Assessment of intraoperative use of Ringer acetate in patients with liver cirrhosis

Hatem A Attalla MD ; Montaser S Abulkassem MD; Khaled M Abo Elenine, MD
Lecturers of Anaesthesia, Faculty of Medicine, Menoufiya University.

Abstract

In this study, Acetated Ringer (AR) and Lactated Ringer (LR) were used as intraoperative infusions in patients with liver cirrhosis during elective surgery under general anaesthesia. Their effect on acid- base balance, serum pyruvate, serum lactate, ketone bodies concentration, liver function, blood glucose level and haemodynamic parameters were evaluated intra and postoperatively.

Thirty patients (grade A, Child-Pugh classification) were divided into two groups according to the type of the infused solution; LR or AR. Postoperative Pyruvate level in AR (1.21±0.39 mg/dl) was significantly higher than in LR group (0.47±0.11 mg/dl). However, the level of lactate in LR group postoperatively (16.80±1.61 mg/dl) increased significantly in comparison to that in AR group (8.87±0.92 mg/dl). The ketone bodies concentration was significantly higher in AR group (2.33±0.42 mg/dl) than in LR group (0.40±0.20 mg/dl). There was no significant changes in pH, HCO_3 *,base excess, liver function, blood glucose level and haemodynamic parameters in both groups either intraoperatively or at the end of the infusion. These results suggest that AR may be more beneficial as an intraoperative fluid than LR.* Acetated ringer decreased the metabolic load to the liver and improved hepatic energy status *in patients with liver dysfunction.*

INTRODUCTION

The need for surgery in patients with liver disease should be considered carefully in view of high reported morbidity and mortality. Risks associated with the perioperative period are decompensation with encephalopathy, renal failure and major difficulties in the management of fluid balance[1].

Intravenous fluid therapy is one of the most crucial aspects in patient care. Over the years different electrolyte solutions have been developed according to the physiologic demands of various medical conditions. The choice of fluid should be based upon the hydration status of the patient, type of concentration, and metabolic abnormalities present[2].

Lactated Ringer's solution (LR) is a hypotonic solution that best approximate extra cellular fluid. LR may be infused safely in large quantities of patients with conditions such as hypovolaemia with metabolic acidosis[3], shock syndromes[3], and burns[4]. Other balanced salt solutions currently available are manufactured using sodium acetate (Ringer acetate, AR) or bicarbonate instead of lactate, the use of which is thought to be generally interchangeable[5].

LR and AR are physiologic solutions that differ only in their bicarbonate source. In the liver, and to a lesser degree, the kidney, lactate is metabolized to pyruvate, which is then converted to either CO_2 and H_2O (80% catalyzed in part by pyruvate dehydrogenase) or glucose (20% catalyzed in part bypyruvate carboxylase). Either of these processes results in the regeneration of the bicarbonate[6].

Acetate is metabolized mainly in the muscles and to a lesser extent in tissues such as Kidneys, heart[7]. Acetate is metabolized to bicarbonate in the following manner. Acetate combines with Co enzyme A to form acetyl-Co A. This reaction is mediated by the acetyl-Co A synthetase and consumes a hydrogen ion in the process. The source of hydrogen ion is carbonic acid, which becomes bicarbonate[7]. In chronic liver

insufficiency, hepatic gluconeogenesis is inhibited and the liver fails to metabolize lactate. The aim of the present study was to evaluate the effects of AR and LR solutions intraoperatively in patients with chronic liver insufficiency. The hypothesis was that acetated Ringer would provide less metabolic load on the liver when administered intraoperatively to patients with impaired liver functions.

PATIENTS AND METHODS

The study was carried out in Menoufiya University hospital. Thirty patients had chronic calcular cholecystitis and evident hepatic cirrhosis, grade A Child – Pugh classification[8] (Table 1), were included in the study. They were scheduled for open cholecystectomy under general anaesthesia.

Exclusion criteria included patients suffering from diabetes mellitus, renal failure, or any cardiovascular or respiratory diseases. Any patient suffered from overt bleeding that needed blood transfusion was excluded from the study. All patients were fasted for food and fluids 8 hours preoperatively.

Patients were randomly divided in to two groups in a single blinded randomized study. Group (I) 15 patients received LR at a rate of 10 ml/Kg/hr.

Group (II) 15 patients received AR at a rate of 10 ml/Kg/hr.

The following preoperative measurements were carried out to all patients in both groups. Complete blood count, platelets count, serum electrolytes, urea and creatinine. Liver function tests as albumin, prothrombin time, ALT, GPT, ALP and bilirubin.

After establishing standard ECG, heart rate (HR), Oxygen saturation and non invasive blood pressure (NIBP) by Capnomac (Ultima, Datex, Finland). Anaesthesia was induced in all patients using fentanyl 1µg/Kg and propofol 2mg/Kg. Atracurium besylate was given in a dose of 0.5mg/Kg followed by manual ventilation for 3 minutes then endotracheal intubation. Maintenance of anaesthesia was carried out with 60% nitrous oxide in oxygen and isoflurane that was changed according to haemodynamic variation and adjusted to end tidal concentration of 1%. Controlled ventilation was adjusted to maintain $ETCO_2$ 35-40 mmHg. Postoperatively, all patients received I.V fluids in the form of equal volumes of dextrose 5% and 0.9% normal saline until patients started oral feeding.

Measurements:-

1. Arterial blood gases sample for evaluation of (pH, HCO_3 and base excess level) was taken preoperatively, after 30 minutes and immediate postoperatively at the end of infusion of either lactate or acetate solution.
2. Plasma pyruvate and plasma lactate levels measured immediate postoperatively and compared with those before operation. (N. pyruvate value 0.3-0.9 mg/dl) (N. lactate value 8-15 mg/dl).
3. Ketone body concentration was done preoperative and immediate postoperatively (N. value 0.3-3 mg/dl).
4. Liver enzymes (serum glutamic pyruvic transferase GPT) N. value 10-45 IU/L. (Alkaline phosphatase ALP) N. value 80-280 IU/L. 24 hours Postoperative values compared to the preoperative ones.
5. Blood glucose level at the end of the infusion compared to the preoperative value. (N. fasting value 70-120 mg/dl).
6. Haemodynamic parameters as HR and MABP were monitored and recorded preoperatively, every 15 minutes for 90 minutes during the infusion of either solution in both groups.

The data were expressed as mean, standard deviation and were analyzed using student (t) test, paired t for data

within the same group and unpaired t for comparison between two groups. Differences were considered significant when $p<0.05$.

RESULTS

As regards demographic data, total infusion volume and duration of surgery, there was no significant difference between the two groups (Table 2).

Arterial blood gases samples for measuring pH, HCO_3 and base excess showed no significant difference comparing intraoperative and postoperative values (at end of infusion) to the preoperative value in both groups. Also there was no significant difference between the two groups at any time of the study (Table 3).

As regards pyruvate level, in group I no significant difference in comparing postoperative value to preoperative value. While in group II (acetate gp) it was significantly increased at postoperative value, also it was significantly higher than that of group I (Table 4).

The Lactate level showed significant increase in the postoperative values in comparison to the preoperative values in group I. While in group II the values did not increase significantly. By comparing both groups, Lactate level was significantly higher in group I at the end of the infusion (Table 4).

Ketone bodies concentration was significantly decreased postoperatively in comparison to preoperative values in group I (Lactate). While in group II (acetate) the ketone bodies concentration showed no changes postoperatively in comparison to the preoperative values. By comparing both groups, Ketone bodies concenration was significantly lower in group I at the end of the infusion (Table 4).

As regards liver enzymes GPT, ALP and blood glucose level, there was no significant difference in postoperative values in comparison to preoperative values in both groups. Also there was no significant difference between the two groups (Table 4).

As regards haemodynamic parameters (HR and MABP), there were no significant difference at any time of the study between the two groups (Fig 1 and 2).

DISCUSSION

Patients with liver disease present a challenge to anesthesiologists because this condition involves not only abnormal handling of anaesthetic agents, but also multiorgan system dysfunction, general debility and specific problems associated with replacement therapy. Moreover, in situations of hepatic insufficiency anesthesia and surgery may precipitate acute failure.

Perioperative fluid management has undergone significant advances over the past few decades. The choice of fluid and its electrolyte composition are important considerations when replenishing plasma volume and other body fluid compartments.

In this study, we compared two crystalloids used intraoperatively in patients with liver cirrhosis, either lactated ringer or acetated ringer to detect the one suitable for those patients a regards their metabolic effects on liver functions.

As regards acid – base changes in this study (pH, HCO_3 and base excess) there were no changes intraoperatively or postoperatively in comparison to preoperative values in both groups. These results were proved in a previous study[9], which compared the intraoperative use of lactate and acetate solutions in different gynaecological operations. There were no changes in acid-base balance; however the study was done on patients with no liver disease. Another two studies[10,11], the first done during hepatectomy and confirm our results where no changes in

Table 1: Child-Pugh Score for assessing hepatic dysfunction.

	1	2	3
Encephalopathy	None	1-2	3-4
Ascites	Absent	Slight	Moderate
Albumin(g/L)	35	28-35	<28
Prothrombin time (Sec.prolonged)	1-4	4-6	>6
Bilirubin(µmol/L)	15-30	30-45	>45

Grade A 5-6 points
Grade B 7-9 points
Grade C >10 points

Table 2: Demographic data, infusion volume and duration of surgery in the two groups.

Diff	Group I Lactated Ringer	Group II Acetated Ringer
Age(years)	53.60±7.91	53.33±8.73
Weight(Kgm)	76.60±11.08	76.80±10.48
Total infusion(ml)	846.67±109.33	836.67±106.01
Duration of surgery(min)	78.27±10.43	77.93±9.05

Data in mean± SD. P significant if <0.05.

Table 3: Changes in pH, HCO_3 and base excess in the two groups.

Diff	Timing	Group I Lactated Ringer (n=15)	Group II Acetated Ringer (n=15)	(t) - between groups	P
pH	Preop	7.38±0.02	7.38±0.01	0.228	0.821
	Intraop	7.38±0.01	7.38±0.02	0.115	0.909
	paired- t	0.292	0.144		
	P	0.774	0.887		
	Postop	7.38±0.01	7.38±0.02	0.242	0.811
	Paired t	0.222	0.354		
	P	0.827	0.728		
HCO_3 (m mol)	Preop	24.20±1.15	24.00±1.41	0.425	0.674
	Intraop	24.27±1.10	24.20±1.15	0.163	0.872
	Paired- t	0.193	0.494		
	P	0.849	0.629		
	Postop	24.00±1.41	24.47±1.13	1.00	0.326
	Paired-t	0.494	0.979		
	P	0.629	0.344		
Base excess (mmol)	Preop	1.80±1.15	2.00±1.41	0.425	0.674
	Intraop	1.73±1.10	1.80±1.15	0.163	0.872
	Paired-t	0.193	0.494		
	P	0.849	0.629		
	Postop	2.00±1.41	1.73±1.10	0.576	0.569
	Paired-t	0.494	0.564		
	P	0.629	0.582		

Data in mean± SD. P significant if <0.05.

Table 4: Pyruvate, Lactate, Ketone body conc, GPT, ALP and glucose level in the two groups.

Diff	timing	Group I Lactated Ringer (n=15)	Group II Acetated Ringer (n=15)	(t)-between gps	P
Pyruvate (mg/dl)	Preop	0.49±0.12	0.48±0.11	0.152	0.880
	Postop	0.47±0.11	1.21±0.39	4.596	0.000*
	Paired-t	0.307	7.153		
	P	0.764	0.000*		
Lactate (mg/dl)	Preop	8.87±0.92	8.73±0.80	0.425	0.674
	Postop	16.80±1.61	8.87±0.92	4.522	0.000*
	Paired-t	4.522	0.423		
	P	0.000*	0.671		
Ketone body (mg/dl)	Preop	2.33±0.42	2.28±0.42	0.304	0.763
	Postop	0.40±0.20	2.33±0.42	4.687	0.000*
	Paired-t	4.269	1.333		
	P	0.000*	0.204		
GPT (serum glutamic pyruvic transferase) (IU/L)	Preop	47.00±11.94	47.33±10.02	0.083	0.935
	24h	47.47±10.08	47.73±12.17	0.065	0.948
	Postop	0.494	0.269		
	Paired-t	0.629	0.792		
	P				
ALP (Alkaline phosphatase) (IU/L)	Preop	140.47±34.26	140.73±35.90	0.021	0.984
	24h	141.60±33.49	141.67±35.79	0.005	0.996
	Postop	1.333	1.793		
	Paired-t	0.204	0.095		
	P				
Blood glucose (mg/dl)	Preop	81.73±8.80	81.87±7.61	0.044	0.965
	Postop	82.53±8.43	83.40±8.10	0.287	0.776
	Paired-t	1.922	2.065		
	P	0.075	0.058		

Data in mean± SD. P significant if <0.05.

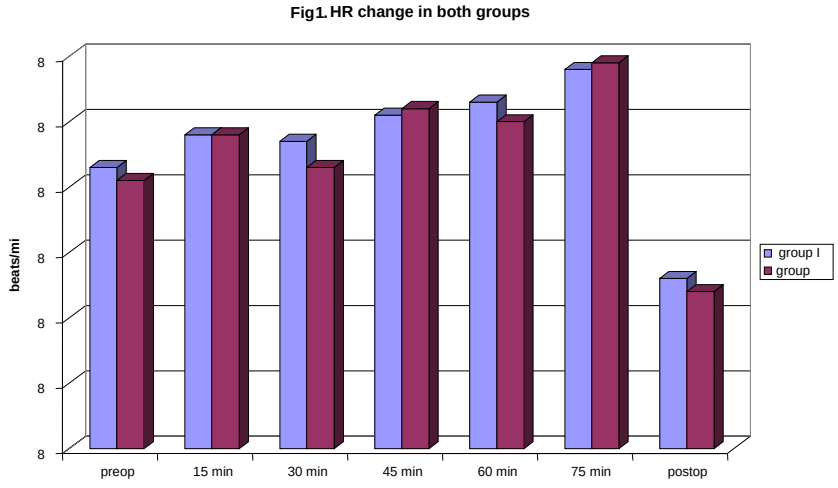

Figure 1. Changes in heart rate in both groups.

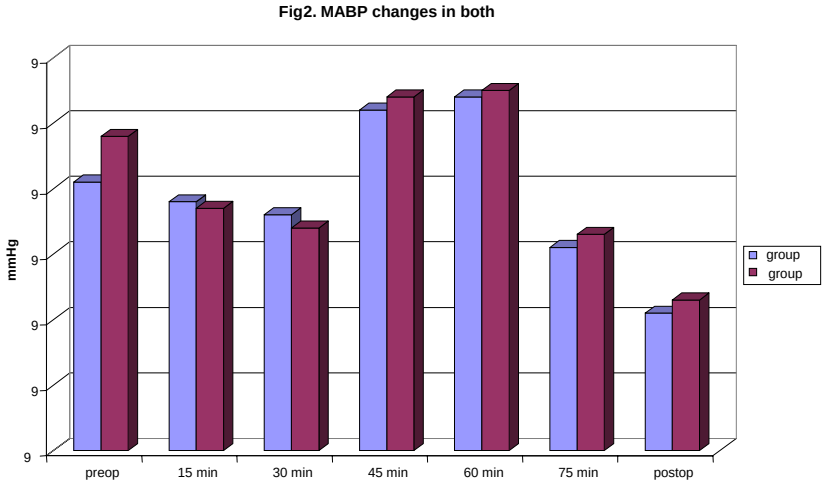

Figure 2. Changes in mean arterial blood pressure in both group.

ABG occurred, the second study was done on rabbits during induced hepatic insufficiency and showed only mild metabolic acidosis in the acetate group in comparison to the lactate group although not at a significant level. Also base excess, HCO_3, PaO_2 and $PaCO_2$ did not differ significantly in the treatment groups.

In contrast with the present results, Onizuka and his colleagues[12], compared the effect of rapid infusion of lactated and that of acetated ringer's solution on base excess, pH and bicarbonate level and found that pH and base excess level were significantly lower in lactated than in acetated group in addition to the higher level of plasma lactate level due to rapid rate of infusion and delayed conversion of lactate to bicarbonate to correct the metabolic acidosis occurred. Also the authors explained this to the better correction of lactic acidosis by acetated solution than by lactated one.

Fukuta et al,[13], induced hemorrhagic shock in rats with hepatic dysfunction and compared the use of lactated and acetated ringers for correction of shock and found marked reduction in blood pH and HCO_3 with increased lactate concentration in using lactated ringer in comparison to acetated ringer and explained that by the efficacy of acetated ringer to correct acidosis and shock even during hepatic dysfunction.

In the present study, pyruvate level was significantly lower in the lactate group than in the acetate group at the end of the operation, which can be explained by the decreased metabolism of lactate to pyruvate in such patients with liver insufficiency[6]. Estimation of the lactate level at the end of infusion of both lactate and acetate solutions in the postoperative period revealed significant increase in lactate level in group I, this can be explained as the main metabolism of lactate occurred in the liver by the process of hepatic gluconeogenesis which was depressed in those patients with liver insufficiency[6], and hence lactate overload occurred postoperatively. This was not the issue in case of acetate infusion, where its metabolism occurred mainly in the muscles and to a lesser extent in the kidney and heart to be converted into bicarbonate[7].

In the present study, blood ketone body concentration was used as an indicator for the period of stress that may occur during surgery and diminished hepatic blood flow[11]. Since ketone bodies are necessary as an alternative source of energy during periods of stress, therefore, maintenance of this energy reservoir may also explain the enhanced hepatic energy

status[14]. It was found that ketone body concentration was maintained by acetated ringer and not by lactated ringer in our study. Nakatani and his colleagues[11], found similar results, where pyruvate level and pyruvate/lactate ratio increased and ketone bodies concentration maintained with acetate infusion in comparison to lactate infusion in rabbits and after a period of hepatic inflow occlusion. They concluded that acetated ringer decreased the metabolic load of the liver and improved hepatic energy status. On the contrary, Kabutan et al[15], found no changes in lactate level and ketone body concentration during infusion of either lactated or acetated ringer solutions. However, their results may be conflicting as some patients undergo hepatectomy with profuse bleeding which will disturb the liver metabolism. Another study[10], compared lactated to acetated ringers intraoperatively during hepatectomy found that lactate level increased significantly in lactated ringer group, also acetate level increased significantly in acetated ringer group. This was explained by the rapid rate of infusion of both solutions during hepatectomy also patients in this study with more advanced stages of liver dysfunction. Sekiguchi et al[16], investigated the metabolic changes during infusions of lactated or acetated ringers intraoperatively during cardiovascular surgery and found that serum lactate or acetate did not increase significantly, however ketone bodies concentration maintained by acetated ringer during the most stressful period with cardiopulmonary bypass.

Ogawa et al[17], recommended the use of acetated ringer solution intraoperatively instead of lactated ringer during hepatectomy in patients with glycogen storage disease, as lactate and pyruvate and base excess showed no changes. Therefore, no need for bicarbonate administration to correct metabolic acidosis, especially in case of lactate accumulation as in glycogen storage diseases.

In this study, the effects of acetate and lactate solutions on liver enzymes (GPT, ALP) were evaluated as well as blood glucose changes. The results showed no changes in these parameters postoperatively compared to the preoperative values. In agreement with another study[16], done on patients during surgery. There were no changes in liver functions and blood glucose level after infusion of lactate and acetate solutions. However this study was done on patients with no liver diseases. In previous studies[10,16], similar results showed no changes in liver functions in the postoperative period after infusion of either lactate or acetate solutions.

Isosu and his colleagues[18], found no additional benefits of acetated ringer over lactated ringer when comparing both infusions in patients with normal liver function and those with liver dysfunction.

In contrast with the present study, Ikeya et al[19], proved that lactated ringer was more useful than acetated ringer with regard to its glucose supply. However, their investigation were done in rats with normal liver function and subjected to acute haemorrhage. Where larger volume of lactate and acetate were used to correct hypovolaemia.

The haemodynamic monitoring (HR and BP) revealed haemodynamic stability during the period of the study. This was confirmed by similar studies[10,16,18], where there were no changes in haemodynamic parameters during the infusion of both solutions intraoperatively and any variations were related to another factor as anaesthetic or surgical effects.

In conclusion, the results of this study showed that the use of acetated ringer rather than lactated ringer was beneficial in patients with hepatic insufficiency, as acetate converted into

bicarbonate in various organ systems regardless of liver function. Therefore acetated ringer decreased the metabolic load to the liver and improved hepatic energy status. It is recommended to use acetated ringer instead of lactated ringer for patients with liver dysfunction.

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