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Original Article

Anaesthesia Section

Postoperative Assessment of Cognitive Dysfunction in Patients Undergoing Transurethral Resection of the Prostate under Spinal Anaesthesia: A Prospective Cohort Study

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ABSTRACT

Introduction: Postoperative Cognitive Dysfunction (POCD) is a common disorder following surgery that threatens the quality of patients' lives. POCD is closely associated with perioperative factors such as age, physical state, surgery duration, anaesthesia method, intraoperative hypotension, and infection. Among these factors, age is the only long-term risk factor for POCD. The relationship between anaesthesia depth and the incidence of POCD is debatable.

Aim: To assess POCD in patients undergoing Transurethral Resection of the Prostate (TURP) and to examine the association between the duration of surgery and serum sodium levels with cognitive dysfunction.

Materials and Methods: A prospective observational study was conducted at the Department of Anesthesiology, PES Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh, India, from January 2020 to June 2021. The study included 100 patients aged over 60 years who were scheduled for TURP surgery under Spinal Anaesthesia. The Mini-Mental State Examination (MMSE) test was performed in the preoperative holding area, and the results were recorded. A decline in cognitive function was defined as a loss of 2 or more points on the MMSE test compared to the preoperative value. Serum sodium levels and MMSE scores were measured before surgery. Serum sodium levels and MMSE scores were also recorded after the 1st hour and 6th hour postoperatively. The data were entered into MS Excel 2007 and analysed using Statistical Package for Social Sciences (SPSS) version 20.0.

Results: In the present study, out of 100 subjects, the majority of patients (33%) belonged to the age group of 66-70 years, and most of the study subjects (79%) were classified as American Society of Anesthesiologists (ASA) II status, followed by ASA III status. The mean age of the study participants was 69.3 years. The mean duration of surgery was 45.6 minutes. A statistically significant difference ($p<0.05$) was observed when comparing the mean serum sodium levels before surgery (138.1±1.5 mmol/L) with those at the 1st hour postoperatively (135.9±1.6 mmol/L) and 6th hour postoperatively (134.4±1.4 mmol/L). The mean MMSE score before surgery and at the 1st hour and 6th hour postoperatively was the same (27.6±0.8), and there was no statistically significant difference between them. The MMSE score did not vary with the serum sodium levels, and this difference was not statistically significant ($p>0.05$).

Conclusion: In the present study, patients undergoing TURP procedures under spinal anaesthesia did not exhibit any POCD, despite a considerable drop in serum sodium levels. It is worth noting that all patients were asymptomatic.

Keywords: Cognitive impairment, Glycine, Prostate, Serum sodium

INTRODUCTION

A standardised MMSE tool was used to assess cognitive skills in patients undergoing TURP preoperatively and postoperatively. Fluid absorption was the factor most strongly correlated with changes in the MMSE score postoperatively. However, the preoperative health status, choice of anaesthesia, and perioperative hemodynamics had no impact on the MMSE score [1,2]. To date, literature provides little evidence regarding the impact of TURP syndrome on mental functions postoperatively, which is an interesting aspect to study, especially in the elderly population. According to the Indian Census 2021, the percentage of the population aged 60 years and above is 10.1% of the total population [3]. Benign Prostatic Hyperplasia (BPH) is a common urological disease among older men. Although BPH rarely causes symptoms before the age of 40, its occurrence and symptoms increase with age. BPH affects approximately 50% of men between the ages of 60 years and up to 90% of men older than 80 years [4]. BPH significantly impacts the Quality of Life (QOL) of many patients [5]. TURP is a surgical option for men with BPH [6]. It involves the use of irrigating fluid to dilate mucosal spaces, remove blood, cut tissue, and debris from the operating field, and improve visualisation [7]. TURP syndrome is a potential complication resulting from the systemic absorption of hypotonic irrigating fluid. It manifests in various clinical symptoms due to the absorption of a large volume of irrigating fluid (1.5% glycine), leading to electrolyte imbalances (hyponatremia and hyperkalemia), confusion, and cognitive impairment in the postoperative period. These symptoms primarily arise from circulatory fluid overload, water intoxication, toxicity of the irrigant solute, and volume of the irrigating fluid [8-10].

POCD can be detected in approximately 10-25% of patients [11]. The incidence of cognitive dysfunction varies from 10% to 46% depending on the type of surgery [12]. Furthermore, POCD is a common complication associated with increased morbidity, mortality, and reduced QOL [13,14]. The MMSE is a widely used cognitive assessment tool that detects POCD in multiple cognitive domains, including orientation, registration, attention and calculation, immediate recall, language, short-term memory, and constructional

ability. The examination typically takes 5-15 minutes, and while it has high specificity, it has low sensitivity in detecting mild cognitive impairment [15,16].

Due to the duration of the procedure, pre-existing neurological conditions, irrigating solute, and volume, a significant number of elderly patients undergoing TURP surgery under general anaesthesia or spinal anaesthesia experienced postoperative cognitive impairment [17]. Two factors contributing to POCD were hyponatremia and glycine toxicity. Analysing serum sodium levels and limiting irrigant volume during the perioperative phase may aid in early identification and management of TURP syndrome [18]. This study aimed to evaluate whether TURP syndrome could cause POCD in elderly patients undergoing TURP by monitoring preoperative serum sodium and MMSE scores, as well as postoperative serum sodium and MMSE scores. Additionally, the study assessed resection time, resected volume of the prostate gland, and the amount of 1.5% glycine associated with POCD.

MATERIALS AND METHODS

The prospective Cohort study was conducted over a period of one year and six months, from January 2020 to June 2021, at PES Institute of Medical Sciences and Research in Kuppam, Andhra Pradesh, India. Institutional Ethics Committee (IEC) approval (No: PESIMSR/IHEC/89) was obtained, and written informed consent was taken from all participants involved in the study. A total of 100 adult male patients aged above 60 years were scheduled for elective TURP surgery under spinal anaesthesia.

Sample size calculation: A sample size of 100 was calculated based on Xue P et al., study, with a prevalence of 7.8% and an absolute precision of 6 [17]. According to these values, the estimated sample size was 76, but for better calculations, the sample size was taken as 100.

Inclusion criteria: The study included patients above 60 years of age, ASA physical status I/II/III, who were scheduled for elective TURP surgeries under spinal anaesthesia.

Exclusion criteria: The study excluded patients unable to read and write or with impaired hearing, patients with a history of metabolic and neuropsychiatric disorders, patients with a history of alcohol consumption and drug dependence, and patients with a past medical history of neurological or other diseases.

Study Procedure

All patients underwent pre-anesthetic assessment prior to TURP surgery. Routine investigations, such as complete blood count, liver and renal function tests, serum electrolytes, electrocardiography, chest X-ray, random blood sugar, echocardiography, and ultrasound abdomen, were performed and optimised if necessary. The MMSE test was conducted in the preoperative holding area, and the results were recorded. The MMSE test has a maximum score of 30 points, with scores of 23 or below indicating cognitive impairment. In this study, a decline in cognitive function was determined by a loss of 2 or more points on the MMSE test compared to the preoperative value. The serum sodium level and the MMSE score were noted before the surgery. All five ASA standard monitors were connected and preloaded with 10 mL/kg of 0.9% normal saline. Aseptic subarachnoid block was performed in the lateral or sitting position using 3 mL of 0.5% Bupivacaine at the L3-L4 intervertebral disc space, resulting in satisfactory analgesia up to the T10 dermatome level. Patients were positioned in the lithotomy posture, and the TURP procedure began with 1.5% glycine irrigation fluid. The height of the irrigation fluid column was maintained at 60 cm, measured from the level of the patients' pubic symphysis on the operating table.

Haemodynamics like Heart Rate (HR), Blood Pressure (BP), Mean Arterial Pressure (MAP), Respiratory Rate (RR), and Oxygen Saturation (SpO_2) were monitored intraoperatively every five minutes. At the end of the surgery, the resected prostate tissue was collected and weighed using a weighing machine in grams. The duration of surgery (resection time) in minutes, and the volume of 1.5% glycine used during the surgery were also recorded. The resection time was calculated as the duration between the first cut on the prostate until the insertion of the 3-way Foley catheter. Throughout the procedure, all patients were closely monitored for early signs of TURP syndrome, like seeing flashing lights or other visual disturbances, facial warmth, and prickling sensations [19]. Preoperative serum sodium levels and MMSE scores, as well as those after the 1st hour and 6th hour postoperatively, were also noted.

STATISTICAL ANALYSIS

The data was entered into MS Excel 2007, and further analysis was performed using SPSS 20.0. Categorical variables were analysed using percentages, while continuous variables were analysed by calculating the mean±standard deviation. The t-test was used for analysing numerical data, and the Chi-square test was applied for categorical data. A significance level of $p<0.05$ was considered statistically significant.

RESULTS

In the present prospective cohort study, conducted on 100 male patients posted for TURP surgery under spinal anaesthesia, all the patients' preoperative laboratory and hemodynamic parameters were normal. In this study, out of 100 subjects, the majority of the study subjects (33%) underwent TURP surgery at the age of 66-70 years, and the majority of the subjects belonged to ASA physical status II. The mean age was 69.3 years [Table/Fig-1].

Variables	(n)	Percantage (%)
Age		
<65 years	32	32
65-70 years	33	33
71-75 years	18	18
>75 years	17	17
ASA physical status		
Grade-II	79	79
Grade-III	21	21

[Table/Fig-1]: Age-wise distribution of study participants (N=100).

In the present study, the mean HR, MAP, SpO_2, and RR were comparable in the study subjects intraoperatively during specified time periods. There was no statistically significant difference in intraoperative hemodynamic parameters among the study subjects ($p>0.05$) [Table/Fig-2].

Serum sodium before surgery: In the present study population, no preoperative serum sodium abnormalities were detected that could lead to TURP syndrome, except in 2% of the population. The majority of the study subjects' serum sodium levels fell within the normal (136-140 mmol/L) range [Table/Fig-3].

Variables	Baseline	5 min	10 min	20 min	30 min	40 min	50 min	60 min	p-value
Mean HR/min	89.40±7.81	90.12±6.35	88.40±4.81	89.56±2.14	90.46±1.09	89.58±2.37	88.76±1.95	90.69±3.21	0.082
Mean MAP (mmHg)	100.87±3.24	100.27±2.15	99.98±1.89	99.56±2.56	100.86±1.73	99.10±2.67	100.95±2.94	99.28±1.94	0.137
Mean SpO_2 (%)	99.87±0.97	99.52±1.21	98.88±0.89	99.80±1.01	98.86±0.79	99.54±1.05	98.67±0.64	99.12±0.84	0.750
Mean RR/min	15.12±0.54	14.56±1.06	15.45±0.16	14.87±1.09	14.63±0.89	15.08±0.57	14.92±1.08	15.23±0.79	0.842

[Table/Fig-2]: Distribution of haemodynamic parameters of the study subjects.

Sodium before surgery (mmol/L)	No. of subjects	Percentage (%)
<135	2	2
136-140	90	90
>140	8	8
Total	100	100

[Table/Fig-3]: Distribution of serum sodium before surgery.

Duration of surgery (resection time): On analysing the distribution of surgery duration, the majority of the study subjects (30%) were clustered in the 46-55 minutes group. However, 95% of the study population fell within the normal range of resection time. The mean duration of surgery was 45.6 minutes. Only 5% of the study population exceeded the normal resection time for prostate gland resection [Table/Fig-4].

Duration of surgery	No. of subjects	Percentage
25 min	7	7%
26-35 min	19	19%
36-45 min	24	24%
46-55 min	30	30%
56-65 min	15	15%
>65 min	5	5%
Total Mean±SD	**100**	**100%**
	45.6±13.5 min	

[Table/Fig-4]: Distribution of study subjects according to the duration of surgery (Resection time).

The majority of the study subjects (59%) required a volume of 15001 to 20000 mL of 1.5% glycine. The mean irrigation volume was 18480±3444.3 mL for a mean resection of the prostate of 37.8±1.3 gm. Within the study population, 31% and 10% required more than 20000 mL and less than 15000 mL of glycine volume, respectively [Table/Fig-5].

Irrigation volume (mL)	No. of subjects	Percentage
<10000	6	6%
10001-15000	4	4%
15001-20000	59	59%
>20001	31	31%
Total Mean±SD	**100**	**100%**
	18480±3444.3 mL	

[Table/Fig-5]: Distribution of study subjects according to irrigation volume (1.5% Glycine).

The present study showed that the mean serum sodium levels before surgery and at post-op 1st hour and 6th hour were compared. There was a decrease in the serum sodium levels at the post-op 1st hour and 6th hour, and this difference was statistically significant (p<0.0001) [Table/Fig-6].

Variables	Mean±SD	p-value
Pre-op sodium before surgery (mmol/L)	138.1±1.5	-
Post-op sodium 1st hour (mmol/L)	135.9±1.6	<0.0001*
Post-op 6th hour serum sodium (mmol/L)	134.4±1.4	<0.0001*

[Table/Fig-6]: Comparison of pre-op and post-op serum sodium 1st hour and 6th hour.
(p<0.05* statistically significant)

Since, the mean MMSE score before surgery and at post-op 1st and 6th hour were the same, it was not possible to test for a significant difference between them [Table/Fig-7].

The mean values of the MMSE score measured at the preoperative stage, at post-op 1st hour, and 6th hour were compared for the duration of surgery that differed with respect to the time taken for the surgeries.

Variable	Mean±SD	p-value
MMSE score before surgery	27.6±0.8	-
MMSE score after surgery 1st hour	27.6±0.8	1.000
MMSE score after surgery 6th hour	27.6±0.8	1.000

[Table/Fig-7]: Comparison of MMSE Score pre-op and post-op 1st hour and 6th hour.

However, the difference in MMSE scores with the duration of surgery at the preoperative stage, as well as at the 1st and 6th hour post-op, was not statistically significant (p=0.4234) [Table/Fig-8].

Variables	Duration of surgery						p-value
	25 min (n-7) Mean± SD	26-35 Min (n-19) Mean± SD	36-45 min (n-24) Mean± SD	46-55 min (n-30) Mean± SD	56-65 min (n-15) Mean± SD	>65 min (n-5) Mean± SD	
MMSE before surgery	27.3±0.5	27.8±0.9	27.5±0.7	27.5±0.7	27.6±0.6	28±1.4	0.4234
MMSE After surgery 1st hour	27.3±0.5	27.8±0.9	27.5±0.7	27.5±0.7	27.6±0.6	28±1.4	0.4234
MMSE After surgery 6th hour	27.3±0.5	27.8±0.9	27.5±0.7	27.5±0.7	27.6±0.6	28±1.4	0.4234

[Table/Fig-8]: Comparison of Duration of surgery and MMSE scores.

The mean values of MMSE scores measured at the preoperative stage, as well as at the 1st and 6th hour post-op, were compared with serum sodium levels classified as <135 mmol/L, 135-140 mmol/L, and >140 mmol/L. However, it was observed from the above table that the MMSE score did not vary with the serum sodium levels, and the difference was not statistically significant (p=0.3423) [Table/Fig-9].

Variables	Serum sodium (mmol/L)			p-value
	<135 N (2) Mean±SD	136-140 N (90) Mean±SD	>140 N (8) Mean±SD	
MMSE before surgery	27±0	27.5±0.8	27.8±0.6	0.3423
MMSE after surgery 1st hour	27±0	27.5±0.8	27.8±0.6	0.3423
MMSE after surgery 6th hour	27±0	27.5±0.8	27.8±0.6	0.3423

[Table/Fig-9]: Comparison of serum sodium and MMSE Score.

Regarding the correlation of the duration of surgery with the postoperative serum sodium levels at the 1st and 6th hour, there was a significant weak negative association between them (p=0.01) [Table/Fig-10].

Variables	Correlation		
	Duration of surgery	Post-op 1st hour sodium	Post-op 6th hour sodium
Duration of surgery (min)	1	-	-
Post-op 1st hour sodium (mmol/L)	-0.4871	1	-
Post-op 6th hour sodium (mmol/L)	-0.4648	-	1

[Table/Fig-10]: Correlation between duration of surgery and post-op 1st and 6th hour serum sodium.
(Correlation is significant at the 0.01 level (2-tailed)*

Similarly, when correlating the irrigation volume with the post-op serum sodium levels at the 1st and 6th hour, there was a significant weak negative association between them (p=0.01) [Table/Fig-11].

DISCUSSION

The POCD is an illness that has been poorly characterised but recognised as a serious concern in elderly people undergoing anaesthesia for decades [20]. Research suggests that approximately a quarter of elderly individuals who undergo major surgery will experience a noticeable decline in cognition, with 50 percent of these

Variable	Correlation		
	Irrigation volume (mL)	Post-op 1st hour sodium	Post-op 6th hour sodium
Irrigation volume (mL)	1	-	-
Post-op 1st hour sodium (mmol/L)	-0.5530	1	-
Post-op 6th hour sodium (mmol/L)	-0.5128	-	1

[Table/Fig-11]: Correlation between irrigation volume and post-op 1st and 6th hour serum sodium:
(Correlation is significant at the 0.01 level (2-tailed)*

patients experiencing long-term impairment. TURP syndrome involves irregularities in the heart, brain, electrolytes, and metabolism [21]. The occurrence of TURP syndrome is related to factors such as the type of irrigating fluid, operation time, patient position, prostate size, fluid bag height, surgeon experience, and intra-prostatic vasopressin injection [22].

In the present study, most of the study subjects fall under ASA physical status II (79%), and 33% of the study subjects underwent TURP surgery in the age group of 66-70 years. The mean age was 69.3 years [Table/Fig-1]. A study by Xue P et al., documented that old age (mean age was 74.84±6.39 years), ASA physical status II patients, and pain intensity after surgery were important risk factors for the development of delirium in patients undergoing TURP [17]. Similar to the present study, studies conducted by Chi YL et al., Bhatta PN et al., and Uddin MH et al., observed that the mean age of the study population was 67.15±9.96, 68.93±10.34, and 64.5±9.86 years, respectively [23-25].

In comparing the mean changes in serum sodium levels, a significant decrease was observed in the postoperative 1st and 6th-hour serum sodium levels (135.9±1.6 mmol/L, 134.4±1.4 mmol/L, respectively) compared to the preoperative serum sodium level among the patients (138.1±1.5 mmol/L) (p=0.0001) [Table/Fig-6]. Similar results were also found in Gupta K et al.,'s study, which showed a statistically significant reduction in postoperative serum sodium (130.3 mmol/L) compared to the preoperative level (141.2 mmol/L) (p=0.0001) [26]. Therefore, they concluded that the significant reduction in postoperative serum sodium could potentially be a cause of TURP syndrome, leading to POCD. Studies conducted by Aziz W et al., Pasha MT et al., and Meena R et al., also reported similar results to the present study, indicating statistically significant changes in serum sodium levels at the 1st and 6th hours after surgery [9,27,28]. None of the patients exhibited any signs or symptoms of TURP syndrome postoperatively. However, Bhatta PN et al.,'s study showed that the postoperative 1st hour and 6th-hour sodium concentrations in both groups decreased from 138.8 to 135.06 mmol/L, but this reduction was not statistically significant (p=0.95) [24]. The results of this study differed from the current study. The MMSE score did not vary significantly with the serum sodium levels (p=0.3423). Therefore, this prospective cohort study concluded that POCD was not common in TURP syndrome patients with a significant reduction in postoperative serum sodium.

According to the present study, the mean resection time was 45.6 minutes [Table/Fig-4], and none of the patients developed TURP syndrome. Aziz W et al., Bhatta PN et al., Gupta K et al., and Meena R et al.,'s studies showed similar mean resection times of 45 to 55 minutes, 42.5±20.04 minutes, 38.75±7.31 minutes, and 40.18 minutes, respectively, which align with the findings of the present study [9,24,26,28]. However, Uddin MH et al.,'s study reported a mean resection time of 63.80 minutes, which contradicted the present study, but none of the patients exhibited any signs or symptoms of TURP syndrome postoperatively [25]. The difference in MMSE score with the duration of surgery at the preoperative stage, 1st hour post-op, and 6th hour post-op was not statistically significant (p=0.4234) [Table/Fig-8]. Thus, the present study concluded that POCD was unlikely to occur within six hours postoperatively for resection times less than 45 minutes.

The distribution of irrigation volume (1.5% Glycine) was analysed. The mean irrigation volume was 18,480±3,444.3 mL. In the present study, 59% of the study population required 15 to 20 L of Glycine [Table/Fig-5]. Studies conducted by Aziz W et al., Bhatta PN et al., and Uddin MH et al., reported mean irrigant volumes of 12.08 L, 23.27±9.02 L, and 23.55±15.20 L, respectively, compared to the present study's volume of 18.4±3.4 L [9,24,25]. After the TURP surgery, the mean weight of the resected prostate tissue was 37.8±1.3 grams, which was similar to the findings of Aziz W et al., and Bhatta PN et al., In those studies, the weight of the resected prostate was greater in the sterile water group (41.25±17.64 g) compared to the Glycine group (35.25±11.71 g) and (41.49±34.46 g versus 15.33±9.74 g), respectively, but the difference was not statistically significant (p=0.093) [9, 24]. Uddin MH et al., reported a mean weight of the resected tissue as 63.80 g, which differed from the present study, and there was no statistically significant difference in postoperative serum sodium levels [25].

An analysis of the MMSE scores before and after surgery showed no significant difference in the mean scores. The mean MMSE score before surgery was 27.6±0.8, and after surgery, it was also 27.6±0.8, which was statistically insignificant and comparable [Table/Fig-7]. A study by Xue P et al., found a similar preoperative and postoperative MMSE score of 27.86±1.76 [17], which aligns with the findings of the present study. This prospective study demonstrated that the duration of prostate resection did not significantly affect MMSE scores in the preoperative, postoperative 1st and 6th hour, suggesting that Postoperative Cognitive Decline (POCD) was unlikely when the prostate resection time was less than 60 minutes (p=0.4234) [Table/Fig-8]. Similar results were reported by Kotekar N et al., where the duration of surgery had no significant impact (p=0.97) [29]. However, S¸eker TY et al., observed a significant decrease in MMSE scores from preoperative to postoperative (72 hr) period (p<0.001), and Aytaç I et al., found significantly lower postoperative (24th hour) MMSE scores compared to preoperative scores in the general anaesthesia group (p=0.003) [30,31].

Regarding the correlation between cognitive scores and serum sodium levels, the present study did not find any significant difference in the mean MMSE scores at preoperative, postoperative 1st and 6th hour (p=0.3423) [Table/Fig-9]. However, there was a significant negative but weak association between the duration of surgery and postoperative serum sodium levels at the 1st and 6th hour (p=0.01) [Table/Fig-10]. Furthermore, a weak association was observed between irrigation volume and postoperative 1st and 6th hour serum sodium levels (p=0.01) [Table/Fig-11].

In a study by Wioletta M et al., it was indicated that older patients experienced greater disturbance of cognitive function in the MMSE test. Additionally, the study demonstrated that higher education levels were associated with lower cognitive disturbance measured by the MMSE test [32].

Central neuraxial block was recommended over general anaesthesia as it allows for early recognition of symptoms and signs of TURP syndrome. Regional anaesthesia may also help reduce the risk of postoperative venous thrombosis. Clinical trials have found no difference between regional and general anaesthesia in terms of blood loss, postoperative cognitive function, or mortality [18,24].

Limitation(s)

The study has several limitations, one of which is that it was conducted at a single center. However, most notably, the study was not blinded, and the psychometric assessment was subjective. The prolonged postoperative decline was self-reported. The findings should be seen as a promising aspect that needs investigation in larger populations with different co-morbidities among the patients, and the utility of different irrigation solutions should be assessed. To generalise the results of the study to a larger population, the

above concern needs to be addressed, and further studies should be conducted along similar lines.

CONCLUSION(S)

In the present study, none of the patients developed cognitive dysfunction in the postoperative period after undergoing TURP surgeries under spinal anaesthesia. It was also observed that the reduction in serum sodium levels was directly proportional to the volume of irrigation fluid used and the duration of the procedure. Glycine was used as an irrigant fluid without significant complications when the duration of surgery was kept to less than 45 minutes.

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