

A study on the relationship between the intraoperative regional cerebral oxygen saturation trends and cognitive decline after lower limb surgeries in elderly patients

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Abstract

Background: The purpose of the study was to assess whether there is a correlation of cerebral oxygenation levels after spinal anaesthesia with the decline in cognitive function. **Materials & Methods:** After thorough PAC of the patients, patients were administered Spinal anaesthesia and haemodynamic parameters (SpO₂, BP, HR) were monitored. Also cerebral oxygenation was monitored through NIRS and rSO₂ values were tabulated intra operatively. Neurocognitive battery of tests were presented to the patient both pre-operatively and intra-operatively and MMSE Memory and Executive functions were compared pre-operatively and post operatively and their variations were correlated with rSO₂. **Results:** POCD was seen in 16% of patients in immediate post operative day (D0) which decreased to 12% on D10. Cerebral oxygen saturation (rSO₂) was monitored in 50 patients undergoing lower limb surgery with central neuraxial anaesthesia. The mean value of rSO₂ of the right side reduced from 65.04 to 59.56 after giving central neuraxial block which further reduced to 57.72 after commencement of surgery which remained the same throughout. At the end of the procedure rSO₂ increased to 60.16 and further returned to near-baseline value of 64.46 at 30 mins post operatively. Similarly, mean rSO₂ of the left side was 64.94 at baseline which reduced to 60.12 after central neuraxial block and stayed at 56.98 till end of procedure which increased to 62.28 at 30 minutes post operatively. MMSE score at baseline (pre-operatively) was 25.92±1.724 which reduced to 24.98±3.820 on post-operative day at D0, which subsequently increased slightly to 26.26±1.871 on Day 5 and came to near baseline values of 25.88±1.734 on Day 10. Memory value at baseline was a mean of 7.68 (on a scale of 12) with a standard deviation of ±0.999 and on Day 0 post operatively was 7.48±0.953 and it came back to 7.58±1.032 on Day 5 and came to near baseline values of 7.66±1.002 on Day 10 post operatively. There was weak correlation of rSO₂ variations with POCD (MMSE scores, Memory values and Executive function). **Conclusion:** Incidence of POCD is in 12% of patients during D10 post operatively. rSO₂ decreased intra-operatively. There was no strong correlation with decline in rSO₂ values during intra-operative period with development of POCD.

Keywords: Postoperative cognitive dysfunction [POCD], regional anaesthesia, spinal anaesthesia, regional oxygen saturation (rSO₂) monitoring, cognitive function test.

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Introduction

Postoperative cognitive dysfunction (POCD) is defined as a new cognitive impairment arising after a surgical procedure. Its diagnosis requires both pre- and postoperative psychometric testing. Its manifestations are subtle and manifold, depending on the particular cognitive domains that are affected. The most commonly seen problems are memory impairment and impaired performance on intellectual tasks [1]. It is defined as a--more than expected post-operative deterioration in cognitive domains, including short-term and long-term memory, mood, consciousness, and circadian rhythm. POCD is diagnosed by specific neuropsychological tests, which are

conducted before and after exposure to anaesthesia. The syndrome may be detected days to weeks after surgery and may also remain a permanent disorder resulting in significant functional impairment and socioeconomic burden for weeks to months after the procedure. Though pathophysiology remains obscure, many potential risk factors such as increasing age, genetic pre-disposition, and pre-existing cognitive impairment have been identified. The use of potentially neurotoxic drugs, low cerebral oxygenation and neuro-inflammation are possible aetiological factors [2]. Postoperative cognitive dysfunction is not uncommon in elderly patients after major surgery [3]. Elderly patients are more prone to develop cerebral desaturation than younger patients due to decreased physiological reserve that accompanies aging and thus the incidence of POCD. There is increased risk of postoperative complications because of numerous comorbidities that accompanies aging including cerebral ischemia and neurodegenerative disorders [4,5]. Anaesthetic agents

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have major impact on POCD. As a rule, the shorter the duration of action of the anaesthetic agent, the shorter will be the duration of cognitive impairment in the immediate post-operative period. Patients are now often premedicated with a sedative that impairs memory, e.g., midazolam; this practice should be critically reassessed. In a clinical study, the author found measurable memory impairment one day after surgery in patients who had been premedicated with midazolam and had then undergone 1–2 hours of general anaesthesia with propofol and remifentanyl [6]. There is clinical evidence that increased depth of anaesthesia may be associated with an increased incidence of POCD [7], although others have failed to confirm this [8]. If anaesthetic agents do contribute to POCD, the effect may be subsumed within the effects of surgery because the incidence was not greater in subjects receiving general anaesthesia. In other studies, it was found out that elderly patients subjected to general anaesthesia displayed more frequent cognitive impairment during the immediate postoperative period in comparison to those who received a regional technique [9]. Regional oxygen saturation (rSO₂) monitoring systems permit the continuous non-invasive measurement of cerebral regional oxygen balance within the frontal cerebral cortex. Using rSO₂ monitoring to manage anaesthesia in elderly patients under-going major abdominal surgery reduces the potential exposure of the brain to hypoxia; this might be associated with decreased effects on cognitive function and shorter PACU and hospital stay. The present study was performed to evaluate the correlation of intraoperative rSO₂ and decline in cognitive function if developed in elderly patients after lower limb surgery.

Materials & methods

The study was an open ended, prospective observational study, conducted in the Woodburn OT complex, IPGMR and SSKM hospital, Kolkata, West Bengal between 1st May 2018 to 30th April 2019. The patients were selected from the age of 50 upwards with ASA 1 and 2 criteria posted for elective lower limb. As it is an observational study, it was decided that 50 people in the age group of >50 years was needed for the study.

Inclusion criteria

- Elderly patients with normal or mild cognitive function
- Age above 50 yrs of either sex
- Patients having ASA status Grade I & II
- Patients undergoing elective lower limb surgeries under spinal anaesthesia
- Patients gave informed consent for surgery and anaesthesia

Exclusion criteria

- Patients' refusal
- Any contraindication to spinal block
- Morbid obesity
- Coagulopathy
- Infection at block site
- Significant cardiovascular, respiratory, renal, hepatic, metabolic disease
- History of substance abuse, psychiatric disorders
- Patients having dementia
- Allergy to local anaesthetics
- Incomplete or failed block requiring GA

Haemodynamic parameters was studied like hear rate, ECG, blood pressure, SpO₂, rSO₂ value etc. Neurological parameters studied like MMSE test, digital subtraction tests, attention span test, tests involving language and comprehension, digit span test, memory tests (immediate, recent and remote), tests to understand visuospatial skills and perception and tests involving executive functions and frontal lobe functions. The study was conducted after obtaining approval from the Institutional Ethics Committee and informed consent from the patients who were undergo elective lower limb surgery under subarachnoid block. Complete pre-anaesthetic evaluation was performed in each patient including detailed history taking, thorough physical check-up, airway examination, cognition function and routine

preoperative investigations. A complete cognitive function test was presented to them one day before the OT. Baseline results were noted. Patients were kept fasting for 8 hours before surgery. Patients were premedicated with oral ranitidine 150mg two hours before surgery. After entering the operating room, monitors were attached for monitoring the peripheral haemoglobin saturation (SpO₂), electrocardiogram (ECG) and non-invasive blood pressure (NIBP) during the study period and baseline parameters were recorded. Patients were administered spinal anaesthesia with 10 mg of 0.5% bupivacaine plus 10 mcg of fentanyl. 26 G needles were used and midline approach was used. Paramedian approach was used in few patients with calcified interspinous ligaments. A 10° and 15° medial angulation of the needle was used to reach the midline. Patient was monitored and allowed to develop motor block and then surgeon was allowed to give the skin incision. All 50 patients had successful motor blocks and no needs of any rescue analgesics were given. No failures were noticed. Supplemental O₂ were given 2 lts/ min through nasal prong during placement of the block and surgery. All the patients were sedated with i.v. midazolam 2 mg and fentanyl 50 microgram to avoid anxiety & discomfort during the procedure. Bilateral rSO₂ sensors were placed on the right and left sides of the forehead prior to spinal anaesthesia. Values were continuously measured using near-infrared spectroscopy (INVOS 4100; Somanetics Inc, Troy, MI, USA). The rSO₂ values were recorded throughout the procedure in all patients. Cerebral oxygen desaturation cut offs were defined as established in the literature in three ways, as follows: an absolute rSO₂ reading of <50% or a reduction of >20% or >25% of the patient's baseline rSO₂ lasting ≥15 seconds. To assess cognitive function, batteries of neuro-cognitive tests were presented to the patient. Reliable change scores to assess cognitive change from baseline to 10 for each patient were used. These scores were calculated for each neuropsychological assessment by first computing the difference from baseline (pre-operative) to 10 days for each subject, and finally standardizing the change score for the study patients by subtracting the control group's mean and dividing the result by the control group's SD. In this way, the scores of the controls were used to adjust for any learning effect in the study patients in the surgical group. Patient demographic characteristics, durations of surgery, tourniquet induced ischemia, and motor block were recorded. Hemodynamic variables (blood pressure and heart rate), respiratory variables (oxygen saturation by pulse oximetry) were measured. All these data were recorded in the operating room for analysis at the following times: T1, prior to induction (baseline); T2, 10 min after spinal puncture; T3-T5, 5 min, 15 min and 30 min, respectively, after the start of surgical procedure; T6, just before end of the procedure (5 mins); T7 at the end of surgery, respectively, after deflating the tourniquet; T8 and T9, postoperatively at 15 min and 30 min after surgery during recovery from the motor block. Patients were given the same battery of tests on day 0 of post-operative stay in the hospital, day 5 post operatively and day 10 post-operative day. The Sample size was kept to 50 subjects in the study. All raw data of study parameters were entered in the Microsoft Excel spread sheet and analysed by Statistica version 6 [Tulsa, Oklahoma: Stat Soft Inc, 2001] and Graph Pad Prism version 5 [San Diego, California: Graph Pad Software Inc., 2007]. Data were expressed as mean ±SD. Variables are made normally distributed by Kolmogorov-Smirnov goodness-of-fit test other than Education, SPO₂ and Memory score values. INVOS monitor for RSO₂ was used for maintaining the RSO₂ values during the intra operative period and immediate post-operative period.

Results

The purpose of the study was to assess whether there is a correlation of cerebral oxygenation levels after spinal anaesthesia with the decline in cognitive function. For the purpose of cognitive function correlation with MMSE and memory were done on day before the surgery, day of immediate post op, 5th day post op and 10th day post op.

Table 1: Demographic parameters (age and weight)

	N	Mean	Standard Deviation
Age	50	72.06	10.277
Weight	50	72.58	12.568

About 50 patients with mean age 72.06 ± 10.277 yrs were enrolled for the study. The weight of patients was in the range of 72.58 ± 12.568 for the study [Table 1]. Heart rate at baseline was 87.64 ± 12.409 . After giving central neuraxial block patient's Heart Rate increased to 89.04 ± 11.403 . After 30 minutes of skin incision, heart rate was further increased to 90.98 ± 10.710 and throughout intra-operatively it remained the same before gradually decreasing to 89.8 ± 10.814 5 minutes before end of the surgery. Heart rate increased to 90.04 ± 10.810 at the end of surgery, decreased to 88.74 ± 10.648 15 minutes after end of surgery and then decreased to 88.62 ± 11.019 30 minutes post operatively [Table 2/ Fig. 1].

Table 2: Heart rate in different time period

Heart Rate	N	Mean	Standard Deviation
HR at baseline	50	87.64	12.409
HR after 10 mins spinal anaesthesia	50	89.04	11.403
HR after 5 mins incision	50	90.78	12.374
HR after 15 mins incision	50	90.94	11.514
HR after 30 mins incision	50	90.98	10.710
HR before 5 mins end of procedure	50	89.8	10.814
HR at end of procedure	50	90.04	10.810
HR at 15 mins post operatively	50	88.74	10.648
HR at 30 mins post operatively	50	88.62	11.019

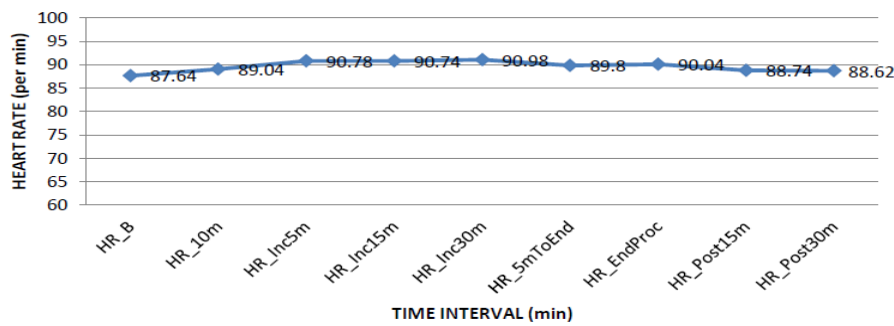


Fig 1: Heart rate progression with time interval

The mean blood pressure of the patients at baseline was 129/77. After giving spinal anaesthesia, patient's blood pressure dropped to a mean of 103/64. Then blood pressure gradually increased to 105/67 after 5 minutes of incision and 109/71 after 15 minutes of incision and 112/75 to 30 minutes after incision and 118/78 till end of procedure. Blood pressure remained at 126/79 at post operative 30 minutes [Table 3/ Fig. 2].

Table 3: Systolic blood pressure in different time period

Systolic Blood Pressure	N	Mean	Standard Deviation
SBP at baseline	50	129.20	14.096
SBP after 10 mins spinal anaesthesia	50	103.48	15.517
SBP after 5 mins incision	50	105.64	15.917
SBP after 15 mins incision	50	109.76	17.260
SBP after 30 mins incision	50	112.80	17.714
SBP before 5 mins end of procedure	50	116.60	16.773
SBP at end of procedure	50	118.64	15.879
SBP at 15 mins post operatively	50	124.24	15.901
SBP at 30 mins post operatively	50	125.88	15.977

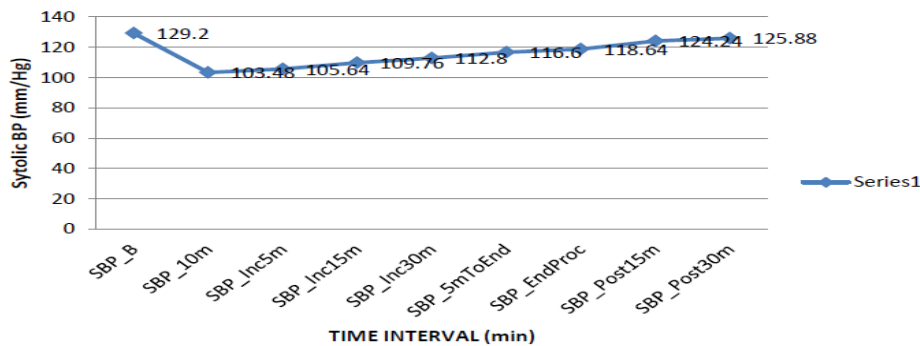


Fig 2: Systolic BP with time

Table 4: Diastolic blood pressure in different time period

Diastolic Blood Pressure	N	Mean	Standard Deviation
DBP at baseline	50	77.12	9.824
DBP after 10 mins spinal anaesthesia	50	64.42	10.606
DBP after 5 mins incision	50	67.36	10.345
DBP after 15 mins incision	50	71.60	10.498
DBP after 30 mins incision	50	75.52	10.510
DBP before 5 mins end of procedure	50	76.16	8.655
DBP at end of procedure	50	78.20	9.615
DBP at 15 mins post operatively	50	78.92	8.743
DBP at 30 mins post operatively	50	79.32	9.541

Diastolic blood pressures at various intra-operative intervals were recorded and tabulated [Table 4/ Fig. 3].

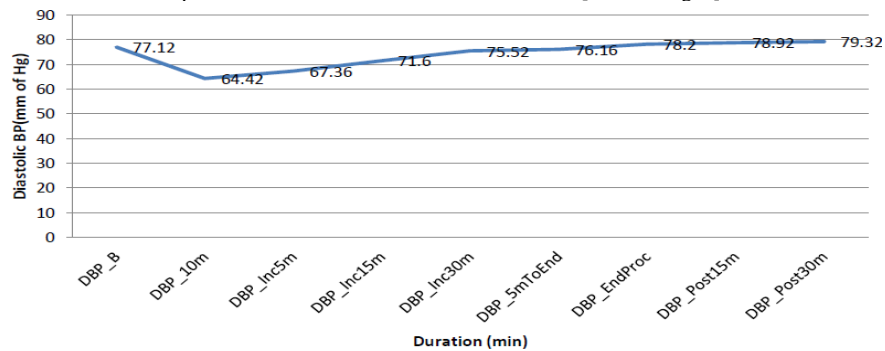


Fig 3: Diastolic BP with time

Seventeen patients had peripheral oxygen desaturation after spinal anaesthesia. Peripheral oxygen desaturation is defined as reduction of saturation of more than 4% from the baseline period. Oxygen saturation of the patients at baseline was at a mean value of 97.36% and which decreased to 96.36% after giving central neuraxial block and inj midazolam 2 mg i.v. was given before incision which kept the oxygen saturation at 96.24% at 5 mins after incision. However, SpO2 started increasing after this point and increased to 96.56 at 15 minutes after incision, 97.38 at 30 minutes of incision and to 96.98 at 5 minutes before the end of procedure and subsequently increased to 97.26% at the end of procedure and further increased to 97.50% till 30 minutes post operatively [Table 5/ Fig.4].

Table 5: SpO2 in different time period

SpO2	N	Mean	Standard Deviation
SpO2 at baseline	50	97.36	1.306
SpO2 after 10 mins spinal anaesthesia	50	96.36	2.284
SpO2 after 5 mins incision	50	96.24	2.378
SpO2 after 15 mins incision	50	96.56	2.062
SpO2 after 30 mins incision	50	96.98	2.114
SpO2 before 5 mins end of procedure	50	97.38	2.156
SpO2 at end of procedure	50	97.26	1.827
SpO2 at 15 mins post operatively	50	97.34	1.649
SpO2 at 30 mins post operatively	50	97.50	1.776

SpO2 was recorded at various intervals intra-operatively and recorded [Table 5].

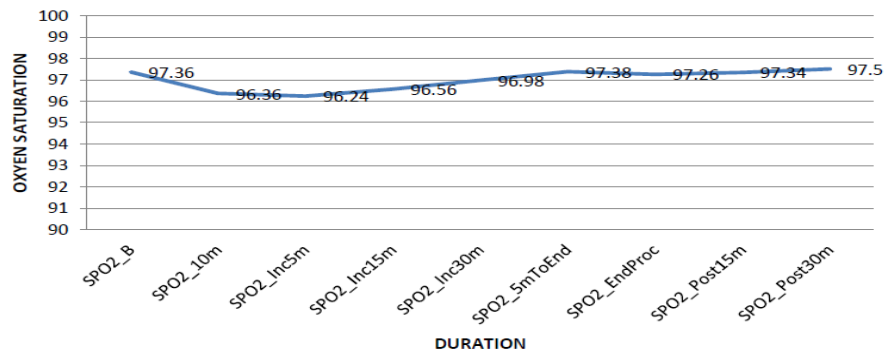


Fig 4: Oxygen saturation with time

About 40% (20 out of 50) patients developed cerebral desturation after spinal anaesthesia. Desaturation is defined as 20% or more from baseline. As depicted, rSO₂ of the right side reduced from 65.04 to 59.56 after giving central neuraxial block which further reduced to

57.72 after commencement of surgery which remained the same throughout. rSO₂ increased to 57.46 at 15 minutes of incision, became 57.76 at 30 minutes of incision and reduced to 57.36 before 5 minutes of end of procedure. Again rSO₂ increased to 60.16 at the

end of procedure, rSO₂ decreased to 59.90 15 minutes post operatively and which increased to 64.46 at 30 mins post operatively. rSO₂ of the left side was also similar 64.94 at baseline which reduced to 60.12 after central neuraxial block which decreased to 58.48 at 5 minutes of incision and reduced to 57.58 after 15 minutes of incision

and increased to 57.74 at 30 minutes after incision stayed at 56.98 till 5 minutes before end of procedure and 60.54 at end of procedure which increased to 62.28 at 15 minutes after procedure and 66.04 till 30 minutes post operatively [Table 6/ Fig. 5].

Table 6: rSO₂ of the right side in different time period

rSO ₂ of the right side	N	Mean	Standard Deviation
rSO ₂ at Baseline	50	65.64	5.882
rSO ₂ after 10 mins spinal anaesthesia	50	59.56	8.237
rSO ₂ after 5 mins incision	50	57.72	9.022
rSO ₂ after 15 mins incision	50	57.46	8.527
rSO ₂ after 30 mins incision	50	57.76	8.317
rSO ₂ before 5 mins end of procedure	50	57.36	9.979
rSO ₂ at end of procedure	50	60.16	9.375
rSO ₂ at 15 mins post operatively	50	59.90	9.067
rSO ₂ at 30 mins post operatively	50	64.46	6.228

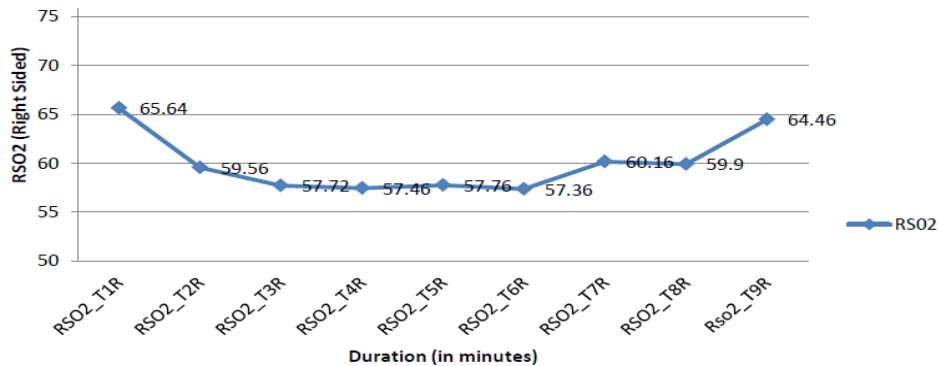


Fig 5: rSO₂ of the right side

Table 7: rSO₂ of the left side in different time period

rSO ₂ of the left side	N	Mean	Standard Deviation
rSO ₂ at Baseline	50	64.94	6.228
rSO ₂ after 10 mins spinal anaesthesia	50	60.12	7.790
rSO ₂ after 5 mins incision	50	58.48	8.728
rSO ₂ after 15 mins incision	50	57.58	9.278
rSO ₂ after 30 mins incision	50	57.74	9.785
rSO ₂ before 5 mins end of procedure	50	56.98	10.501
rSO ₂ at end of procedure	50	60.54	9.314
rSO ₂ at 15 mins post operatively	50	62.28	7.393
rSO ₂ at 30 mins post operatively	50	66.04	6.321

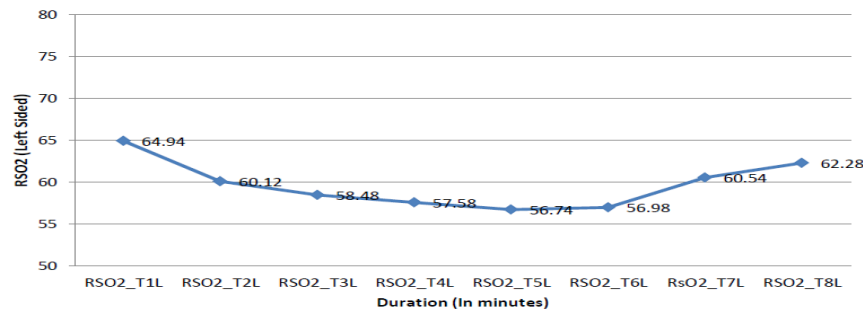


Fig 6: rSO₂ of the Left Side

rSO₂ scores were plotted with time interval intra-operatively [Table 7/ Fig 6].

MMSE Variations: As depicted, mean MMSE at baseline (pre-operatively) was 25.92±1.724 which reduced to 24.98±3.820 on post-

operative day at D0, which subsequently increased slightly to 26.26±1.871 on Day 5 and came to near baseline values of 25.88±1.734 on Day 10.

Table 8: MMSE variations in different time period

MMSE variations	N	Mean	Standard Deviation
MMSE at baseline	50	25.92	1.724
MMSE on Day 0	50	24.98	3.820
MMSE on Day 5	50	26.26	1.871
MMSE on Day 10	50	25.88	1.734

MMSE scores were recorded post operatively and shown [Table 8/ Fig. 7].

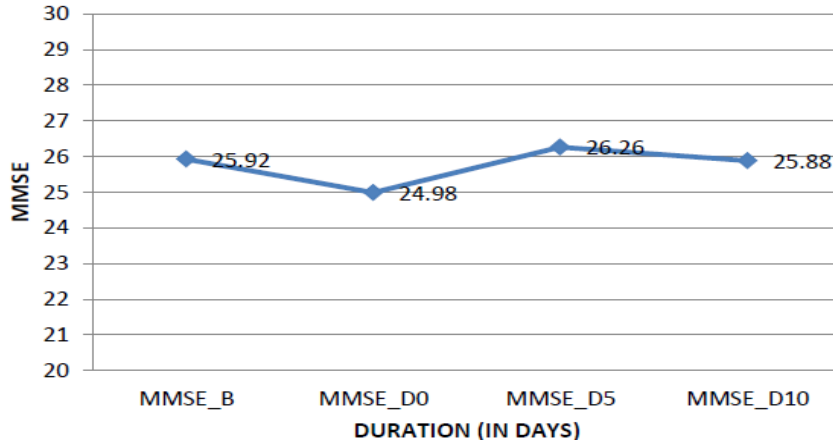


Fig 7: MMSE changes over time

Memory Variations

Memory at baseline was a mean of 7.68 (on a scale of 12) with a standard deviation of ± 0.999 and on Day 0 post operatively was 7.48 ± 0.953 and it came back to 7.58 ± 1.032 on Day 5 and came to near baseline values of 7.66 ± 1.002 on Day 10 post operatively. Memory scoring was done post operatively tabulated as shown [Table 9/ Fig. 8]

Table 9: Memory variations in different time period

Memory	N	Mean	Standard Deviation
Memory at baseline	50	7.68	0.999
Memory on Day 0 post operatively	50	7.48	0.953
Memory on Day 5 post operatively	50	7.58	1.032
Memory on Day 10 post operatively	50	7.66	1.002

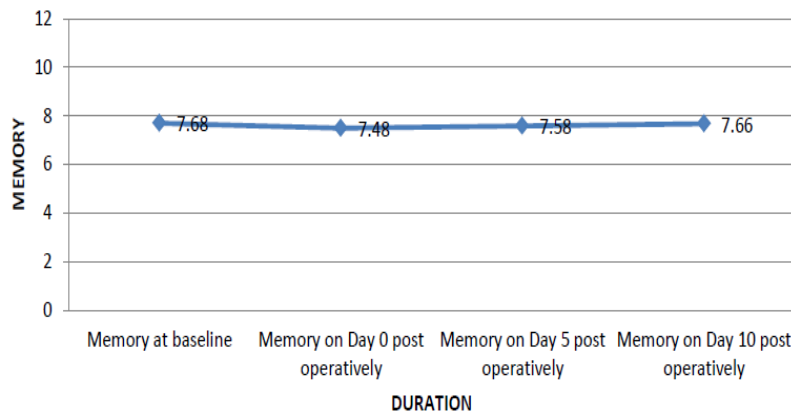


Fig 8: Memory score progression

Discussion

POCD is an established complication of surgery in elderly [10]. The incidence, predictive factors and causes of POCD have not been established with scientific evidence. Lower limb surgeries are most commonly performed under subarachnoid block in elderly population aiming symptomatic benefit and improving the quality of life. A total of 50 patients were taken into consideration in this study (n=50). POCD was detected in 8(16%) patients on the day of surgery, and in 4 (8%) patients on day 5 post operatively and 6 (12%) patients on Day 10 in our study. Canet et al., in their study, reported remarkably

lower incidence of POCD at 1 week from surgery for minor surgeries (6.8%) compared to major surgeries (25.8%). In the present study, we found that 8 out of 50 patients had MMSE score of <24 on the day of surgery, indicating POCD. The number of patients developed POCD was 8 on D0, 4 on D5 and 6 on D10 [11]. The present study was designed to assess the correlation of intraoperative regional cerebral oxygen saturation with postoperative cognition in elderly patients undergoing lower limb surgeries. The trend of rSO2 was recorded and whether episodes of cerebral desaturation observed during regional anaesthesia was correlated with POCD. It was found

that the rSO₂ values weakly correlated with the values of MMSE. This clearly implies the fact that POCD does not correlate strongly with episodes of cerebral oxygen desaturation under central neuraxial block during lower limb surgeries. The baseline rSO₂ values were also compared with the Memory progression over time to determine the correlation between them. There was no significant correlation between the rSO₂ value and memory scoring over time. Episodes of decreased rSO₂ can be caused by various factors and detected during both cardiac and noncardiac surgery. A decreased rSO₂ may be caused by ventilation or oxygenation disorders, changes in hemodynamics, changes in the haemoglobin concentration, or even the patient's position during surgery [12]. It has also been observed in various studies that more the age of the patients, more frequent the incidence of desaturation of cerebral oxygenation intra-operatively and more the post-operative decline. Casati et al. in 2005 observed that cerebral desaturation occurs in nearly 20% of elderly patients undergoing major abdominal nonvascular surgery [13]. In one study, the relationship between intraoperative regional cerebral oxygen saturation trends and cognitive decline after total knee replacement in patients over 65yrs of the age (n=125) under spinal anaesthesia was assessed, and it was observed that there was significant decrease in rSO₂ in all patient during surgery. It was concluded that detection of a trend to asymmetry in rSO₂ values can warn the physicians about the possible post-operative onset of memory decline. Interestingly, all the patients were over 65 years of age (n=125) in whom the relationship between intraoperative regional cerebral oxygen saturation trends and cognitive decline after total knee replacement under spinal anaesthesia were studied [14]. But, in the present study patients included above age 50yrs but below 65yrs which maybe the reason for the decline of rSO₂ was not observed in all patients who were administered central neuraxial block. Birute Kumpaitiene et al [15] in 2018, in a prospective observational study that included 59 patients undergoing coronary artery bypass graft surgery with CPB who underwent neuropsychological tests (Mini Mental State Evaluation, Auditory Verbal Learning Test, digit span test, digit symbol substitution test, and Schulte table) the day before and 10 days after the surgery observed that a decrease in rSO₂ during cardiac surgery is not necessarily related to the development of POCD. The present study was also consistent with this finding and no strong correlation with cerebral desaturation with POCD was found. In the present study, it was also observed that 40% of the patients (20 out of 50) had cerebral oxygen desaturation after spinal anaesthesia. In a study conducted by Vives et al, the incident of cerebral desaturation was similar (46%) after spinal anaesthesia in elderly patients undergoing orthopedic surgery for hip fracture [16]. MMSE was the most important test among other tests to assess cognitive dysfunction in the patients of the present study. In any patient whose score came to be less than <24 was taken to be POCD. The MMSE is helpful in scaling cognitive impairment, documenting cognitive changes over time, and assessing the effects of therapeutic agents on cognition as concluded by Monroe T et al [17]. Memory scoring was significantly decreased from baseline values on Day 0 of surgery which returned to baseline values on Day 10 post operatively in this study. Five patients had a decrease in Memory Values on Day 0 post operatively, which came to the baseline values at the end of Day 5 and persisted on Day 10. Also, correlation with rSO₂ revealed that their memory impairment has no or weak correlation with cerebral desaturation. The finding is similar to two other studies where comparison was made between GA and spinal anaesthesia citing that memory loss in the spinal group was much lesser than GA after 1 week surgery [18, 19]. In the present study, a MAP value of 94 mm of Hg came down to 77 mm of Hg after administering spinal anaesthesia and came up to 87 mm Hg after 30 minutes of anaesthesia and was 91 mm Hg at the end of surgery, which became 95 mm Hg post operatively. MAP values showed changes at 30 minutes of anaesthesia which corresponded with the rSO₂ value.

Similar results were achieved as MAP of 100 came down to 84 after spinal anaesthesia in other study [20].

Conclusion

Incidence of POCD is in 12% of patients during D10 post operatively. There was weak correlation of rSO₂ variations with POCD (MMSE scores, Memory values and Executive function) and rSO₂ decreased intra-operatively. There was no strong correlation with decline in rSO₂ values during intra-operative period with development of POCD.

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