KLİNİK ÇALIŞMA / CLINICAL RESEARCH

THE EFFECTS OF PEROPERATIVE FLUID ADMINISTRATION ON POSTOPERATIVE ACID-BASE AND ELECTROLYTE BALANCE IN PATIENTS UNDERGOING TOTAL GASTRECTOMY

TOTAL GASTREKTOMİ OPERASYONU GEÇİREN HASTALARDA PEROPERATİF SIVI İNFÜZYONUNUN POSTOPERATİF DÖNEMDE ELEKTROLİT VE ASİT-BAZ DEĞİŞİKLİKLERİ ÜZERİNE ETKİLERİ

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SUMMARY

Objective: *This prospective clinical study aimed to compare acid-base and electrolyte balance in patients who were administered perioperative normal saline (group NS) or Ringer's Lactate (Group RL) infusion for total gastrectomy surgery.*

Method: *Fifty patients scheduled to have total gastrectomy surgery for gastric cancer were recruited in the study. We performed arterial blood gas analysis after induction, at 1st, 12th and 24th postoperative hours, and recorded data regarding patients' metabolic conditions with sodium, chloride and potassium levels.*

Results: *The mean pH values of Group RL and NS showed a significant decrease at the 1st postoperative hour, then an increase in the 6th, 12th and 24th hours. The arterial $PaCO_2$, PaO_2, and oxygen saturation values did not show any significant difference in both groups at all times. Serum sodium levels were significantly lower in RL Group during all postoperative period. There was not a significant difference in serum potassium levels. Serum chloride levels at postoperative 6th, 12th and 24th hours were significantly lower in RL Group than NS Group. While Chloride level decreased significantly at the 6th hour in Group NS, compared to the end of the surgery, it did not change significantly at 24th hour.*

Conclusion: *Regarding the metabolic condition, in normal saline group, hyperchloraemic metabolic acidosis was obtained at first postoperative hour as a temporary side effect. Besides, we have observed a tendency for hyponatremia in Ringer's Lactate group. We are in the opinion that normal saline infusion can be confidently used in major abdominal surgeries.*

KEY WORDS: *Gastrectomy; normal saline; Ringer's Lactate; crystalloid.*

ÖZET

Amaç: *Bu prospektif klinik çalışmada total gastrektomi cerrahisi geçiren ve perioperatif %0,9 serum fizyolojik (Grup NS) ya da Ringer Laktat (Grup RL) infüzyonu alan hastalarda asid-baz ve elektrolit dengesinin karşılaştırılması amaçlanmıştır.*

Yöntem: *Gastrik kanser tanısıyla total gastrektomi operasyonuna alınacak olan 50 hasta çalışmaya dahil edildi. Arteryel kan gazı analizleri indüksiyonu takiben, postoperatif 1, 12 ve 24. saatlerde alındı ve hastaların metabolik durumlarıyla sodyum, klorür ve potasyum değerleri kaydedildi.*

Bulgular: *Postoperatif 1. saatte her iki gruba ait ortalama pH değerlerinde anlamlı bir düşüş, ardından 6, 12 ve 24. saatlerde bir yükselme tespit edildi. Her iki grupta da tüm zamanlarda arteryel $PaCO_2$, PaO_2, ve oksijen satürasyonu değerlerinde anlamlı bir fark gözlenmedi. RL Grubu'nda serum sodyum seviyeleri tüm postoperatif dönem boyunca anlamlı olarak düşüktü. Serum potasyum seviyelerinde anlamlı bir fark gözlenmedi. Grup NS ile karşılaştırıldığında RL Grubu'nda serum klor düzeyleri postoperatif 6, 12 ve 24. saatlerde anlamlı olarak daha düşüktü. Klor düzeyi operasyon sonu dönemle karşılaştırıldığında Grup NS'de anlamlı olarak düşmüşken postoperatif 24. saatte anlamlı bir farklılık gözlenmedi.*

Sonuç: *Metabolik durum göz önünde bulundurulduğunda hiperkloremik metabolik asidoz %0,9 serum fizyolojik verilen grupta postoperatif 1. saatte geçici bir yan etki olarak ortaya çıkmıştır. Bununla birlikte RL Grubu'nda hiponatremiye bir eğilim gözlemlenmiştir. Major abdominal cerrahi geçiren hastalarda %0,9 serum fizyolojik solüsyonunun güvenle kullanılabileceği kanaatindeyiz.*

ANAHTAR KELİMELER: *gastrektomi; serum fizyolojik; ringer laktat; kristaloid*

Çıkar çatışması/*Conflict of Interest*: Yazarlar herhangi bir çıkar çatışması bildirmemişlerdir./ *Authors do not report any conflict of interest.*
Geliş tarihi/*Received*: 04/09/2013 Kabul tarihi/*Accepted*: 04/12/2013

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INTRODUCTION

Surgical procedures cause fluid shifts in physiological compartments because of an increase in microvascular permeability and capillary leak in the surgical area (1). In major surgeries, use of appropriate fluid therapy is essential for maintenance of circulatory functions during intra- and postoperative processes. Therefore, changes in electrolytes and acid-base equilibrium resulting from fluid balance are important in patients having major abdominal surgery. Previous studies have reported that because of high chloride level in its content, normal saline infusion leads to metabolic acidosis when it is used in large volumes (2). Theoretically, it may also lead to hyperkalaemia as a result of high extracellular shift in potassium ions (3). Acidosis associated with saline infusion is also accompanied with complications such as immune dysfunction, gastrointestinal dysfunction and decreased renal blood flow. Despite that, saline solution is still the most common crystalloid solution in the world and often used in resuscitation, replacement, or used as maintenance fluid in perioperative period (4). There are some debates regarding the type of crystalloid that should be used in perioperative fluid replacement in adult patients (5). Balanced solutions such as Ringer's Lactate should be carefully used in patients suffering from renal dysfunction, because they can potentially lead to hyperkalaemia due to potassium in their components (6). Holte and Kehlet (7) have underlined in their review that most of the clinical studies regarding fluid administration have been carried out on the patients in intensive care unit; therefore, in order to create evidence-based guidelines there is a need for further studies that analyze fluid therapy in elective surgical procedures. There are previous studies comparing the use of these two crystalloids in renal transplantation (3), abdominal aortic aneurysm surgery (8) and spinal surgeries (9). However, the perioperative effects of the two crystalloids in patients undergoing total gastrectomy for gastric cancer was not studied before. Gastric resections lead to electrolyte imbalance as a side effect (10). Generally patients suffer from different levels of malnutrition after total gastrectomy (11). Therefore, in order to secure normovolemia and hemodynamic instability, fluid management is quite important during perioperative and early postoperative periods of major open abdominal surgeries in which fluid shifts occur. This clinical study aimed to compare acid-base and electrolyte balance in patients who were administered perioperative normal saline or Ringer's Lactate for total gastrectomy surgery.

MATERIALS AND METHODS

Following the approval of the ethics committee (Marmara University Hospital, with the date: 03 October 2012 and the number: B104İSM4340029/1009/82), 50 American Society of Anesthesiologists (ASA) I-III patients, between the ages of 20-70 and scheduled to have total gastrectomy surgery for gastric cancer were recruited in the study. All patients provided written consents before participating in the study. Exclusion criteria included patients' refusal, electrolyte imbalance, metabolic disorders like acidosis or alkalosis, dehydration symptoms such as high density of urine, hypotension, tachycardia or oliguria, and renal dysfunction or cardiac disease. Patients had intramuscular injections of 0.07 mg kg^{-1} midazolam and 0.015 mg kg^{-1} atropine as premedication 45 min before the operation.

Patients included in the study were randomly separated into two groups (n=25). Group assignments were kept in sealed, opaque, sequentially numbered envelopes. At induction both groups had thiopental sodium 5-7 mg kg-1 IV and rocuronium bromide 0.6 mg kg^{-1} IV. Anesthesia was maintained with sevoflurane 1 MAC, 70% N_2O and 30% O_2. A muscle relaxation monitor (TOF Watch SX) was used.

Perioperative 15 mL kg^{-1} IV crystalloid fluid infusion was administered. While the patients in the 1st group (group RL) received perioperative infusion of Ringer's Lactate, fluid requirement of the patients in the 2nd group (group NS) was met with normal saline infusion. Electrocardiogram, invasive blood pressure, temperature, end-tidal carbon dioxide, peripheral oxygen saturation (SpO_2) and central venous pressure (CVP) monitorization were applied on all patients, and the obtained data were recorded at 15-min intervals. Erythrocyte suspension and colloid solutions were used and recorded when there is a need for blood loss compensation in either group. Blood transfusion was administered according to the perioperative blood transfusion guideline of ASA (12).

We performed arterial blood gas analysis after induction, at 1st, 12th and 24th postoperative hours, and recorded data regarding patients' metabolic conditions with sodium, chloride and potassium levels. The same crystalloid infusions were maintained with a dose of 2 mL kg^{-1} h^{-1} till the postoperative 24th hour. We recorded surgical duration, anesthetic duration, urine output, bleeding and transfusion amounts, and amounts of used crystalloid and colloid solutions at the end of the operation.

Statistical analysis

Analyses were carried out using SPSS 21.0 program. Average, standard deviation, ratio and frequency were used for descriptive statistics of data. We used Kolmogorov simirnov test for controlling the distribution of variables. Also, quantitative data were analyzed with the independent Samples T test and the Mann-Whitney U test while qualitative data were analyzed with Chi-square test. Wilcoxon test and Paired Samples T test were preferred for repeated measurements. To reach a difference of 5 mEq L^{-1} in serum chloride level was considered clinically significant. In order to achieve a power of 90% and significance level of 5%, the number of patients required in each group was calculated at 25 patients. P< 0.05 was regarded as statistically significant.

RESULTS

Although 53 patients were in conformity with the inclusion criteria of the study, 3 patients were excluded from the study as they were found out to be inoperable after randomization. Afterwards, we kept the statistics of the data belonging to the 50 patients. There was no significant difference between the two groups regarding their age, weight and gender distribution, total blood loss, total fluid, anesthetic and surgical durations (Table 1). The values of blood pressure, heart rate, temperature, end tidal CO_2 and SPO_2 did not show any significant difference in RL and NS groups before and after surgery (Table 2). The mean pH values of Group RL and NS showed a significant decrease at the 1st postoperative hour, then an increase in the 6th, 12th and 24th hours (p<0.05, Table 3). All postoperative pH values were higher in the RL Group compared to NS Group.

The arterial $PaCO_2$, PaO_2, and oxygen saturation values did not show any significant difference in both groups at all times. In the RL Group, the HCO_3 value at 1st postoperative hour was significantly higher than the NS Group (p<0.05). Postoperative HCO_3 increased significantly in both groups during the 6th, 12th and 24th hours (p<0.05, Table 3). BE was significantly higher in the RL Group at the end of the operation compared to NS Group (p<0.05). However, BE did not show any significant difference in both groups in the rest postoperative period. The BE value increased significantly in RL Group at the end of the operation when compared to the preoperative period (p<0.05). While the mean BE of the RL Group showed a significant increase at 24th hour compared to the beginning of surgery (p < 0.05), there wasn't an increase in NS Group.

Sodium level was significantly lower in RL Group at the end of surgery and at 6th, 12th and 24th hours compared to NS Group (p<0.05, Table 4). While sodium showed a significant decrease at 6th postoperative hour compared to the end of surgery (p<0.05), it did not show a significant change at 24th hour. In NS Group, sodium level showed a significant increase during the whole postoperative peirod compared to the value measured before surgery (p<0.05). However, sodium did not show any significant change during the 6th, 12th and 24th hours compared to the first postoperative hour.

There was not a significant difference in potassium levels before surgery and at the end of the operation as well as in the 6th hour. The levels showed a significant increase in the RL group at 24th hour compared to the preoperative period (p<0.05). Potassium was significantly higher in the RL Group at 24th hour than the NS Group (p<0.05). Although potassium showed a significant decrease in NS Group at the end of surgery in comparison with the beginning of the operation, it did not change significantly within 6th, 12th and 12th hours (Table 4).

Chloride levels at postoperative 6th, 12th and 24th hours were significantly lower in RL Group than NS Group (p<0.05, Table 4). While Chloride decreased significantly at the 6th hour compared to the end of the surgery, it did not change significantly at 24th hour. In Group NS, the Chloride value increased significantly at the posto-

Table 1: The comparison of patient characteristics, total blood loss, total crystalloid infusion, duration of anesthesia and surgery (mean ± SD)

	Ringer's Lactate	Normal Saline	p
Age (years)	55.88±13.34	59.54±10.87	0.296
Male	21 (80.8%)	14 (58.3%)	0.084
Female	5 (19.2%)	10 (41.7%)	
Weight (kg)	69.00±12.38	67.92±11.61	0.752
Total blood loss (mL)	290.58±250.66	260.42±219.67	0.555
Total crystalloid infusion (mL)	2147.31±659.57	2041.67±591.18	0.654
Duration of anesthesia (min)	127.69±43.50	119.79±35.95	0.489
Duration of surgery (min)	106.54±39.89	104.58±37.03	0.859

Table 2: Mean arterial blood pressure, heart rate, peripheral oxygen saturation (SpO_2) and end-tidal carbon dioxide ($ETCO_2$)

		Ringer's Lactate	Normal Saline	p
Blood pressure (mmHg)	O. min	97.69±15.81	95.83±16.09	0.682
	15.min	84.92±19.32	82.33±17.06	0.619
	30.min	83.96±14.17	90.46±21.22	0.206
	End of surgery	80.33±12.85	81.83±13.11	0.691
Heart rate (beat/min)	O. min	86.92±15.09	92.63±14.45	0.180
	15.min	87.54±12.97	91.04±18.30	0.436
	30.min	87.31±13.66	91.25±14.23	0.323
	End of surgery	79.88±13.78	81.79±15.51	0.653
SpO_2 (%)	O. min	98.31±1.44	97.71±2.39	0.444
	15.min	98.73±1.08	98.25±2.05	0.449
	30.min	98.85±0.97	98.63±0.71	0.262
	End of surgery	99.08±1.02	98.92±0.58	0.183
$ETCO_2$ (mmHg)	O. min	34.65±3.50	31.99±4.26	0.052
	15.min	32.96±3.17	32.08±3.23	0.337
	30.min	32.56±3.43	30.96±3.38	0.106
	End of surgery	32.46±3.56	32.18±3.32	0.349

perative 1st hour compared to the preoperative period ($p<0.05$). However, mean Chloride levels did not change at other postoperative hours. In NS Group, Chloride levels decreased significantly at 6th, 12th and 24th hours compared to the postoperative 1st hour ($p<0.05$).

The postoperative mean hemoglobin and hematocrit were not significantly different in RL and NS Groups compared to the preoperative period.

Discussion

The present study compared the use of normal saline and Ringer's Lactate solutions at per and postoperative periods in patients undergoing total gastrectomy. Regarding the metabolic condition, in normal saline group, hyperchloraemic metabolic acidosis was obtained at first postoperative hour as a temporary side effect. Besides, we observed a tendency for hyponatremia in Ringer's Lactate group.

Several studies have emphasized that perioperative normal saline infusion cause to metabolic acidosis, therefore, balanced crystalloids such as RL need to be preferred over saline infusion (13-16). Langer et al (17) indicated in an experimental model that although RL does not make any change in pH value, saline leads to a decrease in it; however, in the mentioned study the pH value was within the normal limits following the saline usage. On the other hand, a retrospective study examining the data of 9799 patients in the intensive care unit concluded that the highest mortality rate was observed in patients with lactic acidosis. However, the mortality rate of patients with dilutional hyperchloremic acidosis did not show a significant difference with patients who did not have metabolic acidosis (18). A review of clinical and experimental studies comparing balanced solutions with saline infusion have reported that neither balanced strategies nor isotonic saline strategies have an effect on renal and gastrointestinal functions, coagulation factors, blood loss or transfusion (19).

In the current study the pH values of saline-receiving group were found to be significantly lower in the postoperative period compared to the values before surgery. On the other hand, the pH value in RL group at the 1st postoperative hour was found to be also significantly lower compared to the preoperative period. Also, in the saline-receiving group the plasma bicarbonate level decreased below 22 mmol L^{-1} only at 1st postoperative hour. However, the change in plasma bicarbonate level compared to the preoperative period was 0.78 ± 2.22, and it was not statistically significant. In Group NS, the mean BE value only in the 1st postoperative period was -3.27 and it was at the limit of metabolic acidosis. However, when preoperative median BE values of the group were evaluated, the average was -2.24. But the change observed in the BE value at 1st hour was not statistically significant.

The tendency to acidosis was observed only at 1st postoperative hour and the significant increase in mean pH level set us considering on other reasons of acidosis, as we maintained the fluid infusion during the 24 posto-

Table 3: Blood gas parameters (mean±SD)

		Ringer's Lactate	Normal Saline	p
pH	Preoperative	7.40±0.04	7.39±0.05	0.100
	Postoperative 1. h	7.38±0.02	7.29±0.04	***0.000***
	Postoperative 6. h	7.39±0.04	7.35±0.04	***0.000***
	Postoperative 12. h	7.40±0.02	7.37±0.04	***0.000***
	Postoperative 24. h	7.41±0.02	7.36±0.03	***0.000***
HCO_3 mmol/L	Preoperative	23.55±1.50	22.47±2.54	0.070
	Postoperative 1. h	23.23±1.64	21.69±1.27	***0.001***
	Postoperative 6. h	24.00±1.58	23.27±1.85	0.139
	Postoperative 12. h	24.83±1.87	24.05±2.10	0.946
	Postoperative 24. h	24.51±2.14	24.65±1.85	0.803
Base Excess mmol/L	Preoperative	-0.62±2.13	-2.24±2.88	***0.028***
	Postoperative 1. h	-1.79±1.75	-3.27±1.91	***0.006***
	Postoperative 6. h	-1.00±1.51	-1.71±1.76	0.131
	Postoperative 12. h	-0.8±2.38	-0.76±2.11	0.944
	Postoperative 24. h	0.22±2.36	0.05±2.46	0.804
Partial arterial oxygen pressure (PaO_2) mmHg	Preoperative	166.92±40.35	164.90±57.48	0.886
	Postoperative 1. h	130.80±41.26	142.33±42.73	0.337
	Postoperative 6. h	95.11±27.70	106.84±35.43	0.197
	Postoperative 12. h	99.21±30.96	98.09±28.86	0.926
	Postoperative 24. h	91.07±23.33	84.55±18.98	0.286
Partial arterial carbon dioxide pressure ($PaCO_2$) mmHg	Preoperative	37.13±4.15	37.18±4.15	0.970
	Postoperative 1. h	41.54±5.21	44.16±4.68	0.069
	Postoperative 6. h	39.87±4.35	40.63±3.88	0.523
	Postoperative 12. h	39.03±3.80	40.52±6.52	0.436
	Postoperative 24. h	39.92±4.10	41.63±4.07	0.146

perative hours. If acidosis had occured only due to the perioperative fluid infusion, we would have observed that it would last as long as maintenance fluid was given. Moreover, metabolic acidosis can develop after major abdominal surgeries due to several different mechanisms other than administration of high volume saline infusion. Lactic acidosis resulting from hypovolemia or decreased perfusion, ketoacidosis developing due to prolonged fasting or diabetes, or hyperphosphatemia may lead to metabolic acidosis (20).

It was documented in the study that while there was a significant increase in postoperative sodium values of saline-receiving group, there was a significant decrease in sodium values of RL Group. While the highest median sodium value reached 142 mEq L^{-1} in NS Group, the lowest median sodium value of RL Group was 130.69 mEq L^{-1} at the postoperative 6th hour and thus reached the limit of hyponatremia that needs therapy. Compared to the preoperative period, the reduction of 7.72 mEq L^{-1} was a high amount, it was found to be statistically significant. As sodium values of these patients had a tendency to increase at 12th and 24th hours, none of them required treatment.

When the patients in the study were compared regarding their potassium values, both groups were found to be normocalemic at all measurement times. When plasma chloride values were studied, there was a little increase in the NS Group only in the first postoperative hour. However, this increase quickly reduced to its preoperative level even though saline infusion was maintained till the 24th hour.

Dilutional hyperchloraemic acidosis is a temporary side-effect caused by high dose saline infusion and recovers between 24 and 48 hours (19). As Liu et al mentioned, although it is known that infusion of normal saline solution has an impact on hyperchloraemic metabolic

Table 4: Serum electrolytes (mean±SD)

		Ringer's Lactate	Normal Saline	p
Sodium (Na) mEq/L	Preoperative	138.41±3.28	136.38±2.17	0.043
	Postoperative 1. h	136.63±4.27	141.28±3.45	***0.000***
	Postoperative 6. h	130.69±24.01	139.77±3.48	***0.000***
	Postoperative 12. h	135.35±5.031	139.07±3.60	***0.000***
	Postoperative 24. h	135.61±4.49	142.08±2.95	***0.000***
Potassium (K) mEq/L	Preoperative	3.56±0.41	3.68±0.19	***0.449***
	Postoperative 1. h	3.66±0.48	3.44±0.37	***0.135***
	Postoperative 6. h	3.79±0.43	3.58±0.27	***0.084***
	Postoperative 12. h	3.72±0.54	3.53±0.42	***0.093***
	Postoperative 24. h	3.80±0.46	3.57±0.25	***0.022***
Cloride (Cl) mEq/L	Preoperative	106.23±4.17	109.13±4.25	***0.019***
	Postoperative 1. h	106.46±4.34	112.38±4.20	***0.000***
	Postoperative 6. h	104.81±4.40	110.88±3.60	***0.000***
	Postoperative 12. h	105.38±4.47	108.20±3.63	***0.012***
	Postoperative 24. h	105.27±4.50	110.38±1.93	***0.000***

acidosis, we do not have information whether it is harmful for the patients or not (21). Only when patients have underlying pathologies such as renal tubular acidosis or enteric fluid loss, saline infusion can cause to progression or exacerbation of disease. Handy and Soni (22) have inferred that there is limited evidence on morbidity resulting from normal saline solution that has been in use for 50 years.

There is a limitation of the present study that should be acknowledged. We did not monitored the parameters of renal and/or gastrointestinal functions of the patients in the postoperative period. However, if parameters regarding these systems had been studied, the results may have contributed to the interpretation of the obtained data.

CONCLUSION

The results of the present study indicated that normal saline infusion during total gastrectomy did not develop hyperchloremic metabolic acidosis except in the first postoperative hour and did not reach the level of hypernatremia; however, we observed a tendency to hyponatremia in patients receiving Ringers' Lactate. Therefore, we are in the opinion that normal saline infusion can be confidently used in major abdominal surgeries.

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