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Post-operative cognitive dysfunction in elderly patients undergoing elective orthopaedic lower limb surgeries under central neuraxial anaesthesia

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***Abstract*---**Introduction: Aging population is a major demographic trend worldwide. Globally, 50% of the elderly individuals are estimated to undergo atleast one surgical procedure. POCD is one of the most common and often poorly understood. POCD is more common in elderly patients undergoing orthopaedic surgeries. This study was conducted to find incidence and its correlation with associated factors for POCD in elderly patients posted for elective orthopaedic surgeries under central neuraxial blockade (CNB). Methods: Study was conducted in 60 patients of either sex, aged >60 years (ASA grade I-III) posted for elective orthopaedic lower limb surgeries under CNB. Mini mental status examination was done preoperatively, on postoperative days 1, 3 and 30. Primary aim was to find out the incidence of POCD; secondary outcomes assessed included correlations with age, sex, level of education, ASA grade, DM, HTN, alcoholism, smoking, type of anaesthesia, intraoperative hypotension, and duration of hospital stay and duration of surgery. Association between categorical variables was assessed with chi-square test. A p-value of<0.05 was considered statistically significant. Results: Among the 60 patients studied

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15(26.67%) patients showed POCD on day 1 which decreased to 18% on day 3 and 12 % on day 30 associated with increasing age, low level of education, higher ASA grade, presence of Diabetes mellitus, associated alcoholism, intraoperative hypotension, increased duration of surgery and increased days of hospital stay. POCD was seen in 44% in ASA grade 2 compared to 4% in ASA grade 1. In patients with DM, POCD was seen in 68% of patients compared to 8% in patients without DM. The incidence of POCD was 60% and 16% in patients with and without alcoholism. Conclusion: POCD is a definite complication after surgery and anaesthesia in the elderly population POCD is common after orthopaedic surgeries in elderly patients (27%). Age, low level of education, ASA PS II and above, associated diabetes, alcoholism, intraoperative hypotension, prolonged duration of surgery and hospitalisation were emerging significant risk factors.

***Keywords*---**post-operative cognitive dysfunction, orthopaedic, central neuraxial blockade.

Introduction

The quality of life, of the patient after surgery is as important as the absence of postoperative complications and mortality rates. Neuropsychological complications such as memory, concentration, language and comprehension disturbances are frequent phenomena in early postoperative period. Post-operative cognitive dysfunction is defined as a “more than expected” postoperative deterioration in cognitive domains, including short-term and long-term memory, mood, consciousness and circadian rhythm. [1] Post-operative cognitive dysfunction (POCD) is relatively more frequent in the elderly patient and is an unwanted complication in the postoperative period particularly in cardiac and orthopaedic pelvic surgeries and most of the time underestimated. The incidence and pathology of POCD have been mostly studied after cardiac surgeries. [2,3] Studies on noncardiac surgeries have reported incidence as high as 46% perioperatively but specific studies on incidence and pathophysiology of POCD in orthopaedic patients are few. Hence, this observational study was planned in our institution to find the incidence of POCD and to correlate the various probable risks and the outcomes so that remedial or prophylactic measures can be initiated early in future management of patients.

Methods

After obtaining approval from the institutional ethical committee and obtaining informed consent from the patient. This prospective, descriptive study was conducted in patients of age more than 60 years, scheduled for elective orthopaedic lower limb surgeries under neuraxial anaesthesia at Medical college Hospital, VIMS, Ballari. The study was conducted in the department of Anaesthesiology, VIMS, Ballari in a period of one year.

Patientsof more than 60 years of age of either sex, posted for elective orthopaedic lower limb surgeries, ASA physical status I-III were included in the study. Patients with pre-existing cognitive dysfunction, Patients who presented with mini mental

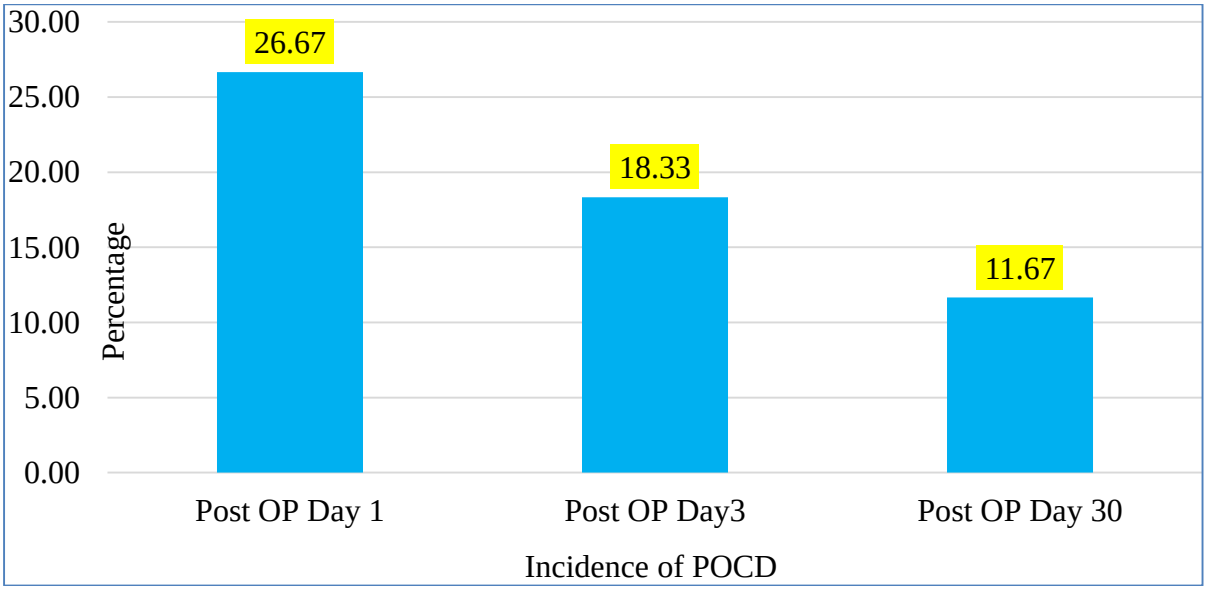
score examination (MMSE) <23, pre-existing cardiac disease, neurological conditions, severe respiratory disease, coagulopathy and known allergy to the drugs used were excluded from the study.

Pre-anaesthetic evaluation was performed and baseline cognition was assessed 24 hours prior to surgery using MMSE. Informed and written consent was obtained. Intra-operatively all standard monitors were applied (Electrocardiography, Pulse Oximetry, Non-invasive Blood Pressure) and Basal readings were recorded. Under strict aseptic precautions appropriate neuraxial anaesthesia was administered. Vitals were monitored and recorded throughout the procedure. Patient was shifted to Post Anaesthesia Care Unit (PACU) after the procedure. Post-operative cognition level was assessed on post-operative day 1, day 3 and day 30 after surgery using MMSE.

All the dataassessed was entered in MS excel Sheet, cleaned and analysed. Related categorical and numerical variables were subjected to suitable statistical tests. The numerical variables are assessed for uniformity of distribution before non-parametric tests. Chi-square test was used for categorical data categorical data. A p value of<0.05 was considered statistically significant

Results

Among the 60 patients studied 15(26.67%) patients showed POCD on day 1 which decreased to 18% on day 3 and 12 % on day 30 associated with increasing age, low level of education, higher ASA grade, presence of Diabetes mellitus, associated alcoholism, intraoperative hypotension, increased duration of surgery and increased days of hospital stay.



The incidence of POCDwas 11%, 75% and 100% in 60-70yrs, 70-80yrs and >80yrs respectively. Age emerged as a significant risk factor for POCD. The incidence of

POCD increased with low level of education. POCD was seen in 9% and 7% in PUC and higher level of education compared to50 and, 82% in middle and primary level of education. POCD was seen in 44% in ASA grade 2 compared to 4% in ASA grade 1. In patients with DM, POCD was seen in 68% of patients compared to 8% in patients without DM.The incidence of POCD was 60% and 16% in patients with and without alcoholism.

Parameter		POCD	NO POCD	P Value
Age	60-70	5(10.9%)	41(89.1%)	<0.001
	70-80	9(75%)	3(25%)	
	>80	2(100%)	0	
Gender	Male	8(25%)	24(75%)	0.755
	Female	8(28.57%)	20(71.43%)	
Educational status	Primary	9(81.8%)	2(18.2%)	<0.001
	Middle	4(50%)	4(50%)	
	Higher	2(6.7%)	28(93.30%)	
	PUC	1(9.1%)	10(90.9%)	
ASA grade	Grade 1	1(3.8%)	25(96.2%)	<0.001
	Grade 2	15(44.1%)	19(55.9%)	
DM	Yes	13(68.4%)	6(31.6%)	<0.001
	No	3(7.3%)	38(92.7%)	
HTN	Yes	8(40%)	12(60%)	0.09
	No	8(20%)	32(80%)	
Smoking	Yes	7(31.8%)	15(68.2%)	0.492
	No	9(23.7%)	29(76.3%)	
Alcoholism	Yes	9(60%)	6(40%)	0.001
	No	7(15.6%)	38(84.4%)	
Anaesthesia	SAB	13(24.1%)	41(75.9%)	0.173
	SAB+EA	3(50%)	3(50%)	
Intraoperative Hypotension	Yes	5(100%)	0	<0.001
	No	11(20%)	44(80%)	
Duration of surgery	< 1hour	0	4(100%)	0.001
	1 – 2 hours	7(16.7%)	35(83.3%)	
	>2 hours	9(64.3%)	5(35.7%)	
Duration of hospital stay	<10 days	0	6(100%)	<0.001
	10-20 days	5(11.90%)	37(88.10%)	
	>20 days	11(91.7%)	1(8.3%)	

Gender, Smoking and type of Anaesthesia were not significant risk factors for POCD.

Discussion

In this study, we found that the incidence of POCD in elderly patients who underwent non-cardiac surgeries was in line with other published literature. Results showed that patients who had POCD performed progressively poorer on days 1, 3, and 30 compared to baseline performance.

The high incidence of cognitive dysfunction after orthopaedic patients can result from long bone fractures, from prolonged immobilization, and partially from perioperative stress in addition to the above-mentioned risk factors. Colonna et al. concluded that the incidence of cerebral embolization after lower extremity arthroplasty was between 40 and 60%.[4] Fatal cerebral embolization constituted complications accompanying long bone fractures,[5] total knee replacements,[6] hip arthroplasty,[7] and vertebroplasty,[8] in which the embolic material passed into the brain through an open foramen ovale,[9] although post-mortem examinations did not reveal it.[4]

In our study conducted on 60 patients undergoing elective orthopaedic lower limb surgeries under central neuraxial blockade, the incidence of POCD was in line with other published literature. POCD was detected in 26% on day and gradually reduced to 19% on day 3 and 11% on day 30.

Age, low level of education, ASA II and more, associated diabetes, alcoholism, intraoperative hypotension, prolonged duration of surgery and hospitalisation were emerging significant risk factors for development of POCD.

Majority of the studies reported have evaluated POCD at ≤ 1 week as early POCD and 3 months post-surgery as a long-term POCD time point. In comparison to early stage POCD, the results show a decline in incidence of POCD at 3 months.[10] In our study POCD evaluation on post-operative days 1, 3, and 30 also showed a gradual decline in the incidence of POCD, suggesting that it is temporary in few patients and could persist long-term in certain patients, probably even beyond 30 days. The results of our study are in line with earlier reports and most importantly, highlights the early onset and early decline in the trend of POCD. Hence long term POCD can be evaluated earlier than 3 months.

Incidence of POCD has been reported to be extremely frequent in elderly patients in our study. The aged brain is different from the younger brain in several important aspects, including size, distribution and type of neurotransmitters, metabolic function, and capacity for plasticity. Hence, POCD is more common in the elderly patients after major surgery, compared to middle-aged patients. Monk et al. documented the presence of POCD on discharge from the hospital[11] in 36.6% of surgical patients aged 18–39, 30.4% of those aged 40–59, and 41.4% of those aged 60 and above (P value = <0.0001 three months after surgery) showing that increasing age is a significant risk factor for POCD. Krenk et al. reported that POCD can arise at any age but tends to last longer and to affect everyday life and the return to work more severely in patients over age 60.[12]

In our study, gender is not a significant risk factor for POCD and was in line with other studies. Interestingly study done by Kotekar et al.[13] females were found at a significant risk for POCD (P value = 0.04).

We found that patients with a higher level of education had a lower incidence of POCD compared to those with lower educational levels. In educated population the brain is exposed to continuous challenging mental activities that could delay the manifestations of cognitive impairment by utilising neuronal reserves and increasing the efficacy of synapses to re-route around damaged areas. A

hypothetical construct coined “cognitive reserve” has been utilised to describe models of cognitive ageing and circumstances where the brain sustains injury.[14] Surrogates of cognitive reserve have included education level and performance on tests of knowledge such as vocabulary. Kotekar et al. found similar results in their study that illiterates (33%) patients were more prone to POCD compared to literates (23%) but was not statistically significant (P value = 0.64). Monk et al.[11] reported that decreased years of education (12.5±3.0) was a significant risk factor (P value = 0.0002) for POCD compared to increased years of education (13.7±2.6 years)

In our study, associated diabetes mellitus was a significant risk factor for POCD. Chronic hyperglycemia in older age is well recognized as a predictor of age-related cognitive impairment.[15] Patients with diabetes are at 50%-140% increased risk of dementia.[16] and even in dementia free range experience a 20 to 50% increased rate of cognitive decline [17]. In a systemic review done by Feinkohl et al.[18] suggested that middle aged to older adults with diabetes are overall at 26% increased risk of POCD compared with diabetic free patients. Glucose induces formation of advanced glycation end products (AGE). AGE reacts with specific cell surface receptors (RAGE) which result in neurodegeneration and atherogenesis, for instance, predicts postoperative cognitive decline in older age. Surgical trauma and anaesthetic drugs might increase the vulnerability of patients with diabetes to such underlying neuropathological changes, resulting in a greater impact of surgery on level of cognitive function in patients with diabetes compared with non-diabetic patients.

In our study alcoholism was significant risk factor for POCD. Alcoholism has been identified as a risk factor for post-operative delirium which is a risk factor for POCD. Chronic alcohol use causes atrophy of the frontal lobes[19,20] and hypometabolism in the frontal cortex.[21-23] This caused impairment in executive functions that is related to frontal lobe dysfunction and impaired memory that is detectable by various neuropsychological tests. After surgery/anesthesia, decrease in the level of cognition are more pronounced involving visuospatial recent memory and executive functions were impaired in alcoholic patients despite an absence of preoperative neurologic abnormalities. Hudetz et al.[24] concluded that alcohol abuse in older patients presents a risk for post-operative impairment in the domains of visuospatial abilities and executive functions that may have important implications for quality of life and health risks. In the same study, Hudetz et al. concluded that patients with a history of alcohol abuse had decreased cognitive impairment after surgery compared to preoperative cognition levels than patients with no such history of alcohol abuse undergoing surgery, even if they stopped drinking for five weeks preoperatively; these patients also had worse cognitive impairment than patients who did not undergo surgery, whether or not they had a history of alcohol abuse

In our study smoking was not a significant risk factor for POCD. The result was in line with other studies. Incidence of POCD was similar in smokers and non-smokers although some studies have suggested smoking as a protective factor in preventing POCD. Wang et al[25] reported that preoperative smoking history was significantly correlated with a decreased risk of POCD. Preoperatively increased serum tumor necrosis factor-α (TNF-α) level had significant correlation with

increased risk of POCD. Nicotine exerts multiple effects on health. Nicotine simulates ACh signaling, which has a variety of functions that unrelated or even antagonistic. In the same study, they found that a preoperative smoking history might reduce the risk of POCD in patients of advanced age, potentially because of nicotine-mediated activation of the cholinergic anti-inflammatory pathway and inhibition of central nervous system inflammation or inflammatory factors (TNF-a, IL-1b, and IL-6)

Type of anaesthesia has been thought to a risk factor for POCD, risk being more with the use of benzodiazepines and inhalational agents. Surgeons and patients presume that Regional Anaesthesia is not associated with postoperative cognitive disturbances and is a safer option compared to General anaesthesia. Benzodiazepines are known for their effect on cognitive function; this could be related to slow and variable metabolism, particularly of diazepam which also has several active metabolites. Several studies however report that benzodiazepines do not play a major role in cognitive dysfunction after anaesthesia.[26] Rasmussen et al. in a randomised study of RA versus GA in 438 patients found no causative relationship (P value = 0.06) between GA (20%) and RA (13%) in long-term POCD although there was increased of POCD with GA. [27] Studies reported by O'Dwyer et al.,[28]Casati et al.,[29] and Somprakit et al.,[30] found no statistical difference in the incidence of POCD after either GA or RA. In a study done by Kotekar et al,[13] there was no significant difference (P value = 0.2) in the incidence of POCD between general anaesthesia (15%) and regional anaesthesia (26%) . In our study there was no significant difference between spinal anaesthesia and combined spinal epidural anaesthesia.

In our study intraoperative hypotension (IOH) was a significant factor for POCD. IOH below cerebral autoregulation causes decreased perfusion and has deleterious impact on brain function. During hypotension, cerebral autoregulation maintains stable blood flow despite changes in systemic blood pressure (BP), which is typically observed within the mean arterial pressure (MAP) range of 60–150 mmHg.[31] These limits are not fixed, and autoregulation pressures tend to be higher in hypertensive patients. Cerebral autoregulation can also be modulated by sympathetic nervous activity, the vascular renin-angiotensin system and any factor (notably changes in arterial CO2 pressure) that decreases or increases CBF.[31] Noteworthy, in chronic hypertension the limits of autoregulation are usually shifted toward higher BP values. In a comprehensive review done by Krzych et al,[188] they concluded that available data are quite inconsistent and there is a paucity of high-quality evidence convincing that IOH is a risk factor of postoperative cognitive impairment. Difference in results between various studies is the major limitation to set up reliable recommendations regarding intraoperative hemodynamic management to protect the brain against hypotension-related hypoperfusion.

In our study Increased duration of surgery and hospital stay are significant risk factors for POCD. Increased duration of surgery exposes the patient to longer duration of anaesthesia and increased surgical trauma which can stimulate inflammation and breakdown of BBB: one of the proposed causative factor for POCD. Canet et al.,[33] concluded that the incidence of POCD at 7 days was remarkably lower after minor surgery (6.8%) than after major surgery (25.8%).

After 3 months, no statistical difference was present between the two groups. Factors such as duration of anaesthesia, surgical trauma, postoperative stress response, hospitalization and post-operative pain and analgesics are implicated to explain the difference in rates of POCD between major and minor surgery.[37-39] Monk et al[11] reported that there was no significant difference (P value = 0.52) in the duration of anaesthesia in patients with POCD (215.0±92.8 minutes) and in patients without POCD (211.5±103.2 minutes). They also observed that patients with POCD (7.2±13.6 days) had a significantly (P value = 0.01) longer duration of hospital stay compared to patients without POCD (5.0±6.3 days)

Limitations of the Study

Patient participation required cooperation and interest, and therefore the included patients represent a group of relatively well-functioning subjects where the incidence of POCD may not correlate with the general patient population at that age. Only patients posted for elective surgery were considered for the study excluding the emergency cases, hence incidence of POCD may not corelate in all orthopaedic surgeries

Conclusion

Post-operative cognitive dysfunction is more frequent in elderly people undergoing elective orthopaedic surgeries with incidence as high as 26%. Age, low level of education, ASA II and more, associated diabetes, alcoholism, intraoperative hypotension, prolonged duration of surgery and hospitalisation were emerging significant risk factors. Hence modifiable risk factors such as diabetes, alcoholism, intra-operative hypotension, duration of surgery and hospital stay etc should be taken care to prevent the occurrence of post-operative cognitive dysfunction.

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