



Anaesthesiology

EFFECT OF INTRA OPERATIVE 0.9% NORMAL SALINE VS BALANCED ELECTROLYTE SOLUTION ON IONIC AND ACID BASE STATUS IN PATIENTS WITH END STAGE RENAL DISEASE UNDERGOING LIVE RENAL TRANSPLANTATION

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ABSTRACT

Introduction Patients undergoing Renal Transplantation are subjected to a wide variety of intraoperative complications including hemodynamic instability, acid-base and electrolyte disturbances because of impaired renal function, and co-morbid diseases. Maintenance of intravascular volume during kidney transplantation is crucial to ensure optimal graft perfusion and function. **Aim** This study compared the effects of normal saline (NS) and Plasma-Lyte-A on acid-base balance and electrolytes during living donor kidney transplantation. **Methods** Patients were randomized to an NS group (n = 15) or a Plasma-Lyte-A group (n = 15). Arterial blood samples were collected for acid-base analysis after induction of anesthesia (base line), before clamp release, 1 hour after clamp release, and at the end of surgery. All samples were analyzed using a blood-gas analyzer. **Results:** In Normal saline group compared to Plasma-Lyte A there was a significant decrease in pH, bicarbonate and base excess. No patient in either group developed clinically significant metabolic acidosis. **Conclusion:** Although we found no difference in immediate graft function between the 2 groups, we concluded that using Normal saline resulted in decrease in pH and hyperchloremia. Such derangements can be prevented by using balanced crystalloids.

KEYWORDS : living donor kidney transplantation, normal saline, plasma-Lyte-A

INTRODUCTION

Patients undergoing Renal Transplantation are subjected to a wide variety of intraoperative complications including hemodynamic instability, acid-base and electrolyte disturbances because of impaired renal function, and co-morbid diseases¹. Maintenance of intravascular volume during kidney transplantation is crucial to ensure optimal graft perfusion and function². Crystalloids alone are usually sufficient to maintain volume during kidney transplantation, carry no infectious risk, and have no specific nephrotoxic effects^{3,4,5}.

Current evidence demonstrates that the use of Ringer's lactate, which contains potassium can potentially aggravate hyperkalemia in patients with impaired renal function⁶, and use of Normal saline can lead to hyperchloremia and consequently hyperchloremic acidosis^{7,8,9}. Moreover, considerable evidence suggests that infusion of hyperchloremic solutions can cause renal vasoconstriction and a consequent decrease in glomerular filtration rate^{10,11,12}. Nevertheless, Normal saline remains the most commonly used infusion solution during renal transplantation¹³.

A Balanced plasma adapted solution is a solution qualitatively and quantitatively similar to plasma. Its use avoids development of hyperchloremic acidosis, while assuring the same volume effect as unbalanced solutions, potentially reducing morbidity and mortality. They also reduce the effects on acid base balance. Mcfarlane et al, compared plasmalyte and normal saline in the intra-operative period and concluded that usage of Balanced salt solutions avoids intra operative changes in electrolytes and acid base status¹⁴.

we designed a study comparing ionic and acid base status, and hemodynamics in Living Donor Renal transplantation patients, managed with Normal saline and Plasma-Lyte A.

METHODS and METHODOLOGY:

Following approval of the Hospital Ethics Committee, written informed consent was obtained from all patients. The study was conducted at the Department of Anaesthesiology in cooperation with Department of Urology of Nizam's Institute of Medical Sciences. This prospective, randomized observational study was conducted on 30 Patients of either gender, aged between 18 -58 years, ASA III scheduled for Living Donor Kidney Transplantation.

Inclusion criteria:

- Patients with ESRD undergoing Living Donor Renal transplantation
- Age group 18 - 58 years

Exclusion Criteria:

- Diabetes mellitus
- Cadaveric kidney transplantation
- Liver dysfunction
- Severe cardiovascular disease

Post inclusion exclusion criteria: intra operative blood transfusion

Sample size was determined using the changes in bicarbonate values in Plasma-Lyte A group and saline group from the study reported by Necmiye Hadimioglu et al¹⁴.

Patients were randomized into two groups of 15 each using computer generated numbers.

- In Group NS, patients received intravenous infusion of Normal saline
- In Group PL, patients received Balanced Salt Solution, Plasma-Lyte

Patients were pre-medicated with oral Alprazolam 0.5 mg and Ranitidine 150 mg on the night before and morning of surgery. After shifting patient to operation theatre, 18 G intravenous and 20G arterial cannulation was done in all patients after local infiltration with 2% Lignocaine. Central venous catheter was inserted after induction of anaesthesia in either internal jugular or subclavian vein. Baseline pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and Systolic pressure variation were noted. Baseline arterial blood gases were done.

All patients received epidural anaesthesia at T9-T10 or T10-T11 level with the aid of a Epidural Anaesthesia set consisting of an 18 gauge epidural needle, a 20 gauge epidural catheter. Epidural catheters were fixed after advancing 5 centimeters into the epidural space.. All patients received continuous epidural infusion of 0.25 % Bupivacaine

at the rate of 6 ml/ hour throughout the duration of surgery which was continued into post-operative period up to 24 hours.

All the patients were pre-medicated with Inj Fentanyl 2mcg/ kg followed by pre-oxygenation for 3 minutes. Then Inj. Thiopentone sodium 5mg/kg was given for induction to loss of eyelash reflex. After checking adequacy of mask ventilation, Inj Atracurium 0.5mg/kg was given for muscle relaxation. Patients were manually ventilated for 3min and then intubated with appropriate size endotracheal tube. Intra-operatively patients were maintained on nitrous oxide, oxygen and isoflurane mixture. Isoflurane administration was adjusted with goal of maintaining arterial blood pressure within 20% of baseline values. Fentanyl and atracurium were administered according to patients requirements. Mechanical ventilation was done by volume controlled mode with tidal volume of 8-11ml/kg and inspiratory and expiratory ratio of 1:2. Respiratory rate was set to keep the partial pressure of carbon dioxide in the ABG within 35+/-5 mm of Hg. Forced-air warming was used to keep patients normothermic

Intra-operatively fluids were given based on the Hemodynamics and values of SPV and CVP. Systolic pressure variation (SPV) was maintained between 5- 15 and CVP was maintained from 10-15mm of Hg and CVP was monitored using a central venous catheter secured into either internal jugular or subclavian vein.

At the end of surgery patients were reversed with inj Neostigmine 0.05mg/kg and inj glycopyrrolate 0.01mg/kg. They were extubated after thorough oral suctioning and monitored in the post anaesthesia care unit.

Arterial blood samples were sent for analysis, at baseline, before clamp release, one hour after clamp release and at the end of operation for measurement of pH, PaCO₂, PaO₂, bicarbonate, Base excess, glucose, Anion gap, osmolality, serum sodium, potassium, chloride, calcium and lactate. All samples were analyzed using a blood-gas analyzer (ABL700, Radiometer, Copenhagen, Denmark). All hemodynamic variables were recorded throughout the duration of surgery for every 30 min. These include Pulse rate, Systolic blood pressure, Diastolic blood pressure, Mean arterial pressure, Systolic pressure variation and central venous pressure

Statistical Methods:

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance.

Student t-test (two-tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters.

Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. For all tests, values were considered to be statistically significant at P value: P≤0.05

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS:-

The demographic characteristics of the recipients were similar in the two groups. Both groups were hemodynamically stable and comparable. No patient received colloid or blood products.

There was a decrease in pH value towards end of surgery in both groups when compared to baseline value. In NS group, pH decreased significantly from 7.43 to 7.33. Changes in base excess corresponded to those in pH with a significant fall in base excess in the saline group, from -1.37 to -5.56. Saline infusion also resulted in a significant decrease in bicarbonate levels in NS group from 22.59 to 20.48 mmol/L.

Lactate was not significantly changed in the two groups. No group experienced significant changes in serum potassium during the surgery Other parameters were comparable in both groups.

		Base line	Before clamp release	One hour after clamp release	End of surgery
pH	Group NS	7.43±0.03	7.39±0.05	7.34±0.04*	7.33±0.04
	Group PL	7.45±0.03	7.40±0.04	7.38±0.04	7.36±0.04
HCO ₃	Group NS	22.59±2.75	21.83±2.27	20.66±1.68*	19.09±1.48*
	Group PL	23.81±2.41	23.19±2.28	22.43±2.08	21.86±2.51
SBE	Group NS	-1.37±2.88	-2.23±2.65	-3.99±1.88*	-5.56±1.81*
	Group PL	0.01±2.36	-0.91±2.50	-1.83±2.28	-2.67±2.57
K ⁺	Group NS	3.63±0.52	3.87±0.77	3.91±0.78	3.77±0.67
	Group PL	3.63±0.45	3.73±0.55	3.84±0.49	3.79±0.59
LACTATE	Group NS	0.75±0.27	0.87±0.29	0.97±0.41	1.25±0.54
	Group PL	0.79±0.21	0.92±0.42	1.04±0.46	1.34±0.60

*statistically significant

Figure 1 : Line diagram depicting comparison of pH in two groups

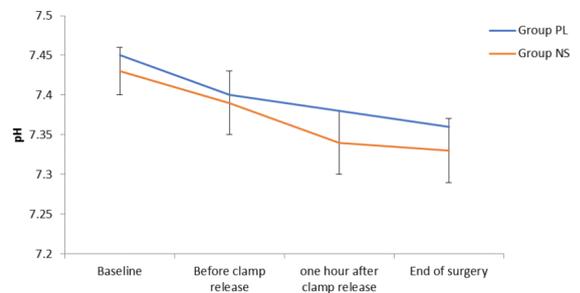


Figure 2: Line diagram depicting comparison of Bicarbonate levels in two groups

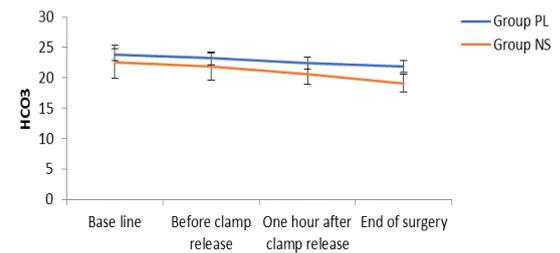


Figure 3: Line diagram depicting comparison of Base Excess levels in two groups

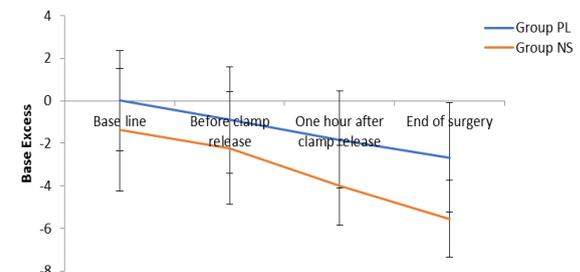


Figure 4 : Line diagram depicting comparison of lactate levels in two groups

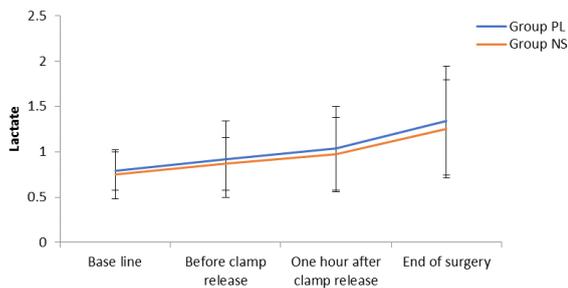
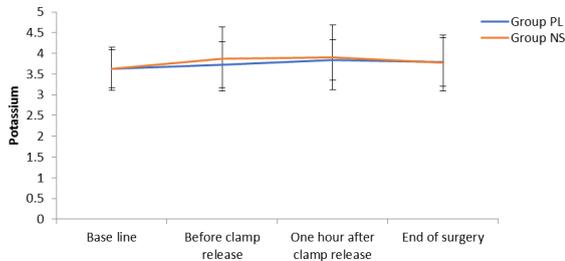


Figure 5 : Line diagram depicting comparison of potassium levels in two



DISCUSSION

The kidneys are essential for adjusting body fluid volumes, electrolyte composition, acid base balance and hemoglobin concentration. They receive about 25% of cardiac output and function as filters for toxins and drugs in the circulation.

Chronic renal failure or more appropriately chronic kidney disease (CKD) refers to a decline in the glomerular filtration rate (GFR). CKD may be categorized as mild (GFR of 60-89 mL/min/1.73m²), moderate (GFR of 30-59 mL/min/1.73 m²) and severe (GFR of 15-29 mL/min/1.73 m²), or end-stage renal disease (ESRD).

The progression of renal disease from one stage to the next results in deleterious effects on multiple organ systems. Acid-base imbalance, electrolyte disturbances and hemodynamic instability are common in patients with ESRD.

Hemodialysis or peritoneal dialysis is typically initiated as the GFR decreases to less than 15 mL/min/1.73 m². The mainstay of therapy remains for ESRD is chronic dialysis, however; a minority of patients is selected for kidney transplantation after exhaustive evaluation.

Kidney transplantation is a process of attaching new kidneys to replace previously diseased kidneys. The grafted kidney's outcome in first few days is generally measured by urine output and serum creatinine values. The most important intraoperative measure, to improve immediate graft function, is to maintain an adequate intravascular volume^{15,16}. Dawidson et al. found that 1 year graft survival decreased from 75% with immediate urine output to only 49% when onset of diuresis was delayed by 12 hours. This suggests that intra vascular volume should be aggressively expanded to promote early diuresis during anaesthesia for kidney transplantation¹⁷. The use of large volumes of fluids during the intraoperative period has typically reported improved graft function.

Normal saline still remains the standard infusion solution in many hospitals. Normal saline is significantly hypertonic and contains a very high content of chlorides hence consequently causes hyperchloremic metabolic acidosis. Administration of large volumes of potassium containing solutions, such as RL, may lead to hyperkalemia. However, with the balanced solutions being available in the market, the trend is drifting towards their use.

There are several studies comparing Normal saline with Ringer's lactate solution. There are limited studies comparing Normal saline to Ringer's lactate solution and balanced solution¹⁴. In Our study, we compared effect of Normal saline and balanced solution i.e., Plasma-Lyte A during intraoperative period on ionic and acid base status and

secondarily for effects on hemodynamics.

Our study indicates that, in Normal saline group compared to Plasma-Lyte A there was a significant decrease in pH, bicarbonate and base excess. The absence of metabolizable anions like acetate in NS explains the cause for the declining trend of bicarbonate & BE. No patient in either group developed clinically significant metabolic acidosis. Our findings are similar to the findings seen in the study done by Hadimioglu et al.

Lactate levels were also comparable between groups. The glucose levels showed increasing trend in both groups. The gluconate in Plasma-Lyte A is thought to increase glucose levels. Except in one patient, all others have blood glucose levels below 200mg/dl. Calcium levels are maintained throughout study and no patient received calcium supplementation.

An ideal crystalloid resuscitation solution would resemble the electrolyte content of Plasma. Plasma-Lyte A is a balanced salt solution having similar electrolyte constitution to that of Plasma and is not associated with the disturbance of the acid base status caused by sodium chloride based fluids.

Most anaesthesiologists avoid potassium containing fluids during renal transplantation with the belief that it may worsen hyperkalemia in case of impaired graft function. However, in the study conducted by Eva Potura and Gregor Lindner et al¹⁸. use of acetate-buffered balanced crystalloid resulted in a difference in hyperkalemia of no more than 17% when compared to use of 0.9NS and did not increase the need for postoperative dialysis. In our study, potassium level was similar between '2' groups and no patient developed clinically significant hyperkalemia.

Hypotension may occur after unclamping the iliac vessels and reperfusion of the graft. It is critical that patient is well hydrated, as renal function is critically dependent on renal perfusion. Hence to decrease the incidence of postoperative acute tubular necrosis, a liberal hydration policy is employed intraoperatively. The Lemmens et al¹⁹. suggested that Aggressive volume expansion is needed to target CVP of 10-15mmHg. This volume expansion is associated with increased renal blood flow and improved graft function.

A study by Tóth et al. showed that there was an increase in serum creatinine levels with MAP below 80 mmHg and decrease in serum creatinine with MAP above 100 mmHg, whereas it remained stable in patients with MAP of 80-100 mmHg²⁰. In our study, systolic blood pressure is maintained between 130-160 mm of Hg and CVP is maintained between 10-15 mm of Hg to optimize cardiac output and renal blood flow.

Human albumin does not improve early graft function in renal transplantation²¹.

The high potassium and calcium content of gelatins renders them inapplicable for perioperative care during renal transplantation²².

In our study, vasopressors and inotropes were not required. Immediate urine production was seen in all patients.

Limitations of this study are following: We only evaluated intraoperative benefits and It would have been interesting if data was gathered about 24-hour urine output, serum creatinine, and blood urea nitrogen concentration on 1st and 3rd postoperative days and to know early graft function. There is a lack of long-term outcome data in terms of renal function/graft function in patients receiving chloride-reduced balanced infusion solutions versus those who received Normal saline.

CONCLUSION

Crystalloids without side effects are the first choice for volume replacement in kidney transplantation. Although we found no difference in immediate graft function between the '2' groups, but in our study it was shown that using Normal saline resulted in decrease in pH and hyperchloremia. Such derangements can be prevented by using balanced crystalloids. Use of potassium containing balanced salt solutions did not cause clinically significant hyperkalemia in ESRD patients. During intraoperative period patient should be adequately hydrated for reperfusion of the graft and immediate graft function. Close monitoring of the CVP, maintaining MAP above 95 mmHg can

prevent hypotension and hence graft dysfunction. The overall anesthetic goal for the newly transplanted kidney is to prevent acidosis, maintain intravascular volume and avoid decreased perfusion to the new kidney

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