Original Research Article

A Comparison of Hemodynamic and Biochemical Changes Between Normal Saline Irrigation and Glycine Irrigation in Transurethral Resection of Prostate

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Abstract

Background: Transurethral resection of prostate (TURP) is the most commonly performed surgery for benign prostatic hyperplasia (BPH). Monopolar TURP using 1.5% glycine as irrigation fluid is the commonest choice. However, recently biploar TURP is introduced which allows 0.9% normal saline to be used as irrigation. This prospective study was to compare the hemodynamic and biochemical changes between 0.9% normal saline irrigation and 1.5% glycine irrigation in TURP. **Material and methods**: It is a randomized study, carried out on 114 patients, divided into two groups of 57 patients each. Group S underwent bipolar TURP using 0.9% normal saline and Group G underwent monopolar TURP using 1.5% glycine under spinal anaesthesia. The changes in hemodynamic and biochemical parameters in both groups were noted. **Results:** The hemodynamic parameters (mean HR and MAP) in both groups gradually declined at 15mins and 30 mins and then increased in postoperative period. Regarding biochemical parameters, both haemoglobin and hematocrit showed gradual fall in both groups and statistically significant difference was only at immediate postoperative period. Serum sodium, potassium and osmolarity also showed gradual fall in both groups throughout the procedure. However, only the decrease in serum sodium concentration was statistically significant at immediate postop and 2hr post-op period between the two groups. (p value 0.037 and 0.008 respectively). **Conclusion:** The changes in hemodynamic and biochemical parameters were equivalent in both groups except serum sodium concentration, which showed significantly less drop in 0.9% normal saline group than 1.5% glycine group.

Keywords: Normal saline, Glycine, Hemodynamic change, Biochemical change, TURP.

Introduction

The prostate is a cone shaped musculo-glandular organ. It is placed immediately below the internal urethral orifice and around the commencement of the urethra. It has 6 surfaces- a base directed upwards, an apex and anterior, posterior and two lateral surfaces. It weighs about 8 grams. According to contemporary classification by McNeal. prostate is divided into 3 zones, most carcinomas arises from peripheral zone and from the central zone most benign prostatic hyperplasia (BPH) arises. [1] Benign prostatic hyperplasia (BPH) is the most common non-malignant illness of the prostate, affecting more than 50% of the aged male population. [2]

Prevalence rate is reported to be >50% in 60-year-old men, and as high as 90% by 85 years of age. [3]

Usually BPH starts in the periurethral transitional zone and as it increases in size, it compresses the outer peripheral zone, which forms the false capsule. There is also an outer fibrous true capsule. [1] BPH increases urethral resistance, leading to the obstructing voiding symptoms like poor flow, straining, sense of incomplete evacuation, frequency, urgency and nocturia.[4Although medical therapy is the first line treatment, a significant percentage of patients require surgical intervention. [5] Transurethral resection of the prostate (TURP) is the standard surgical procedure and also the second most common surgical procedure done in men obove 65 years. [6] In TURP, strips of tissue are cut from the bladder neck to the level of the verumontanum using a high-frequency diathermy current and irrigating fluid. Irrigation is mainly used to dilate the mucosal spaces, remove blood, cut tissue debris from the operating field and enable better vision. However, absorption of excessive irrigation fluid may lead to various complications ranging from hypothermia, circulatory overload, hyponatremia to multi system involvement also known as TURP Syndrome. Despite improvements in the surgical and anaesthetic management, 2.5 - 20% of patients undergoing TURP show one or more manifestations of TURP syndrome and 0.5% - 5% die perioperatively. [6] TURP syndrome may occur very early after beginning of the surgery upto several hours after completion. [7] Awake patient under regional anaesthesia characteristically complains of dizziness, headache, nausea, chest tightness, shortness of breath, restlessness, confusion, abdominal pain etc. Important signs are sudden hypertension and bradycardia, lethargy, disorientation then loss of consciousness, sluggish pupillary reflex, episodes of tonic-clonic seizures. Eventually may lead to cardiovascular collapse and cardiac arrest. These complications related to irrigating fluid are mainly influenced by it's chemical nature and the rate and volume of fluid absorbed. [8] The ideal irrigant would be user-friendly, non-conductive, highly translucent, chemically inert and have similar osmolarity to the serum. Unfortunately no such irrigating fluid is available yet. Till date various irrigation fluids have been used like distilled water, glycine, saline, sorbitol, mannitol etc. In this study 1.5% glycine and 0.9% normal saline were used as irrigation solution for monopolar and bipolar transurethral resection of prostate respectively. Glycine is a non-essential amino acid and a commonly used irrigant. It was introduced in 1948 as an irrigating fluid and has been suggested as a

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suitable irrigating fluid considering lack of allergic reactions, less hemolysis, less renal failure and the low cost. [9] But the osmolarity of 1.5% glycine is 230 mOsm/1 compared to serum osmolarity of 290 mOsm/l and hence risk of cardiovascular and renal complications are there. It's half-life is dose-dependent probably due to intracellular accumulation. [10] Visual disturbances may occur at plasma glycine concentration of 5–8 mmol/litre and at higher concentrations may even produce transient blindness. [11] Concentration more than 10mmol/litre lead to nausea and vomiting and concentration above 21mmol/litre may cause TURP syndrome. On the other hand 0.9% normal saline is the considered most physiologic irrigant for TURP as it's osomolarity (308 mOsmol/L) is closer to serum. But its electrical conducting properties prohibit its use with conventional monopolar cautery. Recent development of bipolar resection systems permits the use of normal saline as an irrigant. Also, use of bipolar cautery has been reported to be associated with less collateral and penetrative tissue damage. [2] Also 0.9 % normal saline using bipolar diathermy has fewer incidence of bleeding and hyponatremia thus allows longer and safer resection. [3] However, with normal saline hyperchloremic acidosis,[12] acute volume overload is more likely. Some incidence of Pulmonary oedema is also reported. [13] This study was undertaken to compare the safety of normal saline irrigation with conventional glycine irrigation using bipolar and monopolar cautery system respectively.

Material and Methods

The present study was to compare the hemodynamic and biochemical changes between normal saline (0.9%) irrigation with glycine(1.5%) irrigation in TURP. Before commencement of the study ethical approval was taken from institutional ethics committee and written consent were taken from the patients. Adult male patients with ASA physical status 1 and 2, scheduled for elective TURP under spinal anaesthesia were included in the study. Patient with significant cardiorespiratory illness, uncontrolled diabetes, severe electrolyte imbalance, neurological disease were not included in this study. Total hundred and fourteen patients were included in this study and they were randomly allocated to one of the two groups using computerized randomisation table. In Group S (n = 57) patients were operated using 0.9% normal saline as irrigation fluid with bipolar cautery and in Group G (n = 57) 1.5% glycine irrigation was used with monopolar cautery system. For bipolar cautery LIGASURE™8 vessel ligating system, Valleylab™,UK and for monopolar cautery FORCE FX™ 8C electrosurgical generator sytem, Valleylab™, UK was used. Preoperatively thorough preanaesthetic check up was done along with routine laboratory investigations like complete haemogram, serum electrolyte (sodium and potassium), liver and renal function tests, chest X-ray and electrocardiogram (12 lead). All the patients were kept NPM as per guideline and their age, weight and height were recorded. Peripheral venous access was secured with 18 G cannula and all patients were preloaded with isotonic saline solution (10 ml/kg). In the operating theatre basic monitors were applied (ECG, pulse oximetry and non-invasive blood pressure) and baseline heart rate, MAP, ECG and SpO_2 of the patients were recorded and monitored throughout the procedure. Surgery was performed under spinal anaesthesia in all patients with 2.5ml of bupivacaine heavy (0.5%) and 25 mcg of fentanyl under strict aseptic conditions. The intrathecal block was performed by paramedian approach between L3-L4 or L4-L5 intervertebral space using 25 G Quincke spinal needle in sitting position. After 10 minutes from injection of local anaesthetic, sensory and motor block were assessed by pinprick test and Bromage score respectively. [14] The irrigation fluid was kept at 60 cm height and total volume of irrigation fluid used in each patient was calculated. Resection time, weight of the resected gland and duration of surgery were also recorded. For intravenous infusion normal saline was used in all patients and no patient had received colloid, plasma products, hypertonic saline, diuretic therapy or blood transfusion during the study procedure. In case of intraoperative hypotension and bradycardia intravenous mephentermine (6-12mg) and intravenous atropine (0.5-1mg) was administered repectively. In this study, hemodynamic parameters (Heart rate and MAP) were recorded preoperatively (HR-1, MAP-1) and then at every 15 minute interval for first 30 minutes of surgery (HR-2, HR-3, MAP-2, MAP-3). Postoperatively parameters were recorded immediately after the end of the procedure and at two hours (HR-4, HR-5, MAP-4, MAP-5). Hemoglobin, Hematocrit, Serum Sodium, Potassium and Serum Osmolarity were the biochemical parameters estimated. Total 9cc venous blood samples were taken in each interval, before starting the procedure (Hb-1, Hct-1, Na+-1, K+-1, OSM-1), then at 30 minutes of the procedure (Hb-2, Hct-2, Na+-2, K+-2, OSM-2), immediately after the end of the surgery (Hb-3, Hct-3, Na+-3, K+-3, OSM-3) and 2hrs after the procedure (Hb-4, Hct-4, Na+-4, K+-4, OSM-4) . All parameters were directly estimated except serum osmolarity, which was derived from the following formula [15] -

Serum osmolarity = 2 × [Serum Na+] + (BUN/2.8) + (glucose/18).

For estimation, 3cc blood from sample was taken in clotted vial for estimation of serum sodium, potassium and urea, 3cc in fluoride vial for blood glucose and rest 3cc for estimation of haemoglobin and haematocrit. Cliinical signs of transurethral resection of prostate (TURP) syndrome was watched for. All the data were recorded in a separate "Case Record Form" by an anesthesiologist not included in the study.

Results

This study was conducted on one hundred and fourteen patients. Fifty seven patients were randomly allocated in each group to compare changes in the hemodynamic and biochemical parameters during monopolar TURP using 1.5% Glycine and bipolar TURP using 0.9% normal saline as irrigation fluid. All data were summerized by routine descriptive statistics namely mean deviation, standard deviation and were compared between groups by using Students' independant "t" test. All the data were analysed using IBM SPSS Statistics version 23 and Graph Pad Prism 5.0. All analysis were two tailed and $p < 0.05$ was the boundary for statistical significance.

Patient characteristics (Age, ASA grade, weight of Prostate), Resection time and Irrigation fluid volume in both groups were comparable as far as possible. Mean HR in both Group G and Group S showed gradual fall at 15mins and 30 mins after spinal anaesthesia from 81.46±10.18 bpm and 81.19±9.35 bpm to 74.19±8.54 bpm and 74.98±7.77 bpm and then to 70.09±7.67 bpm and 70.77±6.56 bpm respectively. However heart rate increased slightly to 73.40±6.62 bpm and 73.95±5.67 bpm at immediate postoperative period and finally to 78.44±7.21bpm and 79.16±7.62 bpm at two hour after procedure in Group G and Group S respectively. The MAP also, in both groups showed a gradual fall at 15mins and 30 mins after spinal anaesthesia from 94.44±5.44 mmHg and 92.81±5.02 mmHg to 81.70±6.38 mmHg and 83.65±4.47mmHg and then to 77.82±5.31mmHg and 77.96±4.43 mmHg in Group G and Group S respectively. Then increased to 83.12±5.30 mmHg and 83.91±4.31mmHg at immediate postoperative period and finally to 89.88±5.51mmHg and 89.04±3.95 mmHg in Group G and Group S respectively. Using students unpaired t test no statistically significant difference was found between the two groups. Therefore, the changes in hemodynamic parameters are comparable in both the groups.

Table 1: Changes in HR & MAP in both groups

Parameters	GROUP G	GROUP S	P value
HR-1	81.46+/-10.18	81.19+/-9.35	0.886
MAP-1	94.44+/-5.44	92.81+/-5.02	0.099
HR-2	74.19+/-8.54	74.98+/-7.77	0.607
MAP2	81.70+/-6.38	83.65+/-4.47	0.062
HR-3	70.09+/-7.67	70.77+/-6.56	0.610
MAP3	77.82+/-5.31	77.96+/-4.43	0.879
HR-4	73.40+/-6.62	73.95+/-5.67	0.639
MAP-4	83.12+/-5.30	83.91+/-4.31	0.385
HR-5	78.44+/-7.21	79.16+/-7.62	0.606
MAP-5	89.88+/-5.51	89.04+/-3.95	0.351

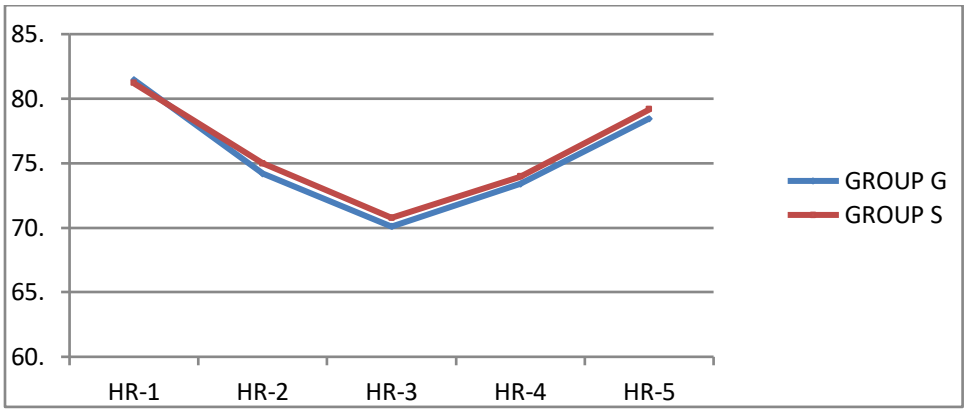

Fig 1: Variation of HR in both groups

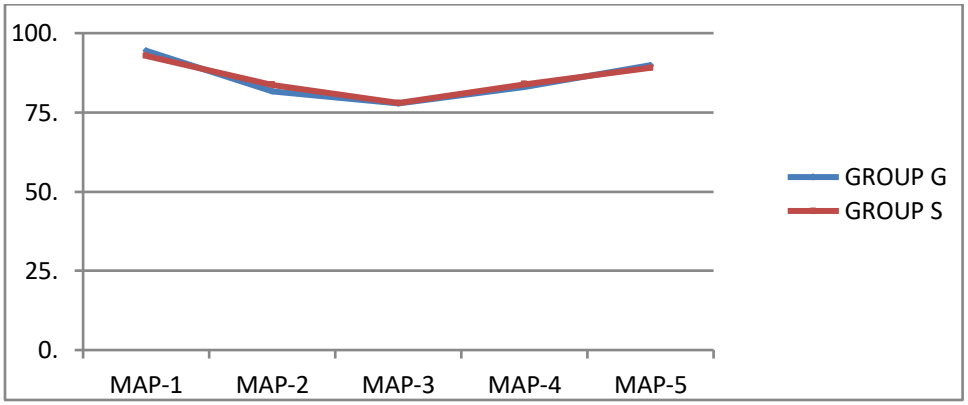

Fig 2: Variation of MAP in both groups

Regarding biochemical parameters both Hemoglobin and Hematocrit values showed gradual fall in both Group G and S and the fall was more in Group G than in Group S. However, the difference was found to be statistically significant only at immediate postoperative period (mean Hb in group G and S were 11±0.51g/dl and 11.21±0.50g/dl respectively, and **p = 0.025** and mean Hct were 32.91±1.47 and 33.58±1.58 and **p=0.021**) . The 2hr postoperative values also showed a more decrease in Hb and Hct in Group G than Group S but the difference was not statistically significant.

Table 2: Changes in Hb & Hct in both groups

PARAMETERS	GROUP G	GROUP S	P VALUE
Hb-1	12.37+/-0.35	12.28+/-0.42	0.256
Hct-1	36.86+/-1.13	36.67+/-1.25	0.387
Hb-2	11.67+/-0.35	11.57+/-0.48	0.206
Hct-2	34.89+/-1.11	34.61+/-1.53	0.266
Hb-3	**11.00+/-0.51**	**11.21+/-0.50**	**0.025**
Hct-3	**32.91+/-1.47**	**33.58+/-1.58**	**0.021**
Hb-4	10.54+/-0.48	10.71+/-0.54	0.096
Hct-4	31.46+/-1.40	32.04+/-1.76	0.055

p value < 0.05 considered significant and marked as bold

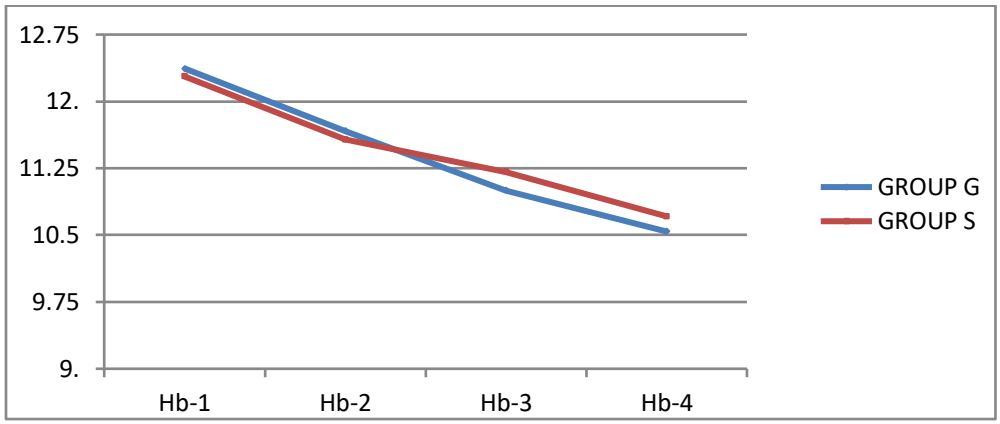

Fig 3: Variation in Hb in both groups

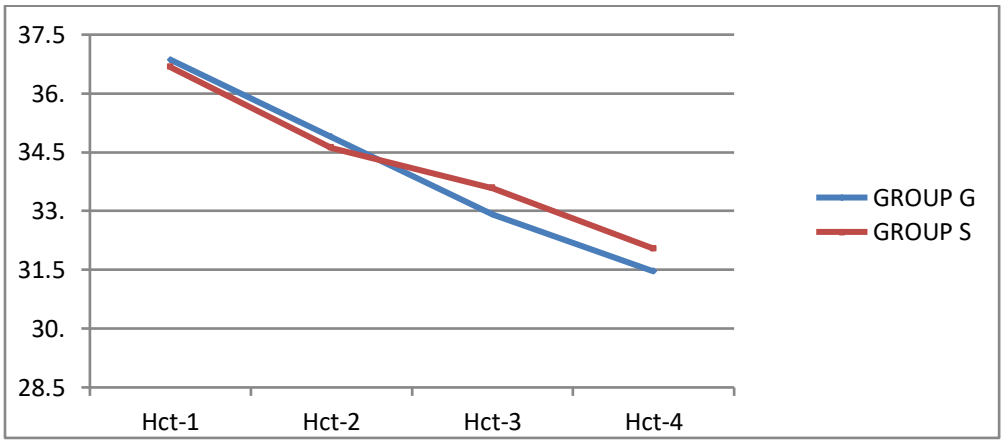

Fig 4: Variation in Hct in both groups

Serum sodium , potassium and osmolarity were also estimated at four intervals and data were compared using students unpaired t test. All the three parameters showed a gradual fall in both groups throughout the procedure. The difference in serum sodium concentration was found to be statistically significant at immediate postoperative and 2hr postoperative period between the two groups. (**p value 0.037 and 0.008 respectively**). At two hour postoperative interval Group G had a mean drop of 3.09±0.22meq/l while Group S had a mean drop of 1.88±0.173meq/l, which was statistically significant (p=0.008) which was significantly greater decline in serum sodium concentration in Group G than Group S. However, serum K+ cconcentration showed a statistically significant fall only at 30mins after the beginning of the procedure (**p value 0.026**) between the two groups and the concentration was less in Group G than Group S. But, the mean drop in glycine group was 0.31±0.07meq/l and in saline group was 0.31±0.00meq/l, which was statistically insignificant (p= 0.076). Regarding serum osmolarity in both Group G and S and the fall was more in group G than Group S. But, the differences were not statistically significant. In Group G the mean decrease was 8.19±1.78mosmol/l and in Group S it was 5.86±1.68mosmol/l. However , there was no incidence of TURP syndrome seen in both the groups.

Table 3: Changes in serum Na+, serum K+ and serum Osmolarity

PARAMETER	GROUP G	GROUP S	P VALUE
Na+-1	140.27+/-2.15	140.25+/-2.49	0.978
K+-1	3.95+/-0.23	4.04+/-0.25	0.051
OSM-1	292.60+/-6.38	291.30+/-6.39	0.281
Na+-2	138.93+/-2.13	139.62+/-2.44	0.115
K+-2	**3.75+/-0.22**	**3.85+/-0.25**	**0.026**
OSM-2	288.82+/-5.04	288.96+/-5.59	0.886
Na+-3	**137.95+/-2.28**	**138.87+/-2.38**	**0.037**
K+-3	3.68+/-0.197	3.75+/-0.26	0.143
OSM-3	286.44+/-4.70	286.86+/-4.99	0.644
Na+-4	**137.18+/-2.32**	**138.37+/-2.32**	**0.008**
K+-4	3.64+/-0.30	3.73+/-0.25	0.076
OSM-4	284.41+/-4.61	285.44+/-4.71	0.241

p value < 0.05 considered significant and marked as bold

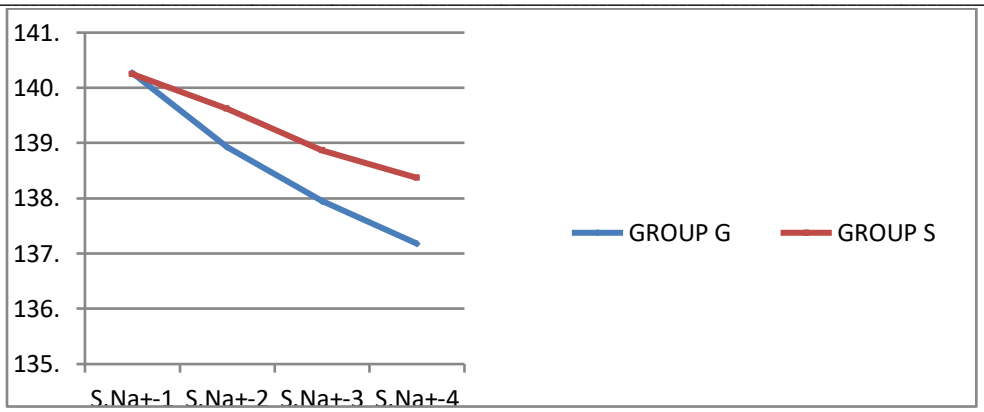

Fig 5: Variation in Serum Na+ in both groups

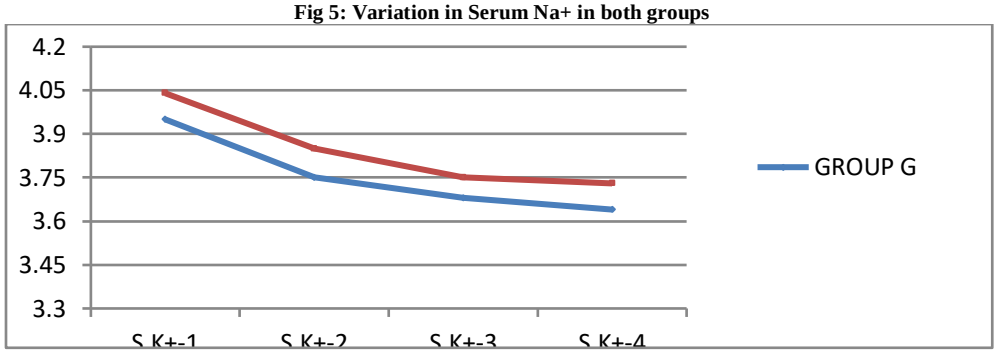

Fig 6: Variation in Serum K+ in both groups

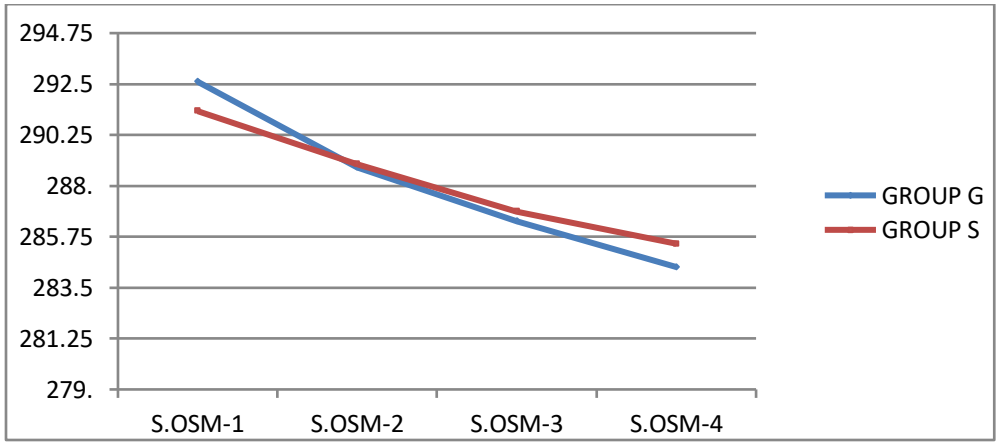

Fig 7: Variation in Serum Osmolarity in both groups

Discussion

TURP is the most commonly done surgical intervention for BPH. Over the years, large amount of data has been accumulated demonstrating its efficacy and safety. Though TURP has a low mortality rate, there is some concern regarding perioperative morbidity especially dilutional hyponatremia, hemorrhage and frank TURP syndrome. Monopolar TURP using glycine (1.5%) irrigation is the most common surgical modality used to treat BPH, however, there are evidences of hyponatremia and TURP syndrome caused by the non-conducting hypo-osmolar irrigation fluid like glycine (1.5%). [16] Mebust et al reported a 2% incidence of TURP syndrome during monopolar TURP using glycine (1.5%). [17] On the other hand, bipolar TURP is a recently introduced modality which helps in better hemostasis and also allows use of normal saline (0.9%) as irrigation fluid. Bipolar TURP using normal saline irrigant decreases the risk of dilutional hyponatremia and TURP syndrome, hence permits a longer operative time. [3]

In this study, hemodynamic and biochemical changes were compared between glycine (1.5%) and normal saline (0.9%) as irrigation fluid using monopolar and bipolar cautery system respectively to compare perioperative safety profile. Biochemical parameters (haemoglobin and haematocrit) showed gradual fall in both the groups, but the difference between two groups was only significant at immediate postoperative period, but finally at two hours after surgery parameters in both the groups were comparable. The mean fall in haemoglobin in Group G was 1.66±0.19g/dl and in the Group S was 1.74±0.06g/dl (p=0.096). While fall in mean haematocrit in Group G and Group S were 4.82±0.64 % and 5.21±0.16% (p=0.055). Similar result was observed in a study by Ho HS et al. who found that there was no significant decrease in Hb level between bipolar and

monopolar group. [18] An international multicentre randomized control trial by Mamoulakis C et al. also reported statistically insignificant difference in haemoglobin drop after monopolar and bipolar TURP (p=0.548). [19] However, in contrary to this, Chee Kong CH et al. have noted a significant lesser blood loss in saline group as compared to glycine group (0.6g/dl vs 1.8g/dl, p= 0.01). [20]

The present study also showed fall in postoperative serum sodium, potassium and osmolarity in both groups and the fall was more in Group G than in Group S . However, only mean fall in serum sodium was significant, while changes in serum potassium and osmolarity were comparable. Group G had a mean drop of 3.09±0.22meq/l while Group S had a mean drop of 1.88±0.173meq/l and p=0.008 . In the study by Chee Hong et al. also serum sodium concentration decreased by 1.03meq/l in Bipolar TURP vs 5.01meq/l in Monopolar TURP and which was significant (p=0.01). [20)] Similarly Ho HS et al., who compared the decline in postoperative serum Na+ between bipolar and monopolar group, found significantly more decrease in serum Na+ in monopolar group (10.7mmol/l) than bipolar group was (3.2 mmol/l). [18] However, in contrast a randomized prospective study by Singhania et al. comparing safety and efficacy of bipolar saline TURP versus standard monopolar TURP ، showed a greater decline in serum sodium concentration (4.12 meq/l vs 1.25meq/l), serum potassium and serum osmolarity in monopolar group compared to bipolar group (5.14mosmol/l vs 0.43mosmol/l) and the differences were not significant. [21]

Interestingly in a study on series of 72 patients it was found that the serum sodium concentration decreased by 10 to 54 mmol/l in 19 patients (26%) while osmolarity changed only in two patients(3%) and 5 patients in that series with largest decrease in serum sodium concentration showed no changes in serum osmolarity. [22]

Hemodynamic parameters in the present study were comparable in both the groups. Intraoperatively, there was transient fall in HR and MAP and then both the parameters increased in postoperative period in both the groups. And the differences were not statistically significant. In a study by Yousef et al. it was found that there was a decrease in the mean value of HR and MAP at ten minutes after induction of anaesthesia in glycine and saline group (57.5±12.6 bpm and 54.6±11.9 bpm for HR and 71.6±19.6 mmHg and 72.5±18.8mmHg for MAP) which was significant. However, thereafter no significant change was found throughout the intraoperative and postoperative period. [23] In contrast the study by Hafez El Saied Hafez et al. showed, the mean HR increased in bipolar group while it was decreased in monopolar group (from 73.40±7.89 bpm to 77.07±7.94 bpm and 70.60±4.84 bpm to 69.80±5.06 bpm respectively) and the difference was significant (p <0.05), while the MAP showed a significant increase in both the group (102.27±3.20 mmHg and 107.67±2.64 mmHg from 99.27±4.03 mmHg and 100.73±3.35 mmHg respectively and p <0.05). [24]

In this study Glycine irrigation with monopolar TURP leads to significant decrease in serum sodium than saline group using bipolar diathermy. However, there was no incidence of clinically evident TURP syndrome in any patient in both the groups. Similarly, in the study by Chee Kong CH et al.also no case of TURP syndrome was reported even though there was a statistically significant drop in serum sodium level. [20] However, in a recent meta-analysis which included 22 studies between 2004 and 2011, not a single instance of TURP syndrome occurred in 1401 patients with bipolar group using normal saline as irrigation, but 35 cases of TURP syndrome occurred (out of a total of 1375 patients) in monopolar group. [25]

Conclusion

The present study concluded that there was significantly less drop in serum sodium in 0.9% normal saline irrigation group in comparison to 1.5% glycine irrigation group however other biochemical and hemodynamic parameters were equivalent in both the groups. However, as this study was conducted on a small size sample including only ASA 1 and 2 patients and followed up only upto 2 hours., therefore further study including larger number of patients with longer follow up is essential.

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