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CAN IV FLUID THERAPY ALTER RENAL FUNCTION? PILOT STUDY ON COMPARISON OF BALANCED SALT SOLUTION, RINGER LACTATE AND NORMAL SALINE

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ABSTRACT

Objective. Kidney dysfunction in patients who had intestinal perforation and were exclusively on IV fluids were compared when different IV fluids were administered. Three IV fluids were compared 0.9% Normal Saline (NS), Ringer Lactate (RL) and Balanced Salt Solution (BSS).

Material and Methods. Study was randomized double blind single centre. 50 patients were recruited in each of three limbs - NS, RL and BSS. Kidney parameters and serum electrolytes were monitored throughout the study period.

Results. In NS limb, patients received a higher chloride load and consequently their serum chloride was higher than other two groups, which as statistically significant (NS=115, RL=103 & BSS=100). The incidence of stage 2 or 3 AKI as per KDIGO stage II or III was more in NS group 8 (16%) than in RL 4 (8%) and in BSS 3 (6%).

Conclusion. This study suggests that IV fluids with physiological levels of chloride maybe better than NS in preventing Renal Injury.

KEYWORDS : Balanced Salt Solution, Kidney Dysfunction, Normal Saline, Ringer Lactate

INTRODUCTION

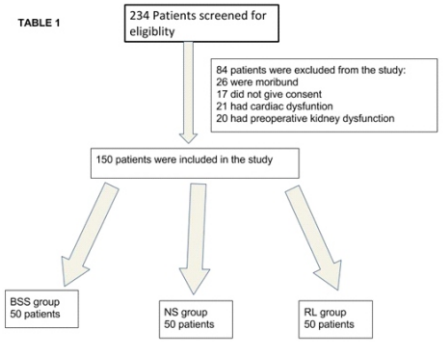
The constituents of the IV fluid administered in ICU patients who are on exclusively on IV fluids play a big role in their outcome[1]. 0.9% Normal Saline was the mainstay of IV fluid therapy of ICU patients as Ringer Lactate (RL) was pushed to the second spot due to ever present danger of Kidney Dysfunction in these patients. Then another IV fluid appeared in the market called as Balanced Salt Solution which the Pharmaceutical Industry projected as a panacea for all ills of IV fluid therapy. To the best of our knowledge and search on Pubmed did not reveal any comparative study of IV fluids and consequent kidney dysfunction of patients. This study was designed to investigate the correlation of Kidney Dysfunction and the kind of IV fluid therapy given to the patient. The patients who remain on IV fluids for longest duration are the patients of Intestinal Perforation. We hypothesized that the constituents of IV fluids would have maximum impact on the outcome of these patients as they remain nil orally and maintained on IV fluids for a mean duration of about 5 days.. Hence we compared renal outcome of patients on these three IV fluids viz., 0.9% NS, RL and BSS (with constituents of 140 mEq sodium, 5 mEq potassium, 3 mEq magnesium, 98 mEq chloride, 27 mEq acetate, and 23 mEq gluconate).

TRIAL SETTING

The pilot study was conducted at a large teaching and quaternary care hospital in North India in time duration from Jan 2015 to Dec 2016. 50 patients each were assigned to the three limbs of the study which were NS limb, RL limb and BSS limb.

PARTICIPANTS

TABLE 1



Adu ısed as intestinal perforation, irrespective of the site of perforation were included in the study. The permission for the study was obtained from the hospital ethical committee. The patients who were competent to comprehend and participate in their treatment decision making were counseled regarding the study and written consent obtained from them. In patients who were sick and in altered sensorium or not able to take decision, their closest relative was the one from which written consent was taken. The exclusion criteria were patients who were moribund and the treating physician think were un-survivable, severe cardiac dysfunction and unfit for volume resuscitation, CKD with KDIGO stage II or beyond and patients who did not give consent.

TRIAL DESIGN

Patients were recruited when they were diagnosed with Intestinal perforation and were posted for surgery and were randomized in the OT. The randomization was computer generated and stratified with the use of a centralized web-based management system (Clininfo). The trial had three limbs, in each limb different IV fluid administered to the patient. In NS limb, 0.9% Normal Saline was administered, in RL limb, Ringer Lactate was administered to the patient and in the BSS limb, either Plasmalyte® of Baxter or Kabilite® of Fresenius Kabi was administered to the patient. The IV fluids were supplied centrally by the controlling investigator in a bag devoid of any markings and neither the doctor administering the fluid knew which limb the patient belonged to and neither the record keeper knew. All the IV fluid bags were similar 500 ml bag with no markings and blinding was adequate double blind. In each limb, all patients were administered with the same IV fluid as per his requirement which was determined by the treating doctor. If required, 25% Dextrose was given separately but the protocol was not breached. Daily few IV bags were issued by the investigator to the clinician for each patient who were kept at the bedside. Whenever required, the same IV bag was used. All unused bags were returned to the investigator at the end of 5 days. Every 24 hours, investigation was done to determine the parameters mentioned in the table below. Patients were in the study for maximum 5 days (exactly 120 hours) after randomization. If the oral feeds were started by the clinician before 5 days, the study terminated and his record was dispatched to the investigator. Termination of the patient in the study was done when the patient stopped requiring IV fluids and was totally on oral fluids and feeds. Even if the patient did require IV fluids after 5 days, the patient was taken off from the study and IV fluid therapy was given as per the choice and decision of the clinician.

The primary end point for the study was (i) increase in Serum Chloride during the hospital stay of the patient, (ii) increase in chances of renal failure as defined by KDIGO (iii) Chloride levels at the end of 5 days. The secondary end point was (i) all cause mortality

at the end of 90 days, (ii) increase in chance for Renal Replacement Therapy in 90 days after surgery.

PROTOCOL

TABLE 2

DAY	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	Discharge
Date						
HR						
BP						
TEMP						
SpO2						
RESP RATE						
Hb						
TLC						
Na						
K						
Cl						
BUN						
S Creat						
Albumin						

Max Creatinine level:

Dialysis Orders:

The above form was filled for all the patients by a separate record keeper who happened to be a resident in anaesthesiology. These forms were completed and send to the investigator.

DATA COLLECTION

For the patients who met the criterion of including in the study, at the time of randomization the following data was collected: Age, sex, body mass index, previous comorbidities, SOFA score at admission, baseline investigations like Hb, TLC, Platelets, BUN, serum creatinine, Na, K, Cl and Albumin levels were recorded.

Daily investigations were done and recorded. At the end of 5 days the protocol was finalized and sent to the investigator. At the time of discharge, the parameters were again recorded and the patient was allowed his normal routine as per his convenience. At the end of 90 days, a telephonic call was placed from the side of the investigator and the following were enquired: (i) whether he is well (ii) was he ever diagnosed with kidney dysfunction all this while (iii) did he ever get dialysis done. The results were tabulated in his chart.

The data was subjected to statistical analysis by Stata 10.

RESULTS

From January 2015 through to December 2016 a total of 234 patients meeting the inclusion criteria underwent GI perforation surgery and were enrolled into the study. Follow-up was completed on 31 March 2016 after hospital discharge of all patients. After excluding patients who did not meet the pre-defined inclusion criteria 150 patients remained for analysis, with 50 patients assigned to each of the three groups. The mean age of enrolled patients was 63 years, 71.4% were male and almost 40% of cases were elective. The mean (SD) of Serum Cl^- at end of 5 days was 15.0 (21.6 - 10.8) and has significant difference between the BSS and RL on one hand and NS group on the other side. Patients assigned to NS limb had lower estimated glomerular filtration rate at baseline but no difference in a validated AKI risk score. Fluid therapy and chloride load Adherence to assigned fluid strategy to completion of postoperative day 5 was high, with a protocol compliance rate of 95% that did not differ between BSS, RL and NS groups. Patients assigned to NS group received a greater total fluid volume (crystalloid and colloid) during the study period [median (interquartile range) 9300 (12600–8200) vs. 8200 (10500–6900)for RL and in BSS group and 8400 ml (10800 - 7000) , p = 0.03 p = 0.01] Patients assigned to a NS group received a greater chloride load than those assigned to BSS & RL groups, both intraoperatively [median (IQR) 436 (344–556) vs. 315 (246–389) RL and 326 (251 - 398) in BSS mmol; p<0.001] and on postoperative days 0 to 4 combined [510 (723–305) vs. 273 (222–339) & 279 (230-340) mmol; p<0.001]. Preoperative S Cl–was similar between patients in the chloride-rich and chloride-limited fluid strategy groups. Intraoperatively, peak S Cl– was higher in patients assigned to a NS group than in those assigned to a RL & BSS groups [median (IQR), 115 (112–118) vs. 103 (97–113) mmol/L and 100 (96-102); p<0.001] and was accompanied by a greater degree of metabolic acidosis. Calculated daily, from the intraoperative period through to postoperative day 5, a time-weighted mean S Cl– was consistently higher in the NS group. Perioperative hyperchloraemia occurred in more than 90% of patients assigned to a NS group and throughout the study period than in BSS and RL groups and the result at the end of the study period revealed [NS 114 (106-121) vs RL 99 (96-104) and BSS 101 (96-105)].

Preoperative S Cr measures were available for 150 of the 150 patients (100.0%). Serum Cr was measured on at least 4 of the first 5 postoperative days in 45 patients (30%) and on each of the first 5 postoperative days in 105 patients (70%). The incidence of stage 2 or 3 AKI as per KDIGO stage II or III was more in NS group 8 (16%) than in RL 4 (8%) and in BSS 3 (6%). This difference was significant [unadjusted relative risk 1.77; 95% confidence interval (CI) 0.71–0.86; p = 0.02]. After adjusting for prespecified covariates, compared to both BSS and RL groups, there was association between NS group and either peak ΔS Cr, transformed to meet the assumptions of multivariable linear regression (regression coefficient 0.03, 95% CI –0.03 to 0.08; p = 0.39) or stage 2 or 3 KDIGO (adjusted odds ratio 1.66, 95% CI 0.65–0.87; p=0.03]. The chloride levels at the end of day 5 was NS group 109 (102-116), BSS 99 (96-102) and RL 99 (97-102).

All cause dialysis event recorded in these 150 patients was 11. NS group 7 and 2 in each group of BSS and RL which was significant (OR = 1.76 with confidence interval of 0.78 - 0.90).

DISCUSSION

0.9% Normal Saline has been thought to be the oldest and most convenient fluid for replacement. All clinicians think that it is a simple and optimal – hence it becomes the most favoured IV fluid. Data from Intercontinental Marketing Services (IMS) Health show that the sales of 0.9% NS in few European countries between 2007 and 2011 were more than all other IV placed together. The figures suggest that 0.9% Normal Saline is used more than it should have been[2]. However, not all is good about this fluid as the composition of this fluid is much different from plasma. Hence, it is not as physiological[3] as one might believe it is and that is why isotonic saline should be labeled **unbalanced – there is nothing Normal about it.** The biggest issue with this solution is unphysiological range of Chloride ion which is 50% higher than that of plasma[3]. Sodium is little on the higher side, though 154 mEq/l is not a drawback. Other ions such as potassium, calcium, magnesium, lactate/bicarbonate/acetate all of which have important function in plasma are missing. The serum osmolality is also significantly higher at 308 whereas the normal osmolality is 275-295 mosm/l. Even 1% variation of osmolality alters the levels of ADH and causes some disturbance in the interior milieu[4,8,9]. 0.9% Normal Saline causes metabolic acidosis and rapid infusion of 2-3 litres decreases pH in adult to lower end of the normal interval, which gets compensated by increasing of minute ventilation by the patient: which may be difficult for a patient with a respiratory compromise[5,6,7]. If this acidosis is not fully compensated, it wreaks havoc on the various intra-cellular metabolic processes – cardiac function is compensated and mayhem breaks loose[3,7,10].

The aspect this study highlighted was the effect of IV fluids on the renal function for a prolonged period of time

CONCLUSION

In conclusion a perioperative fluid strategy designed to restrict IV chloride administration was associated with a difference in the incidence of AKI and other metrics of renal injury in adult patients. Our findings support a strategy of perioperative chloride restriction

as an effective means to reduce the incidence of AKI and dialysis.

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