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Original Article

A comparison of the effects of 1.5% glycine and 5% glucose irrigants on plasma serum physiology and the incidence of transurethral resection syndrome during TURP surgery

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Background: Brain changes, circulatory and electrolyte imbalances are the main complications of transurethral resection of the prostate (TURP) surgery, known as transurethral resection (TUR) syndrome which is the result of excessive absorption of irrigating fluid. For this surgical procedure 1.5% glycine and 5% glucose are commonly used as irrigants.

Objectives: To observe the changes in the serum electrolytes and occurence of the transurethral resection syndrome (TUR) with 1.5% glycine and 5% glucose as irrigant.

Methods: Between June 2008 and May 2010, 120 patients were included in a prospective randomized comparative trial comparing 1.5% glycine with 5% glucose irrigation fluids. We measured blood loss, fluid absorption, biochemistry including serum electrolytes, RBS and perioperative symptoms. Blood samples were taken before and immediately and 24 h after TURP. Irrigating fluid absorption during TURP was measured by serum sodium level. Operative details were recorded, including the type of anaesthesia (with or with no sedation), resection time and weight of resected tissue. Perioperative symptoms were documented prospectively. TUR syndrome was defined as a serum sodium level of ≤ 125 mmol/L with two or more associated symptoms or signs of TUR syndrome.

Results: Two (1.67%) patients had TUR syndrome; all two were irrigated with glycine, although this difference was not statistically significant (p=0.10). There was no difference between the groups in levels of sodium, potassium, urea, creatinine or perioperative blood loss.

Conclusions: Both irrigants were associated with low perioperative morbidity including TUR syndrome. Except for the transient postoperative hyperglycemia in glucose group, both irrigants are nearly equivalent and safe.

Declaration of interest: None

Keywords: TUR syndrome; TURP, 1.5% glycine; 5% glucose; irrigation fluids.

Introduction

Transurethral resection (TUR) syndrome is a multifactorial syndrome, which occurs from absorption of large volume of irrigation fluid during transurethral procedure, typically dur-ing a transurethral resection of the prostate (TURP). Although it is commonly thought to be due to dilutional hyponatraemia exclusively, fluid overload and effects of glycine toxicity contribute significantly to the pathophysiology and symptomatology of this condition.[1] Since the introduction of TURP by McCarthy in 1926, the problem of which irrigation flu-id to use during the procedure has caused wide-ranging debate, up to and including the present. For standard TURP, the criteria for an ideal irrigant are: it must irrigate the surgical field; not be an electrical conductor and not affect diathermy; have good visual acuity and be 'user-friendly'; have similar osmolality to serum; minimal side-effects when absorbed; and can be detectable by the surgeon when excess volume is absorbed.

Several irrigant solutions are available, including sorbitol-mannitol solution and glycine solution; the former is used in Europe but glycine solution is most commonly used in the UK and North America. There is now increasing evidence highlighting the toxicity of 1.5% glycine solution when absorbed during TURP.[1] Glycine solution, used in TURP for more than 50 years, is the most commonly used irrigant. TURP has several recognized complications; one of the more serious and potentially fatal is the TUR syndrome. Glycine is an amino acid present in humans at concentrations <400 µmol/L; at higher concentrations it has shown direct and indirect cardiotoxic effects in animal studies[2] and pathophysiological action in stimulating the release of atrial natriuretic peptide, thereby enhancing sodium loss and contributing to hyponatraemia, which is part of the TUR syndrome.[3]

Kirollos et al. (1997) described that their clinical experience of over 20 years lead them to think that 5% glucose solution used as an irrigant is not toxic and is entirely satisfactory as an irrigating fluid for use during TURP.[4] A solution of 5% glucose is a standard crystalloid. Because glucose is metabolized throughout the body, it requires 13L to be given/absorbed intravenously to expand the intravascular compartment by 1L. Normal serum osmolality is 290 mosmol/kg. The osmolality of 5% glucose is 285 mosmol/kg, as opposed to the osmolality of 1.5% glycine, which is 190 mosmol/kg. This higher osmolality provided by 5% glucose solution may be beneficial in reducing the possible side-effects of cerebral oedema, which can occur after inadvertent absorption of irrigating fluids.

Incidence of TUR syndrome range from 0% to 10%, but it is currently poorly defined and many mild cases can be falsely attributed to old age, anaesthetic complications and exces-sive blood loss.[5] All these evidences suggest that 5% glucose may be safer than 1.5% gly-cine as an irrigating fluid to be used during TURP. Several studies have reported that 1.5% glycine is a better irrigant than 5% glucose during TURP. But no such study has yet been conducted in the context of our country. So a comparative study to evaluate the safety and efficacy of 1.5% glycine and 5% glucose seems to be essential to guide our urologists in this regard.

Methods

Between june 2008 and May 2010, 120 patients undergoing TURP in the Department of Urology, Sir Salimullah Medical College & Hospital (SSMC), Dhaka, Bangladesh, were recruited to a prospective comparative trial, and randomly allocated to either irrigation during TURP with 1.5% glycine or 5% glucose solution. All patients were given an explanation of the study and informed written consent was taken from each patient. Randomization was performed by computergenerated random allocations sequence by simple randomization.

Patients undergoing TURP with spinal anesthesia were included in the study. Patients 1) receiving sedation 2) having diabetes mellitus or other metabolic acidosis 3) undergoing TURP with general anesthesia 4) Bleeding disorders or existing coagulopathy 5) apparent cardiac disease with ECG evidence of ischemia, history of myocardial infarctions and congestive cardiac failure, 6) renal insufficiency as well as 7) any contraindication to spinal anesthesia 8) Significant elevation of serum prostate specific antigen (PAS) were excluded from the study.

All patients were given spinal anesthesia, surgery was commenced when adequate sensory block to T10 at the umbilical level was achieved. Surgical intervention was performed by specialists. Preoperative evaluation of the patients included complete medical history, ultrasound for abdomen and pelvis, routine laboratory investigations (complete blood count, blood urea nitrogen, blood sugar, serum sodium, serum potassium) and PSA. Preoperative as well as immediate postoperative hemoglobin, serum sodium and potassium, blood urea, serum creatinine and random blood glucose were measured. No patients had received colloid, plasma products, hypertonic saline, diuretic therapy or blood transfusion approximately 10 hours before surgery. All patients were pre-loaded with

500ml ringer solution half an hour before induction of spinal anesthesia. No patients received intravenous glucose or glu-cose saline before, during or immediately after surgical procedure.

Hemodynamic monitoring including: heart rate (HR), blood pressure were recorded. Hypotension, defined as 20% fall in blood pressure from preinduction levels or a systolic blood pressure lower than 100 mmHg, was treated immediately by intravenous ephedrine. The amount of irrigation fluids used in each patient is calculated and the height of the irrigating fluid reservoir is fixed at 60cm height from patients' bed. Operative details including operation time, resected tissue weight, irrigating volume used, evidence of prostatic capsule perforation as well as any perioperative complication were recorded. The amount of irrigant absorbed was measured by level of serum sodium, the total irrigation fluid absorbed by each patient was recorded. A standard protocol was for two 8-hourly bags of normal saline to be prescribed; no patient received i.v. dextrose or dextrose saline after undergoing TURP. After TURP, in recovery, blood samples were taken to measure haemoglobin, sodium, potassium, urea, creatinine, glucose. Blood samples were rechecked at 24 h after TURP, and all results compared with values before TURP.

Fluid absorption was quantified by measuring serum sodium in all cases where the solution lacks electrolytes. As a rule, serum sodium was measured at the end of surgery. The hyponatraemia then correlates with the amount of absorbed fluid, although smaller absorption events may be blurred by variability and the sodium content of other infusions. TUR syndrome was defined as a serum sodium level of ≤125 mmol/L with two or more associated symptoms or signs of TUR syndrome. A checklist used to define and score symptoms included in the TUR syndrome (Table 1).

Table 1: Severity score of TUR syndrome

Symptom	Severity score		
	1	2	3
Circulatory			
Chest pain	Duration <5 min	Duration >5 min	Repeated attacks
Bradycardia	HR decrease 10–20 bpm	HR decrease >20 bpm	Repeated decrease
Hypertension	SAP up 10–20 mm Hg	SAP up >30 mm Hg	Score (2) for 15 min
Hypotension	SAP down 30–50 mm Hg	SAP down >50 mm Hg	Repeated drops >50 mm Hg
Poor urine output	Diuretics are needed	Repeated use	Diuretics ineffective
Neurological			
Blurred vision	Duration <10 min	Duration >10 min	Transient blindness
Nausea	Duration <5 min	Duration 5–120 min	Intense or >120 min
Vomiting	Single instance	Repeatedly, <60 min	Repeatedly, >60 min
Uneasiness	Slight	Moderate	Intense
Confusion	Duration <5 min	Duration 5–60 min	Duration >60 min
Tiredness	Patient says so	Objectively exhausted	Exhausted for >120 min
Consciousness	Mildly depressed	Somnolent <60 min	Needs ventilator

Analysis of covariance was used to test for differences between the blood values the day after TURP for the two treatment groups, adjusting for baseline (before TURP) values. Interaction between treatment groups and baseline values were examined and retained if significant at the 5% level. If thy baseline values did not influence the next day values, either a independent sample t-test or a Wilcoxon test was used to assess the next day values as appropriate.

Results

Sixty patients were in the 5% glucose group, the mean age and weight of the patients were 62.6 years and 57.1 kg respectively, mean volume of the irrigant used was 12.1 litres, mean volume of irrigant absorbed was 1.6 litres, mean duration of TURP was 65.4 minutes, mean weight of the resected tissue was 56.5 gm and evidence of prostatic capsule perforation was three in number. Sixty patients who were in the 1.5% glycine group, had mean age and weight of 62.1 years and 58.8 kg respectively, mean volume of the irrigant used was 12 litres, mean volume of irrigant absorbed was 1.61 litres, mean duration of TURP was 63.8 minutes, mean weight of the resected tissue was 63.8 gm and evidence of prostatic capsule perforation was four. Table 2 comapres the biochemical and hematological parameters of the two groups before TURP; there was no statistically significant difference between two groups.

Table 2: Biochemical and hematological values of studied groups before TURP (N=120)

Variable	Glucose group (n=60)	Glycine group (n=60)	P value
S. Sodium (mmol/L)	137.7±1.8	137.7±1.9	0.25
S. Potassium (mmol/L)	4.00±0.22	3.99±0.23	0.40
B. Urea (mmol/L)	27.1±5.8	27.3±4.7	0.36
S. Creatinine (mg/dl)	1.07±0.22	1.12±0.17	0.08
Haemoglobin (gm/dl)	11.3±0.50	11.5±0.54	0.14
RBS (mmol/L)	5.85±0.51	5.83±0.49	0.16

Cell values are mean±SD; Z-tests were used to calculate p value; S-serum; RBS-Random Blood Sugar

Two of the 120 patients developed TUR syndrome (1.6%). All two were irtrigated with 1.5% glycine solution and none of the patients in the glucose group had TUR syndrome. This defference did not reach statistical significance (p=0.10). Of the two patients who had TUR syndrome, one had bradycardia, nausea, blurring of vision and both were hypoten-sive, drowsy, confused, had pricking sensantion and experienced uneasiness.

Table 3: TUR syndrome by irrigation fluid groups after TURP (N=120)

Irrigation fluid	TUR syndrome		Total	P Value
	No	Yes		
Glucose 5% group	60	0	60	0.10
Glycine 1.5% group	58	2	60	
Total	118	2	120	

TUR syndrome: transurethral resection syndrome; p value measured from chi-sqaure test

Table 4 comapres the biochemical and hematological parameters of the two groups after TURP; there was no statistically significant difference between two groups.

Table 4: Biochemical and hematological values of studied groups immediately after TURP (N=120)

Variable	Glucose group (n=60)	Glycine group (n=60)	P value
S. Sodium (mmol/L)	131.6±2.9	131.6±3	0.28
S. Potassium (mmol/L)	3.86±0.24	3.90±0.27	0.38
B. Urea (mg/dl)	23.9±3.4	24.9±2.9	0.45
S. Creatinine (mg/dl)	0.94±0.15	0.98±0.16	0.10
Haemoglobin (gm/dl)	10.8±0.56	10.9±0.58	0.23
RBS (mmol/L)	7.14±0.73	6.10±0.50	0.19

Cell values are mean±SD; Z-tests were used to calculate p value; S-serum; RBS-Random Blood Sugar

Table 5 comapres the biochemical and hematological parameters of the two groups 24 hours after TURP; there was no statistically significant difference between two groups. There was no statistically significant difference between the studied groups in levels of serum sodium, potassium, blood urea, serum creatinine, haemoglobin level preoperatively, immediately after and 24 hours after TURP (P>0.05 in cases of all the variables). There were some decrease in the serum sodium and potassium postoperatively when compared with preoperative values. But this defference did not reach statistical significance (P>0.05 in all cases). In glucose group, there was a significant elevation in the postoperative mean value of blood sugar level (P=0.0011) which returned back within 24 hours.

Table 5: Biochemical and hematological values of studied groups 24 hours after TURP (N=120)

Variable	Glucose group (n=60)	Glycine group (n=60)	P value
S. Sodium (mmol/L)	136.7±1.9	136.5±1.6	0.25
S. Potassium (mmol/L)	3.90±0.21	3.87±0.26	0.30
B. Urea (mg/dl)	23.2±3.7	23.8±2.7	0.38
S. Creatinine (mg/dl)	0.95±0.19	0.97±0.16	0.08
Haemoglobin (gm/dl)	10.40±0.63	10.64±0.71	0.16
RBS (mmol/L)	6.60±0.72	6.25±0.77	0.20

Cell values are mean±SD; Z-tests were used to calculate p value; S-serum; RBS-Random Blood Sugar

Discussion

Endoscopic surgery of the genitourinary tract requires the use of an irrigating fluid. The absorption of some irrigant occurs during almost every TURP. Volumes of irrigation fluid absorbed can be difficult to predict, although the volume tends to be greater in extended and bloody operations. Currently surgeons are more aware of the dangers of irrigant absorption and most would attempt to limit the duration of TURP; however TUR syndrome still occurs.

Collins et al. carried a comparative study between the effect of 1.5% glycine and 5% glucose irrigants on plasma serum physiology and the incidence of transurethral resection syndrome during TURP and showed that five of 250 patients had TUR syndrome (2%).[6] Of the five patients who had TUR syndrome, one had bradycardia, three had hypotension, four were drowsy, one was nauseous, two had prickling, two experienced uneasiness, one had blurred vision and two were confused; none had chest pain.[6]

Although all five patients with TUR syndrome were in the glycine group and none of the patients in the glucose group developed TUR syndrome, this difference did not reach statistical significance (Fisher's exact test, p=0.06, n=233. There was no significant difference between the groups in sodium levels or for the changes in potassium, urea, creatinine, osmolality, calcium, haemoglobin or haematocrit. All five patients with TUR syndrome had glycine levels above the normal range (150–399 μmol/L), a fluid absorption of 3.6 (2.6–4.1) L, and a re-section time of 47.6 (35–58) min; four had prostate capsule perforation noted during TURP. They also showed that there was evidence of an association between TUR syndrome and raised glycine levels at the end of TURP (Fisher's exact test, p=0.01, 231 men). None of the patients in the glucose group developed TUR syndrome, although one had a serum sodium value of < 125 mmol/L after TURP but did not fulfil the criteria for TUR syndrome, as he had no symptoms or signs of TUR syndrome.

Akan et al. investigated the incidence of TUR syndrome using 1.5% glycine, 5% glucose and 0.9% NaCl as irrigant during TURP & found that there was no statistically significant difference in the mean value between the studied groups regarding the preoperative hemo-globin, serum sodium, serum potassium and random blood sugar.[1] Statistically insignificant decrease in the postoperative serum sodium was observed in glycine and glucose groups, while insignificant increase was observed in saline group (142.6±12.6 mmol/l). Insignificant reduction in serum potassium in glycine and saline group was observed, but more pro-nounced decrease in glucose group (3.67±0.92 mmol/l) was measured postoperatively. TUR syndrome developed in 17 patients in the glycine group but non in neither glucose nor saline groups. Other studies concluded that bipolar saline is a safe and eliminates the risk of TUR syndrome in high-risk patients with large prostates.[7-10]

There are several limitations of this study. As the serum glycine level cannot be measured in Bangladesh, it cannot be measured the association between the incidence of TUR Syndrome and serum glycine level. Fluid absorption during TURP should be measured by 1% ethanol in breathed air which is added in irrigating fluid.[11] In this study it was measured by the level of sodium in serum.

Conclusions

Endoscopic transurethral resection of the prostate performed using monoplar 5% glucose as irrigating solution during surgery, when compared with monoplar 1.5% glycine was associated with lower perioperative morbidity including TUR syndrome. Except for the transient postoperative hyperglycemia, in glucose group, both irrigants are nearly equivlent and safe.

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