ORIGINAL ARTICLE

POSTOPERATIVE COMPLICATIONS WITH GLYCINE AND STERILE DISTILLED WATER AFTER TRANSURETHRAL RESECTION OF PROSTATE

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Background: Transurethral resection of prostate (TURP) is considered the gold standard for the surgical treatment of BPH. Irrigant fluid absorption by the patient is a potentially serious complication of TURP and can lead to dilutional hyponatremia and TURP syndrome. Other common complications of TURP include urinary tract infection and secondary haemorrhage. The objective of this study was to compare the frequency of postoperative complications (Urinary Tract infection and dilutional hyponatremia) between 1.5% glycine and sterile distilled water used as irrigant in BPH patients after TURP. **Methods**: This randomized controlled trial was conducted in department of Urology, PIMS Islamabad, from August 2013 to February 2014. A total of 170 adult male patients between 50-80 years of age undergoing TURP with prostate volume more than 30cc on ultrasound. 85 patients each were randomly allocated to two groups. In group-A, glycine was used as irrigant solution during TURP while in group-B distilled water was used. Serum sodium levels were measured at 6th postoperative hour to look for dilutional hyponatremia. On the 15th postoperative day they were inquired about any clinical features of urinary tract infection. Also urine routine examination was performed to look for the presence of WBCs in the urine. **Results:** Post-operative dilutional hyponatremia was observed in 13 (15.3%) patients in Group A and in 10 (11.8%) patients in group-B. The difference between both the groups being non-significant (*p*-value=0.501).Frequency of postoperative urinary tract infection on 15th postoperative day in group-A was 23(27.1%) while in group-B it was 16 (18.8%), the difference among both the groups being insignificant (*p*-value=0.202). **Conclusion:** Although the frequency of postoperative complications like UTI and dilutional hyponatremia was less with sterile distilled water, yet, the difference was statistically not significant.

Keyword: TURP, Benign Prostatic hyperplasia, Irrigant solutions, Dilutional Hyponatremia, Urinary Tract Infection

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INTRODUCTION

Benign prostatic hyperplasia (BPH) results from enlargement of prostate gland.[1] Approximately 80% hyperplastic growth of prostate begins in men at the age of 50 years and by age eighty, almost 90% of men have histologic evidence of BPH.[2] The open prostatectomy and transurethral resection of prostate (TURP) have been the surgical options for men with obstructive symptoms. Nevertheless, TURP is considered by many as a simpler and safer procedure than open prostatectomy.[3]

TURP was first introduced in 1926 and popularized in 1930s. Research has demonstrated that TURP is clinically effective in improving the quality of life for patients with BPH and is considered the gold standard for the surgical treatment of BPH.[4] TURP, like other endoscopic operations of the genitourinary tract, requires an irrigating fluid. The irrigating fluids used in conventional TURP are nonconductive solutions, which include distilled water, 5% dextrose, glycine, sorbitol or mannitol solutions. All the nonconductive fluids are hypotonic, because increasing osmolality to isotonic level will compromise endoscopic visibility due to increased turbidity and significant light refraction.[4] Glycine solution has been used in TURP for more than 50 years. Although glycine is an endogenous amino acid without an allergic potential and is transparent, yet it is non-physiological because it lacks electrolytes and excessive absorption has recognized complications. A large volume of perioperative fluid absorption is known to cause TUR syndrome and it can be potentially fatal. Deaths have been reported in patients undergoing TURP in upto 5% cases.[5]

Although fatal complications are less frequent today due to better understanding of the risks, there is now increasing evidence highlighting the toxicity of 1.5% glycine solution when absorbed during TURP. Laboratory studies in animals showed that glycine influences cardiovascular functions and it has direct and indirect cardiotoxic effects in animals.[5]

Like any other surgical procedure, TURP by using either 1.5% glycine or sterile distilled water is associated with early and late postoperative outcomes. Early complications include urinary tract infection, secondary haemorrhage, blood transfusion, prostatic capsule perforation, temporary urinary incontinence.[6] Other complications include hypervolemia and electrolyte imbalance called as TURP syndrome which results from absorption of large quantities of the irrigating fluid.[7] UTI after TURP using glycine as irrigant can occur in upto 37.7% cases.[8] Dilutional hyponatremia, water intoxication and ammonia toxicities have been postulated as the cause of TURP syndrome.[7] TURP syndrome presents as neurologic and circulatory disturbances and is characterized by dyspnoea, nausea, hypertension, increased central venous pressure cerebral oedema, cardiogenic shock and renal failure.[7] Dilutional hyponatremia after TURP using glycine as irrigant can occur in upto 70% cases.[7] Acute hyponatremia with blood sodium concentration below 115-120 mmol/L could be potentially serious to the patient.[7]

Although glycine is an ideal non electrolyte solution, but it is expensive, not easily available and is associated with potential complications as mentioned above. Sterile distilled water has also been used as irrigating fluid in TURP.[4] Distilled sterile water is cheap and available in abundance. Also distilled water has been shown to be a safe irrigating fluid for TURP.[9,10] In a study conducted in Nigeria the incidence of UTI after TURP using distilled water as irrigant was 7.5%.[9] In a study in Iran the incidence of hyponatremia after TURP using sterile water as irrigant was 2.5%.[10]

The choice of ideal irrigating solution remains controversial. Different irrigant solutions are used in different urologic centres as still there is no consensus about which irrigant solution is the best for irrigation. Some authors report various complications of 1.5 % glycine use.[5] Similarly some authors mention various problems associated with use of sterile distilled water such as hyponatremia, water intoxication and bacterial contamination.[11] No comparative study has ever been done in Pakistan to compare the frequency of post-operative complications with 1.5% glycine and sterile distilled water. Similarly no comparative study has been done between the two irrigant solutions internationally in last 10 years. Hence, I conducted a comparative study to compare the frequency of postoperative complications between the two groups, that is, those with 1.5% glycine and those with sterile distilled water. If findings of this study show that the postoperative complication frequency is same in both groups (1.5% glycine and distilled water), then distilled water can be used as safe irrigating fluid for TURP in our clinical setting.

MATERIAL AND METHODS

This randomized controlled trial was conducted at the Department of Urology, Pakistan Institute of Medical Sciences, Islamabad, Pakistan from August 2013 to February 2014**.** Permission to conduct the study was taken from the Hospital Ethics Committee before the commencement of the study. The consecutive (non-probability) sampling technique was used. All patients with age 50–80 years diagnosed to have BPH and scheduled for TURP were included in this study. Patients with history of diabetes, deranged liver functions, congestive cardiac failure and known bleeding disorders were excluded from the study. Patients with urinary tract calculi, associated bladder tumour and patients using anticoagulant and antiplatelet drugs following issues were also excluded from the study. Informed consent was taken from all the patients before the enrolment. All the patients diagnosed to have BPH and undergoing TURP were screened for enrolment in the study. Those who fulfilled the inclusion criteria were enrolled. Inclusion criteria was strictly followed. The diagnostic workup for BPH was done on each patient including detailed history, digital rectal examination and urinary tract ultrasonography. Further, baseline laboratory investigations were carried out including complete blood picture, urine analysis and culture, blood sugar and urea, serum electrolytes and creatinine, ECG, chest radiograph. Bleeding and Clotting profile which includes bleeding time, prothrombin time (PT) and activated partial thromboplastin time (APTT) were also performed. Blood grouping and cross matching was obtained before the procedure. All patients underwent TURP after controlling pre-existing urinary infection with appropriate antibiotics. All TURP procedures were carried out under spinal anaesthesia using the continuous irrigating resectoscope of 24Fr. Peri-operative antibiotics were given to all patients.A total of 170 patients were included in the study. Patients were divided in two groups by lottery method. In group-B of the patients distilled water was used as irrigant solution and in group-A 1.5% glycine was used as irrigant solution during TURP. Head of pressure in fluid delivery system was kept at 60cms from operating table. Volume of irrigating fluid and resection time was recorded for each patient. Three way Foleys catheter (24 Fr) was passed and continuous irrigation was carried out. Afterwards, all patients were shifted to the ward. Serum electrolytes were examined for each patient at 6^{th} hour postoperatively to access for the dilutional hyponatremia (less than 135 mmol/L). Urethral

catheter was removed on the 48th to 72th hours postoperatively and patients were discharged on 3rd postoperative day on oral antibiotics for 5 days. Patients were called in urology out patients department on the 15th postoperative day and were inquired about any features of Urinary tract infection such as fever, burning micturition and suprapubic pain. Also urine routine examination was performed. When the urine routine examination showed more than 5 WBCs/HPF and patient was symptomatic then the patient was considered as having urinary tract infection

Sample size of 85 patients in each group (total 170 patients) was determined using WHO calculator the sample size taking into account the level of significance at 5%, power of test as 80%. Anticipated population proportion as 37.7%[8] and anticipated population proportion as 7.5%[9] was used for the comparison groups.

RESULTS

Mean age of patients in group-A was 67.15±7.067 and in group-B 65.04±8.462 years. Preoperative mean serum Na in group-A was 139.81±2.603 mmol/L and in group-B it was 139.80±2.558 mmol/L, whereas postoperative serum Na 137.66±2.767 mmol/L in group-A and 137.91±2.671 mmol/L in group-B (Table-1).

Post-operative dilutional hyponatremia was observed in 13 (15.3%) patients in Group A and in 10 (11.8%) patients in group-B. The difference between both the groups being non-significant (*p*-value=0.501) as shown in table-2.

Frequency of postoperative urinary tract infection on 15th postoperative day in group-A was 23(27.1%) while in group-B it was 16 (18.8%), the difference among both the groups being insignificant (*p*-value=0.202) as summarized in table-3.

Table-1: Serum sodium levels of patients in both the groups

	Two Groups	N	Mean	SD
Pre Op Na	1.5% Glycine	85	139.81	2.603
	Sterile Distilled Water	85	139.80	2.558
Post Op Na	1.5% Glycine	85	137.66	2.767
	Sterile Distilled Water	85	137.91	2.671

Table-2: Comparison of dilutional hyponatremia in both the groups

		Two Groups		Total
Dilutional hyponatremia		1.5% Glycine	Sterile Distilled Water	
	yes	13	10	23
		15.3%	11.8%	13.5%
	No	72	75	147
		84.7%	88.2%	86.5%
Total		85	85	170
		100.0%	100.0%	100.0%

p-value=0.501

Table-3: Comparison of UTI of patients in both the groups

		Two Groups		Total
		1.5% Glycine	Sterile Distilled Water	
UTI	Yes	23	16	39
		27.1%	18.8%	22.9%
	No	62	69	131
		72.9%	81.2%	77.1%
Total		85	85	170
		100.0%	100.0%	100.0%

p-value=0.202

DISCUSSION

Benign prostatic hyperplasia is a common ailment of elderly men that causes lower urinary tract symptoms which are not only distressing but cause significant morbidity.[12] BPH adversely effects the quality of life and has huge financial burden as 25–30% of patients will eventually require treatment.[13] Though the mortality rates from BPH in most developed countries has been on the decline since 1950 owing to better treatment facilities yet mortality rates for most developed countries in the 1980s were 0.5–1.5/100,000.[14] The histologic prevalence of BPH examined in several autopsy studies reaches 50–60% for men in their 60s, and is 80-90% for men in their 70s and 80s.[15]

The Baltimore Longitudinal Study of Aging showed good agreement between the clinical prevalence and autopsy incidence in men of all ages.[16] BPH arises from the transitional zone of the prostate which is located around the urethra, hence also called the periurethral zone.[17–20]

TURP still considered the standard by the Canadian Urologic Association and as the "benchmark for surgical therapies" by the American Urological Association. Moreover, the European Urological Association considers TURP "the treatment of choice for prostates sized 30–80 mL. TURP has been demonstrated to be efficient, cost-effective and, most importantly, durable with low long-term complications and re-treatment rates.[21] TURP is associated with significant improvement in symptom score, maximal urine flow rate and post-void residual urine volume.[22] Like any other surgical procedure, TURP is associated with complications such as failure to void, surgical revision, urinary tract infection, bleeding which requires transfusions, retrograde ejaculation, stricture, incontinence, and electrolyte imbalances in the form of the transurethral resection (TUR) syndrome.[21,23]

In a study conducted by Alhasan *et al*[9], the mean of age of patients was 67.2±9.8 with a range of 47-110 years. In our study, the age of patients with 1.5% glycine and sterile distilled water was 67.15±7.067 and 65.04±8.462 respectively.

Perioperative morbidity from this procedure ranges between 18% and 26% and the mortality rate may be as high as 1%.[24] Although of retrospective nature, study of Mebust *et al* immediate postoperative morbidity rate was 18%.[25]

In our study the overall frequency of postoperative UTI was 22.9% (27.1% for glycine and 18.8% for sterile distilled water). Similarly the overall frequency of dilutional hyponatremia was 13.5% (15.3% for glycine and 11.8% for sterile distilled water). These results are comparable to the morbidity rates mentioned earlier. In another study, Uchida *et al* analyzed data of 3,861 men who underwent TURP between 1971 and 1996 (early group 1971–1985 and late group 1985–1996) at a single institution and found that morbidity rate reduced over the last 25 years (20.2% vs 17.2%).[26] These rates are also comparable to our complication rates. Similarly Reich and colleagues published a contemporary prospective evaluation of 10 654 patients who underwent TURP statewide. The mortality rate was 0.10% and the cumulative short-term morbidity rate was 11.1%.[27] A meta-analysis by the BPH guideline panel showed that the morbidity rate associated with TURP ranges from 7% to 43%.[28]

The main early postoperative complication of TURP is still urinary tract infections.[29] Despite the high level of safety and low incidence of mortality associated with transurethral resection of the prostate (TURP), urinary tract infections (UTIs)-the most common complication associated with this procedure-continue to be an important source of postoperative morbidity and costs.[30] The reported incidence of postoperative UTI is between 6% and 60%.[31] In our study the overall frequency of postoperative UTI was 22.9% (27.1% for glycine and 18.8% for sterile distilled water), which falls within the range mentioned above. Rassweiler *et al*[32] mentioned that percentages reported in literature vary from 4% upto 20%. Similarly, in a French multi-centric study the incidence of post-TURP infection was 21.6%.[33]

In a study done in Denmark by Mogensen *et al*[8], where glycine was used as an irrigating fluid, the incidence of UTI after TURP was 37.7%. In our study the frequency of UTI in patients in whom glycine was used as irrigating fluid was 27.1% which is lower than the frequency mentioned by Mogensen *et al.* In a study done in Iran by Ketabchi *et al*[34], where glycine was used as irrigant solution, the frequency of UTI after conventional TURP was 17.34%. Lim *et al*[35] have reported a fall in the incidence of postoperative urinary tract infection (UTI) from 25% in the 1970s and 16% in the 1980s to 6% in 1999 in TURP cases where glycine was used as irrigant solution. Similarly in our study, the frequency of UTI when distilled water used as irrigant solution was 18.8%. A study done by Alhasan *et al*[9] in Nigeria showed a UTI frequency of 7.2% when distilled water was used as irrigant solution. Similarly, a French multicenter prospective study conducted by Vivien *et al*[36], reported that the incidence of UTI following TURP was 19.3%.

In our study the frequency and percentage of patients with post-operative complication like hyponatremia in glycine and sterile distilled water patients were 13 (15.3%) and 10 (11.8%) respectively. As compared to the study conducted by Muhammad *et al*[8] in 2010 which found that the frequency and percentage of patients with hyponatremia were 28(70%), when glycine was the irrigant solution in TURP. Similarly the frequency of dilutional hyponatremia was 35% when water was as irrigant solution in TURP in a study done by Memon *et al.*[11]

Moorthy *et al*[37] in their study explained that the mean preoperative serum sodium levels of patients in glycine and sterile distilled water irrigant groups were 145.7±0.7and 136.7±0.9 respectively. And the post-operative sodium levels with glycine and sterile distilled water were 140.5±1.1and 133.4±0.8 respectively. Similarly in our study, the mean of pre-operative serum sodium levels of patients in both groups were 139.81±2.603 and 139.80±2.558. And post-operative serum sodium levels of patients in both glycine and sterile distilled water groups were 137.66 and 137.91 respectively.

CONCLUSION

Although the frequency of postoperative complications like UTI and dilutional hyponatremia was less with sterile distilled water, however the difference was statistically not significant. Hence we can say that there was no difference in the frequency of postoperative complications between 1.5% glycine and sterile distilled water in BPH patients after TURP. Therefore sterile distilled water and can be used as safe irrigating fluid for TURP in our clinical setting.

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