair 4	Creatinine 4 - Creatinine 5	0.037	0.16	0.032	-0.02	0.10	0.265
Pair 5	Creatinine 5 - Creatinine 6	-0.092	0.58	0.11	-0.32	0.14	0.421
Pair 6	Creatinine 6 - Creatinine 7	0.096	0.59	0.11	-0.14	0.33	0.411

Patients were divided into two main groups comparing CVP values less than 12 mmHg vs CVP more than 12 mmHg at time of declamping. The serum Creatinine levels among the study subjects with CVP levels of 12 and above when compared with CVP levels of 12 and less was found to be not significant statistically on following 7 days Post transplant. The creatinine levels revealed a falling trend among the both the CVP groups on all the post operative days. [Table3].

Table3. *Serum creatinine levels as compared in the CVP <12 mmHg and CVP >12 mmHg groups*

		Sum of Squares	Mean Square	F	P value
Creatinine 1 *CVP group	Between Groups	3.736	3.736	3.735	.065
	Within Groups	25.007	1.000		
	Total	28.743			
Creatinine 2 *CVP group	Between Groups	2.516	2.516	1.847	.186
	Within Groups	34.067	1.363		
	Total	36.583			
Creatinine 3 *CVP group	Between Groups	1.958	1.958	1.077	.309
	Within Groups	45.442	1.818		
	Total	47.400			
Creatinine 4 *CVP group	Between Groups	.718	.718	.913	.348
	Within Groups	19.662	.786		
	Total	20.380			
Creatinine 5 *CVP group	Between Groups	.730	.730	.990	.329
	Within Groups	18.433	.737		
	Total	19.163			
Creatinine 6 *CVP group	Between Groups	1.946	1.946	.991	.329
	Within Groups	49.080	1.963		
	Total	51.027			
Creatinine 7 *CVP group	Between Groups	.519	.519	.712	.407
	Within Groups	18.226	.729		
	Total	18.745			

We further created groups of patients based on MAP into MAP less than 100 mmHg and MAP above 100 mmHg revealing non-significant differences in creatinine levels on consecutive 7 post op days [Table 4].

Table4. *Serum creatinine trends compared in the MAP <100 mmHg and MAP >100 mmHg groups*

		Sum of Squares	Mean Square	F	P value
Creatinine 1 *MAP group	Between Groups	.072	.072	.062	.805
	Within Groups	28.671	1.147		
	Total	28.743			
Creatinine 2 *MAP group	Between Groups	.205	.205	.141	.711
	Within Groups	36.378	1.455		
	Total	36.583			
Creatinine 3 *MAP group	Between Groups	.694	.694	.372	.548
	Within Groups	46.706	1.868		
	Total	47.400			
Creatinine 4 *MAP group	Between Groups	.259	.259	.322	.575
	Within Groups	20.121	.805		
	Total	20.380			
Creatinine 5 *MAP group	Between Groups	.031	.031	.040	.843
	Within Groups	19.132	.765		
	Total	19.163			
Creatinine 6 *MAP group	Between Groups	.440	.440	.218	.645
	Within Groups	50.586	2.023		
	Total	51.027			
Creatinine 7 *MAP group	Between Groups	.157	.157	.211	.650
	Within Groups	18.588	.744		
	Total	18.745			

4. DISCUSSION

The availability of living donor and costs are major barrier to transplantation worldwide as well as in our country, out of 1.2 billion people only 3.25 per million indivisuals undergo Renal Transplant on an average per year which is far below when compared to other counties like Spain and United States. [9] Irrespective of improved transplant techniques, DGF incidence rates varies from 4-10 %. [9]

Hence , in an implanted Kidney adjusting hemodynamic parameters suited to indivisual needs becomes necessary to achieve a favourable results .Patients with renal failure often have dyselectrolytemia and uncertain intravascular volume status [10] , resulting in a narrow margin of safety for intravenous fluid resuscitation and maintenance with either renal injury or Pulmonary edema being at either extremes. The overall anaesthetic management stresses on the fact that good perfusion to the graft post vascular declamping is possible after maintaining optimal hydration of the recipient [11] Post declamping of vessels, the accumulated vasoactive mediators during ischemia period are released invariably resulting in a decline in CVP, continuous measurement of CVP is therefore an absolute requirement to ensure good plasma volume expansion. [12]

There has always been a speculation as to whether an increased intra vascular fluid status reflected by increased CVP> 11mmHg resulted in a good graft function reinforced by the fact that chances of Acute Tubular Necrosis were directly co –related to patient's hydration status.[14,15] While others advocated this value to be between 10 to 12.[13]. In our study we took a CVP cut off of 12mmg but found it not to have any satisfactory statistical significance by keeping it above or below cut off limit as compared to drop in serum creatinine levels of the following 7 days post surgery.

Mean Arterial Pressure predicts organ perfusion and needs to be maintained above 60mmHg to

maintain perfusion to vital organs of the body , so in order to verify the significance in respect to graft functioning after we divided our patients in to groups having MAP more or less than 100mmHg but could not acknowledge any statistically significant difference compared to serum creatinine on consecutive 7 post operative days MAP values , which was in concordance with recent study by Aulukh et al who derived similar results [16] while some authors even revealed a MAP < 93mmHg was consistent with delayed graft functioning.[8] . Our average MAP was 110 & consistent efforts were aimed to maintain MAP above100 mmHg by considerate use of intravenous fluids or vasopressor support if required.

The Use of Osmotic diuretics like mannitol proven to reduce the chances of ATN [12] and are incorporated in our Institutional practise. All our transplants had an early graft functioning and no patient received postoperative dialysis.

However we had certain constraints in the study being its retrospective nature, small sample size & associated sample bias. Recent studies in this area have pointed that even though conventional parameters for hemodynamic assessment are relevant, promotes over hydration which can develop prompt vascular permeability falsely implicating need for more intravenous fluids thus indicating that these parameters may not be good predictors of fluid responsiveness. Innovative less invasive techniques to determine response to hydration, cardiac function at any given point of time like pulse contour analysis (PCA), dynamic pulse wave motion, thoracic electrical bioimpedance/ bioreactance and CO2 rebreathing can be extended in field of transplantation to guide fluid management and seems promising in future [18,19]

5. Conclusion

Based on the results of our study and scrutiny of literature we can uphold that maintaining thorough hydration in the perioperative period certainly leads to improved patient and graft outcomes. Traditional CVP & MAP guided management although continues to be still relevant and commonly practiced in evolving centres but in light of improved understanding of this subject and indivisualized needs, a more evidence based approach catering to patient's physiological needs and assessment of responsiveness would be constructive. Prospective corresponding studies would be warrented in this field to integrate the newer modalities to the current clinical practices.

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