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Original Research Article

Effect of general and sub-arachnoid anesthesia on the incidence of postoperative delirium and cognitive impairments in elderly Chinese patients

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Abstract

Purpose: *To investigate the effect of general and subarachnoid (spinal) anesthesia on the incidence of postoperative delirium and cognitive impairments in elderly Chinese patients.*
Methods: *Elderly Chinese patients (n = 281) aged 65 – 79 years (mean age = 74.12 ± 4.15 years) who underwent proximal femoral fracture surgery were recruited over a 1-year period for this study. The patients were evaluated using neuropsychological assessment battery (NAB) 24 h before surgery, and on the first day 1 month after surgery. Data on activity of daily living (ADL) (in this case toileting at the time of discharge) were recorded and analyzed.*
Results: *There was no significant difference in the number of patients that developed postoperative delirium between the two anesthesia groups ($p > 0.05$). Although the trail making test (TMT) scores (parts A and B) were increased on the first day 1 month after surgery, there were no significant differences in NAB results between the two groups ($p > 0.05$). Patients who received subarachnoid (spinal) anesthesia had significantly higher dependency for toileting at the time of discharge than those who received general anesthesia ($p < 0.05$).*
Conclusion: *These results show that general and subarachnoid (spinal) anesthesia do not cause postoperative delirium and cognitive dysfunction in elderly Chinese patients who underwent proximal femoral fracture surgery.*

Keywords: *Anesthesia, Cognitive function, Delirium, Elderly patients, Surgery*

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INTRODUCTION

Postoperative cognitive impairment (POCI) is a functional mental disorder that arises after a surgical procedure [1]. It affects verbal and visual memories and leads to lack of concentration and attention deficit [2]. Postoperative cognitive impairment is characterized by high morbidity and mortality among elderly patients [3]. Results of studies on POCI are divergent in their conclusions [3,4]. It has been speculated that the incidence of POCI after hip fracture surgery will continue to increase in China up to 2050. Temporal fluctuations peak during the initial postoperative period and return to the initial state within a week after surgery [1]. The severity of POCI is determined by co-morbidities in patients and type of surgery [2,5]. The type of anesthesia

used during surgery is thought to contribute to POCI. Regional anesthesia is generally preferred for elderly patients by most anesthesiologists [6]. However, studies have shown that there is no marked difference in incidence of POCI several weeks after surgery between patients on general and regional anesthesia [4,7]. Although anesthetics used in surgeries have profound effect on the central nervous system (CNS), it is difficult to describe the individual effect [3]. The actual contribution of anesthesia to POCI is largely unknown [8].

Hip or proximal femoral fracture refers to fracture of the femur in bone areas distal to the articular cartilage of the hip, to a level approximately 5 cm below the lower border of the lesser trochanter [9]. Proximal femoral fracture impacts on the quality of life of patients [10].

The aim of this study was to investigate the effect of general and subarachnoid (spinal) anesthesia on the incidence of postoperative delirium and cognitive impairments in elderly Chinese patients.

METHODS

Materials

Fentanyl was obtained from Taylor Pharmaceuticals (USA). Propofol was product of Fresenius Kabi AG (Germany). Rocuronium was bought from Hospira (USA). Spinal cord needle (Quincke 25 G) was purchased from Becton, Dickinson, and Company Ltd. (USA). Ropivacaine was product of AstraZeneca (UK), while epinephrine was obtained from Mylan (USA).

Patients and general information

Elderly patients (n = 281) aged 65 – 79 years (mean age = 74.12 ± 4.15 years) who underwent proximal femoral fracture surgery in Suzhou Ninth People's Hospital, Soochow University, Suzhou, Jiangsu, China, were recruited over a 1-year period for this study.

Patients with disease(s) of the CNS (dementia and Parkinson's disease), as well as those on antidepressant therapy, were excluded from the study. There were 130 male patients and 151 female patients. The study protocol was approved by Institutional Ethical Committee of Suzhou Ninth People's Hospital, Soochow, China, and the study guidelines were in accordance with the laws of China and Declaration of Helsinki (2008). Written informed consents were signed by the patients and their family members.

Experimental design

The patients were randomly assigned to 2 groups: general anesthesia and subarachnoid anesthesia groups. Patients in general anesthesia group (n = 154, mean age = 74.12 ± 4.15 years) received fentanyl at a dose of 3.5 µg/kg body weight (bwt) and 1.5 mg propofol/kg bwt. Intubation was facilitated with 0.6 mg rocuronium/kg bwt. Mechanical ventilation was carried out with a 50 % oxygen-air mixture to achieve tidal volume of 6 – 8 mL/kg bwt, respiratory rate of 10 – 12 breaths/min, oxygen saturation > 97 %, and end-tidal carbon dioxide of 35 mmHg.

Subarachnoid anesthesia group patients (n = 127, mean age = 73.12 ± 6.15 years) with L3-L4 or L4-C5 intervertebral space were administered 20 µg fentanyl/kg bwt and 0.75 % ropivacaine via spinal puncture. In the event that hypotension (reduction in systolic blood pressure > 30 % from pre-procedural value) occurred, 1 mg epinephrine/kg bwt was intravenously injected. The patients were evaluated using NAB 24 h before surgery, and on the first day after 1 month of surgery.

Assessment of confusion

Acute onset and fluctuating course, inattentiveness, disorganized thought, and altered level of consciousness were used for deciding the absence or presence of delirium. Confusion assessment was performed daily after surgery for 7 days [11].

Mini-mental state examination (MMSE)

A total of 11 questions covering five areas of cognitive function (temporal orientation, spatial orientation, attention, calculation, recall, and language) were used for MMSE. The maximum score was 30 and score < 24 was considered as cognitive impairment [12].

Beck Depression Inventory-II

A total of 21 items were rated on a 0 to 3 scale. The total score ranged from 0 to 63. Scores ≥ 20 were taken as indicative of depression [13].

Trail making test (TMT)

Part A: Patients were made to draw a line serially connecting Chinese numerals 1 to 25. Ability to complete the task within 150 sec was

indicative of normal state or absence of cognitive impairment.

Part B: Patients were made to draw lines linking 12 Chinese zodiac animals and their pictures. Ability to complete the task within 150 sec was indicative of normal state or absence of cognitive impairment [14].

Auditory-verbal learning test (AVLT)

The AVLT measures verbal learning in terms of immediate and delayed free recall, recognition, and retroactive and proactive interference [15]. The AVLT score was calculated and scores ≤ 23 were considered normal [16].

Digit symbol substitution test (DSST)

The DSST requires response speed, sustained attention, visual spatial skills and set shifting. Patients were made to draw lines linking Chinese symbols and digits within 2 min. Scores ≥ 80 were taken as normal [17]. The higher the score, the better the patient's performance.

Verbal fluency test (VFT)

Patients were asked to name animals within 1 min. Ability to name at least 15 animals within the stipulated time was indicative of normal state or absence of cognitive impairment [18].

Measurement of ADL (toileting)

Toileting as an index of ADL was used as a measure of patient's independence. It was classified into total dependence, partial dependence, and independence. Data on ADL at the time of discharge were recorded and analyzed.

Statistical analysis

The sample size was calculated based on the assumption that 7 ± 1 % patients would develop postoperative delirium. Power analysis was performed using an online calculator, assuming α = 0.05 with a power (β) of 80 %.

Qualitative data are expressed as relative frequency (percentage), while quantitative data are presented as mean ± standard deviation (SD). Groups were compared using Student's *t*-test, Chi-squared test, Fisher exact test, and Mann-Whitney test as appropriate. All statistical analyses were performed using SPSS (25.0). Values of $p < 0.05$ were taken as indicative of statistically significant differences.

RESULTS

Clinical and demographic characteristics of patients

There were no significant differences in patients' preoperative demographic characteristics, clinical conditions, NAB outcome, and operative characteristics between the two anesthesia groups ($p > 0.05$; Table 1).

Results of neuropsychological tests battery

There was no significant difference in the number of patients who developed postoperative delirium between the two anesthesia groups ($p > 0.05$). Although the TMT scores (parts A and B) were increased on the first day 1 month after surgery, there were no significant differences in NAB results between the two groups ($p > 0.05$). These results are shown in Table 2.

ADL results

Patients who received subarachnoid (spinal) anesthesia had significantly higher dependency for toileting at the time of discharge than those who received general anesthesia ($p < 0.05$; Table 3).

DISCUSSION

Postoperative cognitive impairment (POCI) is a common adverse event after surgery. Its manifestations are subtle and diverse, depending on the particular cognitive domains that are affected. The diagnosis of POCI requires both pre- and postoperative psychometric testing. Elderly patients in particular are vulnerable to memory disturbances and other types of cognitive impairment after surgical operation. Emergence from anesthesia is often accompanied by signs of delirium such as fluctuating mental status and inattentiveness. Several studies have evaluated the effects of general anesthesia and non-general anesthesia on POCI. However, the results reported in these studies are inconsistent. The cerebral cortex is the basis of cognition. Factors that cause functional abnormalities in the cerebral cortex result in cognitive impairment [2,3]. The clinical manifestations of POCI range from mild cognitive abnormalities to severe memory impairment such as loss of judgment and personality changes.

Table 1: Preoperative demographic characteristics, clinical conditions, neuropsychological assessment battery and operative characteristics (n, %)

Parameter		Anesthesia group		
		General	*Subarachnoid (spinal)*	
		n = 154	n = 127	*P*-value
Age (years)		74.12 ± 4.15	73.12 ± 6.15	
Sex	Male	69 (45)	61 (48)	0.631
	Female	85 (55)	66 (52)	
Weight (kg)		59.22 ± 7.82	60.23 ± 6.45	0.245
Education	Primitive	65 (42)	49 (38)	0.827
	Below graduation	55 (36)	48 (38)	
	Graduate and above	34 (22)	30 (24)	
Ethnicity	Han Chinese	139 (90)	115 (90)	0.992
	Mongolian	12 (8)	9 (7)	
	Tibetan	2 (1)	2 (2)	
	Uighur Muslim	1 (1)	1 (1)	
American Society of Anesthesiologists status	I	67 (43)	55 (43)	0.998
	II	69 (45)	57 (45)	
	III	18 (12)	15 (12)	
New York Heart Association status	I	62 (40)	51 (40)	0.947
	II	71 (46)	57 (45)	
	III	21 (14)	19 (15)	
Hypertension		55 (36)	42 (33)	0.706
Diabetes		25 (16)	23 (18)	0.751
Asthma		7 (5)	6 (5)	0.998
Chronic obstructive pulmonary disease		5 (3)	2 (2)	0.463
Duration of Surgery (min)		65.00 ± 11.00	68.00 ± 15.00	0.055
RBC transfusion		18 (12)	17 (13)	0.719
Hospital stay (days)		9.15 ± 2.14	9.02 ± 2.15	0.613
Mini-mental state examination		25.62 ± 1.45	25.71 ± 1.18	0.574
Beck Depression Inventory-II		6.85 ± 2.81	6.89 ± 2.85	0.906
Trail-making test Part A (sec)		89.15 ± 12.15	88.47 ± 13.45	0.657
Trail-making test Part B (sec)		112.43 ± 14.15	114.52 ± 15.43	0.238
Auditory-verbal learning test		17.14 ± 1.42	17.47 ± 1.52	0.061
Digit symbol substitution test		95.43 ± 7.11	95.44 ± 6.45	0.991
Verbal fluency test		18.89 ± 1.02	18.93 ± 1.15	0.758

Table 2: Results of NAB 1 month after proximal femoral fracture surgery

Parameter	Anesthesia group						Comparisons between groups at EL
	General			*Subarachnoid (spinal)*			
	n = 154			n = 127			
	BL	EL	*P*-value	BL	EL	*P*-value	*P*-value
Mini-mental state examination	25.62 ± 1.45	25.12 ± 1.52	0.300	25.71 ± 1.18	25.45 ± 1.25	0.089	0.051
Beck Depression Inventory II	6.85 ± 2.81	6.91 ± 2.85	0.853	6.89 ± 2.85	7.15 ± 2.95	0.476	0.489
Trail-making test Part A (sec)	89.15 ± 12.15	94.22 ± 15.47*	0.002	88.47 ± 13.45	97.42 ± 16.48*	< 0.0001	0.093
Trail-making test Part B (sec)	112.43 ± 14.15	123.42 ± 17.41*	< 0.0001	114.52 ± 15.43	124.52 ± 18.29*	< 0.0001	0.607
Auditory-verbal learning test	17.14 ± 1.42	17.01 ± 1.22	0.389	17.47 ± 1.52	17.22 ± 1.02	0.125	0.124
Digit symbol substitution test	95.43 ± 7.11	95.44 ± 6.15	0.989	95.44 ± 6.45	94.12 ± 7.15	0.124	0.097
Verbal fluency test	18.89 ± 1.02	16.81 ± 0.98*	< 0.0001	18.93 ± 1.15	16.72 ± 0.93*	< 0.0001	0.434

*$P < 0.05$, compared with BL value (BL = 1 day before surgery; EL = first day 1 month after surgery)

Table 3: Activity of daily living (toileting) in patients at the time of discharge (n, %*)*

Parameter	Anesthesia group		*P*-value
	General	*Subarachnoid (spinal)*	
	n = 154	n = 127	
Total dependence	48 (31)	55 (43)*	0.036
Partial dependence	51 (33)	43 (34)	
Independence	55 (36)	29 (23)	

*$P < 0.05$, compared with general anesthesia

Age has been the only widely accepted risk factor for development of POCI [8]. However, there are inconsistencies and controversies surrounding the level of involvement of anesthesia in POCI. Although it has been speculated that general anesthesia could be the cause of POCI, other studies have shown no significant differences in its incidence between patients receiving general and non-general anesthesia [8]. At present, there are inconsistent conclusions regarding comparative incidence of POCI in patients receiving general anesthesia and subarachnoid (spinal) anesthesia. The results obtained in this study showed that there were no significant differences in NAB on the first day 1 month after surgery between general and subarachnoid (spinal) anesthesia groups. Patients who received subarachnoid (spinal) anesthesia had significantly higher dependency for toileting at the time of discharge than those who received general anesthesia. These results are not in agreement with those obtained in previous studies involving Greek, Turkish and Japanese patients [1,6,19]. In this study, the TMT scores were within normal limit. It has been reported that pre-existing neurocognitive impairments, preoperative demographic characteristics, preoperative clinical condition, and operative characteristics of patients affect TMT scores [20–22]. The results of this study indicate that subarachnoid (spinal) anesthesia worsened the ADL (toileting) of patients after proximal femoral fracture surgery. This finding is not in agreement with those of a previous study [23]. Spinal anesthesia disturbs bladder function [24]. It interrupts micturition reflex via blockage of efferent fibers and afferent nerves [23]. Higher Charlson Comorbidity Index scores are associated with a disturbance of daily living (toileting) after proximal femoral fracture surgery in elderly patients [24]. General and spinal anesthesia have been shown to slow the recovery of bladder functions in elderly patients after proximal femoral fracture surgery.

There was no significant difference in the number of patients who came down with postoperative delirium between the two anesthesia groups. These results may have been due to the complexity of the surgical procedure, and they are in agreement with those of a randomized trial involving Greek patients [1].

Limitations of the study

The likely limitations of this study are: (1) small sample size/population; (2) non-inclusion of a normal control group; (3) short follow-up period; (4) failure to carry out multivariate analysis for an independent predictor of postoperative cognitive dysfunction and delirium; (5) non-inclusion of other ADL parameters; (6) failure to carry out comparison of hemodynamic parameters and postoperative pain management; (7) analysis of ADL (toileting) data of patients who stayed in hospital only; (8) use of a single population (Han Chinese); and (9) failure to include other surgical parameters that could affect postoperative cognitive dysfunction.

CONCLUSION

The results obtained in this study suggest that general and subarachnoid (spinal) anesthesia do not cause postoperative delirium and cognitive dysfunction in elderly Chinese patients who underwent proximal femoral fracture surgery.

DECLARATIONS

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Availability of data and materials

The datasets used and analyzed during the current study available from the corresponding author on reasonable request.

Conflict of interest

The authors declared that they have no conflict of interest or any other competing interest regarding results and/or discussion reported in the research.

Contribution of authors

Both authors have read and approved the manuscript for publication. Wei-Xia Ren was project administrator, contributed to

methodology, literature review, resources, investigation, and supervision of the study. Ran-Ran Wu contributed to methodology, literature review, resources, formal analysis, and data curation of the study, draft and edited the manuscript for intellectual content. Both authors agree to be accountable for all aspects of work ensuring integrity and accuracy.

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