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The Use of Glucose 5% as Irrigating Fluid During Hysteroscopy Reduces the Incidence of Hypontremic Encephalopathy. Double Blinded Randomized Study

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Abstract

Background: Excessive absorption of irrigating fluid during endoscopic surgical procedures produces central nervous system changes, circulatory disturbances and electrolyte imbalances. Wecompared glycine 1.5% versus glucose 5% as irrigating solutions in patients undergoing hysteroscopy for various diagnostic or therapeutic purposes.

Patients and methods: One hundred patients were randomized into two equal groups according to the irrigation fluid used. Fifty patients used glycine 1.5% solution as irrigating fluid (**glycine group**) and 50 patients used glucose 5% solution (**glucose group**) as irrigating fluid during hysteroscopy.Patient's demographics, operative time, postoperative amino acid glycine assay and peri-operative complications were observed

Results: No difference was found in the immediate pre-operative mean values of serum sodium, potassium, hemoglobin, and hematocrit in both groups. Elevated glycine levels were observed in 14 patients, hyponatremia developed in 11 patients, and encephalopathy developed in 6 patients in the glycine group.Patients in glucose group developed significant post-operative hyperglycemia, none of the patients developed manifest hyponatremia or encephalopathy

Conclusion: The use of glucose 5% solution as irrigating fluid during hysteroscopy produced transient postoperative decrease in serum sodium, potassium and significant hyperglycemia. None of the patients developed hyponatremic encephalopathy in glucose group.

Keywords: Hysteroscopy; Irrigation solution; TURP syndrome; Glycine solution; Glucose 5% solution

Introduction

Hysteroscopic surgical procedures are more commonly used because of their high diagnostic accuracy; resection of lesions and their high safety profile. Endometrial ablation for treatment of dysfunctional uterine bleeding can be performed using electrosurgical diathermy;however these procedures are not without potential complication [1]. The use of an irrigatingfluid is mandatory for proper visualization of the operating field and to wash away debrisand blood; while excessive absorption of these hypotonic fluids could lead to hypervolemia and manifest hyponatremia and may even progress to encephalopathy [2]. Menstruate women are more vulnerable for development of hyponatremic encephalopathy mostly due to increased anti-diuretic hormone level in these patients [3,4]. Glycine is a commonly used irrigation fluid because it is devoid of any allergic potential; transparent and inexpensive in cases of low economic states. However; the solution is un-physiological and absorption of more than 2000 ml could leads to pathological manifestation that ranges from nausea; vomiting; confusion and arterial hypotension up to myocardial infarction and even death [5].

The glucose 5% solution is readily metabolized when absorbed and excessive absorption is without recognizable complication [6]. The aim of this study is to compare peri-operative morbidity especially hyponatremic encephalopathy in women undergoing hysteroscopic procedures usingglycine 1.5% versus glucose 5% as irrigating solutions.

Patients and Methods

The study was approved by an Investigational Review Board of Faculty of Medicine; Tanta University; an informed written consent was obtained from all patients participating in the study. This study was registered in the Pan African Clinical Trail Registry under unique identification number PACTR 201209000409253.

A total of one hundred patients undergoing operative hysteroscopy were enrolled into the study. Patients were randomly allocated into two equal groups according to the irrigating fluid used; fifty patients usedglycine 1.5% solution (glycine group)and fifty patients used glucose 5% (glucose group) as irrigating fluid during hysteroscopy.

Randomization was performed using closed envelopes contain either (G1) card for glycine group or (G2) card for glucose group. Glycine and glucose solutions used for irrigation were prepared in clear containers where their label are removed and relabeled as (G1) for glycine group and (G2) for glucose group. Envelopes; cards and irrigation fluids bags were prepared by anesthetist who is not participating in the study in collaboration with hospital pharmacist.An anesthetist who is not aware by the study design or data collection enrolled the patients

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in their corresponding group till the desired number of patients was achieved. None of the patients or physician responsible for follow up or data collection was aware by group assignments.

Hysteroscopy was performed using 24 Ch continuous irrigating resectoscope (Storez;Tottling; Germany). Endometrial ablation was performed used 24 Ch cutting loop and 24 Ch roller loop as a working element for resectoscope for monopolar current (Storez; Tottling; Germany). The amount of irrigation fluids used is calculated depending upon gravimetric methods; the height of the irrigating fluid reservoir is fixed at 60 cm height from patients' bed to maintain the intrauterine pressure limited to 60 cm H_2O during hysteroscopy procedure.

All patients had been designed to receive spinal anesthesia. Evaluation of the patients included full medical history; ultrasound for abdomen and pelvis; in addition to routine laboratory investigations. Patients with bleeding diathesis or coagulopathy; diabetes mellitus and apparent cardiac; pulmonary or renal disease were excluded as well as patients with any contraindication to spinal anesthesia.

One hour before induction of spinal anesthesia; all patients were pre-loaded with 500 ml ringer solution. Hemodynamic monitoring including:heart rate; electrocardiogram and mean arterial blood pressure were recorded.Immediate pre-operative as well as post-operative hematocrit; hemoglobin; serum sodium; potassium; blood urea; serum creatinine and random blood glucose were measured.

Hypontremic encephalopathy is a central nervous system dysfunction secondary to severe hyponatremia (serum sodium of 125mmol/l or less); these central nervous system manifestations include headache; nausea; vomiting; mental confusion; anxiety; parasthesia or visual disturbance that may progress to seizures; respiratory arrest andnon-cardiogenic pulmonary edema [7].

Glycine Assay Using Thin Layer Chromatography

Thin layer chromatography is used as a semi-quantitative method for amino acid glycine separation and assay.The principle of the separation depends on differences in both the degree of adsorption by the adsorbent and solubility in the solvent used for separation; using a uniform thin layer of adsorbent on a supporting glass plate then plates are dried in an oven at 100-120°C[8].

Statistics

Student t test was used for analysis of continuous variables. Chi-squared statistic was used to test the differences in proportions. Descriptive statistics were reported as percentages for proportions while;mean and standard deviation for continuous values. The results were considered significant at the 5% critical level (a two-sided) P value (0.05).

A sample size analysis determined that 49 patients per group were required to detect difference of at least 20% in serum sodium with a power of 80%; α of 0.05 and allocation ratio of 1:1; so we included 50 patients in each group.

Results

There is no significant difference between the two groups regarding the patients' demographics; type and duration of surgery. Endometrial resection was performed in sixty patients; thirty-two in glycine group and twenty-eight in glucose group. Eighteen patients performed diagnostic hysteroscopy in glycine group compared to twenty-two patients in glucose group (Table 1).

Parameters	Glycine group (n=50)	Glucose group (n=50)
Age (years)	32.6 ± 12.5	34.5 ± 14.2
Weight (Kg) mean ±SD	75.4 ± 10.5	72.8 ± 11.8
Height (cm)mean ±SD	162 ± 15.9	164 ± 17.5
Operative time (min)	39.5 ± 10.2	37.3 ± 12.8
Type of surgery†:		
Endometrial ablation	32 (64%)	28 (56%)
Diagnostic hysteroscopy	18 (36%)	22 (44%)

Student t test was used.
†Chi-squared test was used.

Table 1: Patients characteristic in both groups.

	Pre-op Gly/Glu	10min Gly/Glu	20min Gly/Glu	30min Gly/Glu	60min Gly/Glu	post-op Gly/Glu
HR	79.6/78.8	62.5*/61.4*	67.2/68.5	72.1/74.8	61.6*/62.4*	60.5*/61.8*
MABP	75.5/76.5	60.6*/61.4*	69.9/70.8	76.2/77.2	87.6/86.5*	89.5/88.4*

Gly/Glu: Glycine/Glucose groups.
MABP: mean arterial blood pressure (mmHg)
HR: heart rate (beat/m)
Student t test was used
*Significant change (p<0.05%)

Table 2: Homodynamic Changes in the Studied Groups.

The hemodynamic changes regarding heart rate and mean arterial blood pressure were compared in both groups. There was a non-significant difference in the pre-operative mean heart rate values between both groups (79.6 ± 11.5 beat/min & 78.8 ± 10.6 beat/min). The heart rate mean values showed significant decrease after 10 min (62.5 ± 10.8 beat/min & 61.4 ± 10.3 beat/min); 60min (61.6 ± 9.1 beat/min & 62.4 ± 10.7 beat/min) and in the immediate postoperative period (60.5 ± 9.5 beat/min & 61.8 ± 10.5 beat/min) in the glycine and glucose groups respectively in comparison to pre-operative mean values. However, insignificant change in the heart rate mean value was found after 20 min (67.2 ± 10.6 beat/min & 68 ± 11.3 beat/min) and 30 min (72.1 ± 10.7 beat/min & 74.8 ± 9.4 beat/min) in both groups in comparison to pre-operative mean values (Table 2).

There was a non-significant difference in the preoperative mean arterial blood pressure between groups. Significant decrease 10 min after induction of anesthesia to mean values of 60.6 ± 10.5 mmHg & 61.4 ± 11.7 mmHg in both groups respectively in comparison to pre-operative mean values. After 20 and 30 min no significant change was found (69.9 ± 11.6 mmHg & 70.8± 12.5 mmHg) and (76.2 ± 10.4 mmHg & 77.2 ± 9.5 mmHg) in both groups respectively in comparison to pre-operative mean values. However, significant increase was found after 60 min (87.6 ± 10.5 mmHg & 86.5 ± 10.2 mmHg) and in the immediate post-operative period (89.5 ± 9.5 mmHg & 88.4 ± 10.2 mmHg) in the both groups respectively in comparison to pre-operative mean values (Table 2).

There was a non-significant difference in the mean value of the pre-operative hemoglobin; serum sodium; serum potassium and random blood sugar.The mean value of fluid absorption in glycine group was 560 ml; while it was 520 ml for glucose group.

The pre-operative hemoglobin was 11.7 ± 1.8 gm/dl and 11.5 ± 2.5 gm/dl, which decreased to 10.2 ± 1.5 gm/dl and 10.5 ± 1.45 gm/dl in glycine and glucose groups respectively.

Insignificant decrease in the post-operative serum sodium in both groups was observed but more marked in glycine group; the pre-operative mean value of serum sodium was 135.62 ± 3.79 mmol/l in glycine group and decreased to 129.7 ± 15.4 mmol/l; while pre-operative mean value in glucose group was 137.2 ± 14.2 mmol/l which decreased

to 134.5 ±10.2 mmol/l. Insignificant reduction in post-operative mean value of serum potassium was observed which is more pronounced in glucose group; the mean pre-operative value was 4.52 ± 0.3 mmol/l and decreased to 3.55 ± 0.75 mmol/l; while in the glycine group the pre-operative mean value was 4.35 ± 0.45 mmol/l and decreased to 3.95 ± 0.85 mmol/l post-operatively. The pre-operative random blood sugar was 95.8 ± 25.9 mg/dl in glycine group which revealed no significant elevation in the postoperative period to a mean value of 117.5 ± 15.2 mg/dl, while the mean pre-operative mean value in glucose group was 105.2 ± 18.4 mg/dl which revealed a significant elevation to mean value of 185.5 ± 29.5 mg/dl; which returned back to normal values within 6 hours (Table 3).

An elevated glycine level was observed in 14 patients; hyponatremia developed in 11 patients and encephalopathy developed in 6 patients in glycine group. The mean value of glycine absorption was 980 ml in hypontraemic patients and 1375 ml for patients who developed encephalopathy. Two patients in glycine and one patient in glucose group needed blood transfusion; that experienced a decrease in hemoglobin concentration to less than 9 g/dl (Table 4).

Discussion

This study was designed to evaluate the use of glucose 5% solution as irrigating fluid during hysteroscopy; patients used glucose 5% manifested transient post-operative decrease in serum sodium; more manifested decline in serum potassium and significant immediate post-operative hyperglycemia. None of the patients developed hyponatremic encephalopathy in glucose group; compared to 11 patients who developed hyponatremia and 6 patients developed encephalopathy in glycine group.

During roller ball ablation fluid absorption is directly from disrupted endometrial and myometrial surfaces; this absorption is infusion pressure dependant and indirectly from the peritoneal surfaces after trans-tubal spillage. Menstruate women are more susceptible to hyponatremic encephalopathy due to elevated ADH levels due to increased estrogen and progesterone which causes the release of ADH [3].

Serum Na response to fluid irrigation is 40% greater in females. The amount of extracellular water which is the distribution volume for sodium is about 200 ml/kg body weight in males and 150 ml/kg body weight in women [4].

Systemic absorption of these fluids could produce significant consequences. These consequences depend on the rate; volume and nature of the fluid absorbed. Absorption of small amounts of fluid occurs in 5-10% of patients with mild symptoms. Large volume fluid absorption is rare; but leads to critical manifestation that require intensive care admission [5]. There are several irrigating fluids available for use during endoscopic surgery. The choice depends to large extent upon the price and properties of the fluid [9]. Glycine solution is the most commonly used irrigate; it is a non-essential amino acid with serum level less than 400 µmol/l; higher concentration produces serious potential complication such as hyponatremia [10].

The hyponatremia associated with glycine absorption is partly due to dilution effects; beside the loss of sodium in urine, which represents an absolute loss [11]. Elevated serum glycine increases the release of atrial natriuretic peptide in excess of that expected from the volume absorbed; which will further promote natriuresis. Hyponatraemia; leads to cerebral edema; which manifest itself by restlessness; agitation; confusion; altered sensation; seizures and coma [12].

Glycine is an inhibitory neurotransmitter and high glycine levels cause abnormal electroencephalographic activity; visual disturbances and transient blindness [13].

Glucose 5% is a partially safe fluid when used as irrigating fluid. It is more physiological because it can be given intravenously with lower incidence of complication.Glucose 5% solution is considered a standard crystalloid; because it is metabolized throughout the body. Intravenous infusion of about 13 L of glucose 5% only expands the intravascular compartment by 1 L. The osmolality of glucose 5% is about 285 mosmol/kg; which is close to normal serum osmolality 290 mosmol/kg; while that of glycine is 190 mosmol/kg. This higher osmolality provided by glucose 5% solution may be beneficial in reducing the possible side effects of cerebral edema [12]. Previous studies concluded that the use ofglycine 1.5% solution as irrigating fluid in endoscopic surgery is associated with higher glycine levels; higher incidence of hyponatremia and the associated complications; while glucose 5% is a safer alternativein endoscopic surgery [9,10,14].

Parameters	Glycine group (n=50)	Glucose group (n=50)
Hemoglobin (gm/dl)	10.2 ± 1.5	10.5 ± 1.45
Sodium (mmol/l)	129.7	134.5
Potassium (mmol/l)	3.95	3.55
Random blood sugar (mg/dl)	117.5	185.5*
Fluid absorption (ml)	560	520

Student t test was used.
*Significant change (p<0.05%)

Table 3: Chemical, hematological and fluid absorption mean values in the studied groups in the immediate postoperative period.

Parameters	Glycine group (n=50)	Glucose group (n=50)
Hyponatremia	11*	0
Hyperglycinemia	14*	0
Encephalopathy	6*	0
Blood transfusion	2	1

†Chi-squared test was used.
*Significant change (p<0.05%)

Table 4: Peri-operative complications in the studied groups.

Conclusion

The use of glucose 5% solution as irrigating fluid during hysteroscopy produced transient post-operative decrease in serum sodium; potassium and significant hyperglycemia. None of the patients developed significant hyponatremia or encephalopathy.

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