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Research Article

Effect of preoperative hypervolemic hemodilution with hydroxyethyl starch (130/0.4) on hemodynamics, blood loss and renal function after laparoscopic gastric bypass surgery

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KEYWORDS

Laparoscopic gastric bypass surgery;
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Hemodynamic;
Blood loss;
Renal function

Abstract *Background:* In a trial to overcome the adverse effects of pneumoperitoneum during laparoscopic gastric bypass surgery (GBP) on renal function this study investigated the effects of third generation HES 130/0.4 (6%) on renal function and blood loss during laparoscopic GBP.
Patients and methods: This study was carried out on 83 adult patients of both sexes scheduled for (GBP) surgery. Patients were randomly classified into Group I (42): received HES 130/0.4 10 ml/kg to a maximum volume 1000 ml, and Group II (41): received ringer acetate solution 10 ml/kg to a maximum volume 1000 ml within 30 min pre-operatively.
Mean arterial blood pressure (MABP) and heart rate (HR) were measured before starting of fluid infusion, and every 15 min till the end of surgery. Blood loss was assessed intraoperatively and postoperatively.
Intraoperative urine output was observed. Renal functions (blood urea, serum creatinine, and creatine clearance) were evaluated preoperatively and after 24 h postoperatively.
Results: Intraoperative and postoperative blood loss was comparable in both groups. Changes in mean arterial blood pressure (MABP), and heart rate (HR) were comparable in both groups except significant increase in MABP in group I from 30 min till 150 min intraoperatively (p values were 0.04, 0.03, 0.02, 0.04, 0.01, respectively). Creatinine clearance increased significantly at postoperative assessment time in group I, ($p = 0.04$). There was no significant difference between both groups regarding serum creatinine and blood urea. Intraoperative urine output significantly increased in group I, ($p = 0.02$).
Conclusion: Infusion of HES 130/0.4 has role in prevention of oliguria and provides renal protection without effect on hemostasis and intraoperative or postoperative blood loss.

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1. Introduction

Nowadays, usage of Laparoscopic gastric bypass surgery for treatment of obesity is increasing. It has many advantages for the patients as minimal incision, minimal trauma, decreased postoperative pain and reduced hospital stay [1]. However, this technique has potential complications as insufflation of carbon dioxide to create a pneumoperitoneum increases the intra-abdominal pressure which may compromise the renal function, which depends on different factors as the level of intra-abdominal pressure, baseline renal function, intravascular volume status, duration of procedure, and position of the patient during procedure [2–4].

This renal impairment is usually transient without sequelae but it may progress to be of clinical value especially in patients with impaired renal function or presence of co-morbidities such as diabetes, elevated intra-abdominal pressure, and hypertension [5].

HES is a colloid product often used for intravascular volume expansion in adults, especially in shock state caused by hemorrhage, burns, surgery, or trauma. It is a heterogeneous macromolecular agent derived from starch. It has a longer half-life and maintains hemodynamic stability more efficient than crystalloids. Its molecular weight is sufficiently low to allow for adequate metabolism and renal elimination, while maintaining osmotic activity. This helps to prevent the accumulation of HES in plasma after repeated doses. In recent studies, the advantage of it in intravascular volume expansion compared to crystalloids has been marginal [6]. In experimental studies, colloids demonstrate more rapid resuscitation and improved tissue perfusion compared to crystalloids [7]. Furthermore, complementary laboratory and clinical research has demonstrated the negative effects of large volume infusion of crystalloid that could affect kidney function indirectly [8].

This study was done to evaluate the effect of HES 130/0.4 6% on renal function, urine output, and postoperative bleeding following laparoscopic gastric bypass (GBP) surgery.

1.1. Patients and methods

After approval by our institutional ethical committee, written consent was obtained from all patients before getting them involved in the study. The steps of the study, the aims, the potential benefits and dangers, all were discussed with each individual patient. 88 enrolled, randomized and allocated into 2 groups and received intervention.

Exclusion criteria included hemoglobin < 10 gm/dl or hematocrit $< 30\%$, patients with clinically evident limitation of cardiac or pulmonary function, untreated hypertension, patients with impaired renal function, patients with liver disease, patients with bleeding disorder, and current anticoagulant therapy.

Preoperative examination was done by history taking, physical examination, and laboratory investigations including complete blood count, liver function, renal functions, ECG, chest X-ray, echocardiography, serum electrolytes, PT and PTT, and Pulmonary function test.

All patients were premedicated with 150 mg ranitidine and 10 mg of metoclopramide one hour before the procedure.

On arrival to the pre-operative preparation room, the patients were classified into 2 groups: Group I (44): received HES 130/0.4 10 ml/kg to a maximum volume 1000 ml preoperatively within 30 min, and Group II (44): received ringer acetate solution 10 ml/kg to a maximum volume 1000 ml preoperatively within 30 min.

Randomization was performed using a computer random number generator and the assignment entered in sealed envelopes that were opened by a chief nurse who did not participate in patients' care after obtaining informed consent.

On arrival to operating room the patients were attached to monitor displaying the following: ECG, noninvasive blood pressure, pulse oximetry, end tidal carbon dioxide, and heart rate. The patients were pre-oxygenated for 3 min before induction.

The anesthesia was induced by fentanyl 2 μg/kg, propofol 2 mg/kg and atracurium 0.5 mg/kg. After manual ventilation for three minutes endotracheal tube (ETT) was inserted and confirmed by clinical observation of chest wall movement, auscultation of chest and presence of square wave of capnogram. Then, the patients were connected to mechanical ventilation. The respiratory rate and tidal volume were adjusted to maintain an ETCO2 between 32 and 35 mmHg.

After securing the ETT, central venous catheter was inserted through right internal jugular vein for fluids, drugs infusion and measure the central venous pressure, urinary catheter was placed for monitoring of urine output and arterial line was inserted for blood sampling and blood gas.

Anesthesia was maintained by 100% oxygen and isoflurane 1–1.5%. Top up doses of atracurium and fentanyl were given when needed and the concentration of anesthesia was adjusted to maintain the BP and HR within 20% from baseline.

1.2. Fluid therapy

On arrival to the pre-operative preparation room, Group I received HES 130/0.4 10 ml/kg to a maximum volume of 1000 ml, and Group II received ringer acetate solution 10 ml/kg to a maximum volume of 1000 ml.

The subsequent fluid loss intraoperatively was replaced by ringer solution in a volume 1:1. Blood loss will be replaced by ringer solution in a volume 3:1 up to loss of 500 ml of blood and the subsequent blood loss was replaced by blood.

After completion of surgery, inhalational anesthesia was stopped and muscle relaxant was reversed with atropine and neostigmine and the patient allowed to breathe spontaneously.

The ETT was removed when the patients fulfilled the criteria of extubation (spontaneous eye opening, purposeful movement, intact reflex). After extubation the patients were transferred to postanesthesia care unit.

1.3. Measurements

Mean arterial blood pressure (MABP) and heart rate (HR) were measured before starting of fluid infusion as baseline, and every 15 min till the end of surgery. Blood loss was assessed intraoperatively and postoperatively. Intraoperative urine output was observed. Renal functions (blood urea, serum creatinine, and creatine clearance) were evaluated preoperatively and after 24 h postoperatively.

1.4. Statistical analysis

Sample size calculation was based on the assumption that creatinine clearance is the primary endpoint and 40 patients were

needed to get an 80% power to detect a 35% difference between groups with a 5% (two-sided) type I error. For possibility of dropout of some patients 10% was added to each group so 44 patients were included in each group. The statistical analysis was done using SPSS Version 20 for Macintosh. Demographic, hemodynamic and laboratory data were compared with the *t*-test, Mann–Whitney *U*-test or χ^2-test as appropriate. The level of statistical significance was set to allow an alpha error of 5% (value of 0.05).

2. Results

83 patients completed the study protocol: 42 patients in group I and 41 patients in group II, and 5 patients were excluded because of changing the procedure plan to open surgery because of either intraoperative bleeding or extensive adhesion. There were no significant differences between patients in each group as regards age, sex, body mass index, pneumoperitoneum pressure and pneumoperitoneum duration (Table 1).

Intraoperative and postoperative blood loss was comparable in both groups, p value >0.05, Table 1.

MABP was significantly higher in Group I than Group II at 30, 60, 90, 120 and 150 min (p values were 0.04, 0.03, 0.02, 0.04, 0.01, respectively), Table 2.

Table 3, summarizes the changes in renal parameters and showed that, at baseline, variables were similar and within the normal range in both groups. The comparison shows that creatinine clearance was significantly higher in group I compared with group II, p value 0.04. There was no significant difference between both groups regarding serum creatinine and blood urea. Intraoperative urine output was significantly higher in group I compared with group II p value 0.02.

3. Discussion

Laparoscopic bariatric surgery, particularly laparoscopic GBP, is a complex operation often associated with a longer operative time than other commonly performed laparoscopic procedures. A longer operative time during laparoscopic GBP translates to longer exposure of the host to the adverse physiological effects of pneumoperitoneum. Therefore, anesthetist giving anesthesia for laparoscopy in morbidly obese patients should understand the basic physiologic changes occurring during pneumoperitoneum, recognize the clinical changes, and make appropriate intraoperative adjustments to minimize the adverse changes. One of the measures to minimize the effects of increased intraabdominal pressure on renal and cardiac function is optimization of intravascular volume.

The reduction in intraoperative urine output has been well documented during laparoscopic operations [9,10] and the degree of intraoperative oliguria is dependent on the level of increased intraabdominal pressure; higher intraabdominal pressures resulted in a greater degree of oliguria [10]. Intraoperative urine output in morbidly obese subjects decreased immediately

Table 1 Patients characteristics, pneumoperitoneum pressure and duration; data are presented as mean ± SD or numbers.

	Group I $N = 42$	Group II $N = 41$	P
Age	32.5 ± 11.5	30.4 ± 10.6	0.8
Sex male/female	18/24	17/24	0.4
Body Mass Index (BMI)	53.6 ± 5.9	52.4 ± 7.8	0.6
Pneumoperitoneum pressure (mmHg)	13.6 ± 0.5	13.4 ± 0.6	0.4
Pneumoperitoneum duration (min)	180.7 ± 15.7	175.5 ± 20.8	0.7
Intra-operative blood loss (ml)	150.8 ± 20.8	170.6 ± 18.7	0.6
Post-operative blood loss (ml)	50.7 ± 15.5	55.7 ± 14.7	0.5

Table 2 Hemodynamic data including mean arterial blood pressure and heart rate in both groups; data are presented as mean ± standard deviation.

Hemodynamic data	Group I	Group II	P value
MABP (mmHg)			
T0	95 ± 5.7	96 ± 5.6	0.3
T1	90 ± 7.8	80 ± 8.7	0.04*
T2	92 ± 6.7	82 ± 6.8	0.03*
T3	94 ± 7.6	84 ± 7.8	0.02*
T4	92 ± 5.8	80 ± 6.8	0.04*
T5	90 ± 4.9	85.3 ± 6.5	0.01*
T6	87 ± 6.7	86.4 ± 4.3	0. 5
T7	86.3 ± 5.5	86.3 ± 5.8	0.7
HR beat/minute			
T0	79 ± 6.5	82 ± 8.6	0.3
T1	86 ± 6.8	90 ± 4.6	0.2
T2	84 ± 5.6	85 ± 6.5	0.6
T3	83 ± 4.7	81 ± 5.8	0.4
T4	86 ± 5.8	88 ± 4.8	0.5
T5	84 ± 4.7	85 ± 4.5	0.5
T6	79 ± 5.4	80 ± 6.8	0.6
T7	81 ± 4.5	82 ± 7.5	0.4

T0 = Base line, T1 = 30 min after induction, T2 = 60 min after induction, T3 = 90 min after induction, T4 = 120 min after induction, T5 = 150 min after induction, T6 = 180 min after induction, T7 = 210 min after induction.
* p value <0.05 (significant difference between both groups).

Table 3 Renal functions including creatinine clearance, serum creatinine, blood urea and urine output; data are presented as mean ± standard deviation.

	Group I $N = 42$	Group II $N = 41$	P value
Creatinine clearance preoperatively (mL/min)	115 ± 27.6	118 ± 28.7	0.4
Creatinine clearance postoperatively (mL/min)	140 ± 15.7	100 ± 6.7	0.04
Serum creatinine preoperatively (mg/dL)	0.7 ± 0.04	0.8 ± 0.06	0.3
Serum creatinine postoperatively (mg/dL)	0.8 ± 0.07	1.2 ± 0.1	0.5
Blood urea preoperatively (mg/dL)	20.8 ± 5.8	22.6 ± 4.3	0.5
Blood urea postoperatively (mg/dL)	30 ± 7.8	42 ± 6.9	0.06
Intra-operative urine output (l)	1.5 ± 0.04	0.5 ± 0.01	0.02

after initiation of pneumoperitoneum during laparoscopic GBP and remained lower than during open GBP [11].

The reduction in intraoperative urine output during laparoscopic operations could be explained by: Pneumoperitoneum has a direct pressure effect on the renal cortical blood flow [12] and renal vasculature, resulting in reduced renal blood flow [13], release of certain hormones such as antidiuretic hormone (ADH), plasma rennin activity, and serum aldosterone may diminish urine output [14].

Hydroxyethyl starch (HES) 130/0.4 is indicated for the treatment and prophylaxis of hypovolemia. As its molecule is smaller than the other available hydroxyethyl starch products, it is associated with less plasma accumulation and can be safely used in patients with renal impairment. Previous studies have demonstrated that it has comparable effects on volume expansion and hemodynamics as other available HES products. It is also associated with fewer effects on coagulation and may be an acceptable alternative to albumin for volume expansion in situations in which other starches are contraindicated secondary to risk of coagulopathy [15].

In a trial to overcome the adverse effects of pneumoperitoneum during laparoscopic GBP on renal function we investigated the effects of third generation HES 130/0.4 (6%) on renal function and blood loss during laparoscopic GBP. We revealed that, infusion of HES 130/0.4 has role in the prevention of oliguria and provide renal protection without effect on hemostasis and intraoperative or postoperative blood loss. This could be explained by the state of hypervolemia which occurred after infusion of HES 130/0.4 and remained in the circulation longer than crystalloid which led to stable hemodynamics during surgery and no episodes of hypotension with near normal mean arterial blood pressure which provides adequate renal perfusion and adequate urine output intraoperatively and normal renal function postoperatively so we can conclude that the state of hypervolemic hemodilution with HES 130/0.4 after induction of anesthesia can overcome the adverse effect of prolonged pneumoperitoneum on renal function and provide renal protection during GBP. Also, the HES 130/0.4 has rapid metabolism and renal excretion and is more superior as regards renal safety when compared to older type of HES.

Demyttenaere et al. [16] concluded that both renal function and renal blood flow (RBF) are decreased during pneumoperitoneum. The magnitude of the decrease is dependent on factors such as preoperative renal function, level of hydration, level of pneumoperitoneum, patient positioning, and duration of pneumoperitoneum.

In agreement with the present study, Jover et al. [17] concluded that, prehyderation with HES can be an effective method in renal protection during laparoscopic cholecystectomy. Also Osthaus et al. [18] revealed that the negative effects of prolonged pneumoperitoneum (PP) on hemodynamics and acid-base balance can be obviated by a liberal plasma volume stabilization regimen with colloids. Also, an experimental study by London et al. [19] concluded that Intravascular volume expansion alleviates the effects of CO2 pneumoperitoneum on renal hemodynamics in a porcine model. Hypertonic saline (7.5% NaCl) solution may maximize renal blood flow in prolonged pneumoperitoneum, but it does not completely prevent renal dysfunction in this setting. This study suggests that routine intraoperative volume expansion is important during laparoscopic live donor nephrectomy.

Regarding, intraoperative and postoperative blood loss, the present study found that the infusion of new HES has no effects on homeostasis and no major blood loss has occurred. This is in agreement with Jungheinrich et al. [20] who showed that the perioperative infusion of hydroxyethyl starch 130/0.4 (6%) in orthopedic surgery resulted in a normal coagulation profile 5 h post surgery, in contrast to hydroxyethyl starch 200/0.5. This could be explained by rapid normalization of decreased von Willebrand factor and factor VIII due to the faster elimination of hydroxyethyl starch 130/0.4 compared with hydroxyethyl starch 200/0.5 [21–23].

The increased therapeutic safety index of the third-generation hydroxyethyl starch 130/0.4 compared with hydroxyethyl starch 200/0.5 was acknowledged by European regulatory authorities by increasing the maximum daily dose to 50 mL/kg bodyweight, which is the highest dose for any hydroxyethyl starch type approved so far [24].

In contrast to the present study, Chan et al. [25] concluded that the use of HES is unnecessary and should be avoided in most elective bariatric surgery cases as it leads to coagulation abnormalities and increases the risk of postoperative bleeding.

4. Conclusion

Infusion of HES 130/0.4 has role in prevention of oliguria and provides renal protection without effect on hemostasis and intraoperative or postoperative blood loss.

Conflict of Interest Disclosure

The authors have no conflict of interest.

Criteria for authorship

Sabry M. Amin conceptualized and designed the study; drafted the article; and revised the article.

Sameh M. Fathy did the literature search; analyzed and interpreted the data; and edited the manuscript.

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