Effect of a Single-dose Dexmedetomidine on Postoperative Delirium and Intraoperative Hemodynamic Outcomes in Elderly Hip Surgery; A Randomized Controlled Trial Dexmedetomidine for Postoperative Delirium

Chidchanok Choovongkomol, M.D.[1], Sothida Sinchai, M.D.[1], Kongtush Choovongkomol, M.D.[2]

[1]Department of Anesthesiology, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima, Thailand, [2]Department of Orthopedics, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima, Thailand.

ABSTRACT

Objective: Postoperative delirium (POD) is common in elderly patients. The growing evidences suggesting the potential benefits of dexmedetomidine (DEX) infusion in reducing POD. However, the administration of a single-dose DEX remains controversial. This study aims to investigate the effect of a single-dose DEX on POD in elderly patients undergoing hip surgery.

Materials and Methods: This prospective, randomized, double-blinded trial enrolled patients aged over 65 years who underwent hip surgery under spinal anesthesia. Patients were assigned to either the DEX (received intravenous DEX 0.3-0.5 μg/kg after incision), or the normal saline solution (NSS). Delirium assessments were conducted at the post anesthetic care unit (PACU) and at 24, 48 and 72 hours postoperatively using the Confusion Assessment Method (CAM).

Results: A total of 200 patients were randomized, with 100 in the DEX and 100 in the NSS. The incidence of POD was significantly lower in the DEX compared to the NSS ($P < 0.001$, RR 0.45, 95%CI: 0.28, 0.73). This difference remained significant at each postoperative assessment time point. There was no significant difference in sedation score and perioperative hemodynamics, except for a slightly lower intraoperative heart rate (P=0.015) and systolic blood pressure (P=0.029) observed at the PACU in the DEX, but these differences were not clinically significant. Additionally, the length of stay after surgery in the DEX was significantly shorter compare to the NSS (P=0.006).

Conclusion: A single-dose dexmedetomidine can reduce the incidence of POD within 72 hours postoperatively in elderly patients undergoing hip surgery without compromising intraoperative hemodynamic stability.

Keywords: Elderly; Dexmedetomidine; Delirium; Postoperative complications; Hip fractures; Hemodynamics
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INTRODUCTION

Hip fractures are a prevalent issue among the elderly population. Surgical intervention has emerged as the definitive and efficacious method for reducing morbidities and mortality.[1,2] However, due to the aging population, patients frequently present with multiple medical comorbidities, which may increase the likelihood of complications after surgery.[1,2]

Postoperative delirium (POD) represents a significant and common complication, particularly among elderly population with reported incidence rates ranging from 10 to 70%[3-6], depending on the surgical procedure and studied

Corresponding author: Chidchanok Choovongkomol
E-mail: thisismemoen@gmail.com
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population. Notably, vascular, cardiac and orthopedic surgeries especially urgent or semi-urgent repair of hip fractures exhibit a higher occurrence of POD.[6-8] The etiology of POD is multifactorial, stemming from patient-related factors such as advanced age or coexisting medical conditions, operative factors such as prolonged operative time or severe blood loss, and environmental factors such as staying in the ICU, where patients may have difficulty recognizing the time or being in an unfamiliar place. Some of these factors can be preventable, but others cannot. POD contributes to unfavorable outcomes, including prolonged hospitalization, increased costs of care, higher rates of morbidities and mortality, as well as, compromised functional and cognitive recovery.[4,6,8-10] Patients may develop post-operative cognitive dysfunction[11], leading to permanent brain damage if POD is not detected early.

Dexmedetomidine (DEX) is a highly selective α-2 adrenergic receptor agonist that has a range of potentially beneficial effects in the postoperative period. It possesses anxiolytic, sedative, analgesic and neuroprotective properties while causing minimal respiratory depression.[12,13] In recent years, the role of DEX in the perioperative period has garnered attention. Several studies have demonstrated that the perioperative used of DEX can substantially decreased the incidence of POD in the elderly patients.[13-18] However, the prescribed dose of DEX, along with its infusion technique - 1 mg/kg over 10 minutes than 0.3-0.8 μcg/kg/hr until the end of the operation - is a considerable dosage that can pose challenges of clinicians during perioperative management. Studies suggest that administering DEX via intravenous infusion may result in unstable hemodynamics and heightened levels of sedation in elderly patients.[15,17,20]

Accordingly, this study was designed to investigate the effect of a single-dose of DEX on the incidence of POD in elderly patients undergoing hip surgery. Moreover, we hypothesized that a smaller single-dose of DEX, compared to the prescribed dose, would be adequate to reduce POD with minimal impact on hemodynamics and sedation status. This consideration takes into account the pharmacokinetics and pharmacodynamics of DEX in the geriatric population, which advise reducing the dose by half. By employing this approach, we anticipate that anesthesiologists will be empowered to effectively prevent POD in elderly patients undergoing hip surgery.

MATERIALS AND METHODS

This prospective, randomized, double-blinded, placebo-controlled trial, based on the CONSORT 2010 guidelines[21], was conducted after obtaining approval from the author's affiliated institution (Institutional Review Board number 100/2022, approval date: August 18th, 2022) and registered prior to patient enrollment at the Thai Clinical Trials Registry (TCTR20221004001, approval date: October 4th, 2022). Written informed consent was obtained from all elderly patients with hip fractures before their enrollment. The study was conducted at a tertiary referral center in Thailand from October 2022 to June 2023.

The inclusion criteria were patients aged 65 years or older who were scheduled for hip surgery under spinal anesthesia with an appropriate peripheral nerve block during that time. The exclusion criteria were patients who had: 1) a known history of anaphylaxis to DEX, 2) comorbidities with delirium or dementia before the operation, 3) a history of stroke and residual neurological deficit, epilepsy, or Parkinson's disease 4) a psychological disease or the use of psychological drugs 5) conversion from spinal anesthesia to general anesthesia due to failure, 6) a history of sick sinus syndrome, severe sinus bradycardia (HR < 50 bpm) or second- or third- degree atrioventricular block without a pacemaker, 7) severe hepatic dysfunction (Child–Pugh grade C or higher), or renal failure requiring renal replacement therapy, or 8) unstable hemodynamics (HR< 60 bpm or > 150 bpm, BP < 90/60 mmHg or > 180/100 mmHg).

All investigators responsible for preoperative screening, data collection and assessment were trained and qualified by psychiatrists prior to the study. Cognitive function and delirium status were evaluated before the operation using the Thai Mini-Mental State Examination (MMSE)[22,23] which allows a maximum score of 30. A score of 14, 17 or 22 or higher (depending on the preoperative patient status) is considered normal. Additionally, the Confusion Assessment Method (CAM)[24] was employed before the operation.

Upon entering the operating theater, all patients were monitored for SBP, DBP, SpO_2 and ECG. A peripheral intravenous line was established in the upper limb, and a crystalloid solution (normal saline solution, lactated Ringer's or acetated Ringer's) was administered at a rate of 5-10 ml per kilogram before the initiation of anesthesia. All hip surgery was performed under spinal anesthesia with an ultrasound-guided peripheral nerve block for postoperative analgesia. An anesthesiologist used 0.5% isobaric bupivacaine (Marcaine®) at a dose of 10-15 mg for spinal anesthesia to achieve sensory level at less thoracic level 10, and 0.33% bupivacaine at a dose of 60-100 mg for an ultrasound guided-iliaca fascial space block which was a proper peripheral nerve block for postoperative analgesia.

All patients were randomized after confirming their

normal test results on the MMSE, CAM and ensuring that spinal anesthesia and an iliaca fascial space block were sufficient for the surgery. Randomization was performed using a block size of four, with each block contained a computer-generated random sequence of two groups in equal numbers. The first group received dexmedetomidine (Precedex® 200 µg/2 ml) at a dose of 0.3-0.5 µg/kg, administered intravenously through a slow injection within 10 minutes after the start of the operation. The second group received an equivalent volume of normal saline solution (NSS). An anesthesiologist, who was not otherwise involved in the trial, would open opaque envelopes for each group and prepared the trial syringe, ensuring that the solutions in identical-looking 10-ml syringes, matched the assigned sequential randomization numbers. Both investigators and patients were therefore completely blinded to treatment allocation. However, in case of emergencies or unexpected deterioration in a patient's clinical status, the attending anesthesiologist could adjust or discontinue drug administration if they deemed clinically necessary. Unmasking was allowed only when clearly needed for clinical purposes.

Throughout the operation, all patients would receive standard anesthesia care. No additional anesthetic, sedative agents or pain relief medication were allowed during the operation, except in necessary situations with the agreement of attending anesthesiologists. At the end of the operation, patients would be transferred to the post-anesthetic care unit (PACU) for close monitoring for one hour.

The primary end point of this study is postoperative delirium, while the sedative score as a secondary endpoint. Two investigators would independently assess delirium and sedation score, using the CAM for non-ventilated patients or the CAM for the Intensive Care Unit (CAM-ICU) for ventilated patients[24,25] and the Richmond agitation sedation scale[26], respectively, at the PACU, and at 24, 48 and 72 hours postoperatively. In cases of discrepant results, the investigators would re-assess the patients together to determine the reliable responses. Delirium is a complex condition that naturally fluctuates over time, so we decided to evaluated it consistently each morning.

All patients who were identified as having POD by the CAM or the CAM-ICU were referred to a consulting psychiatrist for the diagnosis and treatment of delirium. In terms of postoperative pain control, all patients would receive multimodal analgesia, which included a peripheral nerve block, non-opioid analgesic drugs such as acetaminophen or nonsteroidal anti-inflammation drugs (NSAIDs), unless contraindicated. The used of opioid drugs was minimized to the necessary extent.

For other secondary endpoints, hemodynamic values were documented and reported every 5 minutes throughout the perioperative and recovery periods as part of standard anesthetic care. We selected the greatest change in hemodynamic values from the preoperative baseline to represent the worse outcome associated with DEX. Similarly, for safety outcomes, we compared the changes in hemodynamic status to the preoperative baseline during each period. The definition of bradycardia is heart rate(HR) less than 60 bpm, or a decreased of more than 30% from baseline; tachycardia is HR more than 100 bpm; hypotension is Systolic blood (SBP) less than 90 mmHg, or a decreased of more than 30% of the baseline; hypertension is SBP more than180 mmHg, or an increase of more than 30% from baseline; hypoxia is pulse oxygen saturation less than 90%. The intervention included adjustment of study drug dose and/or administration of medication, fluid, oxygen or physical therapy. Additionally, we recorded and reported all intraoperative and in-hospital complications, the total length of stay during this visit and the length of stay after the operation.

Statistics

The sample size was calculated based on the primary endpoint from the study conducted by Xie S and Xie M.[25] In their study, the incidence of delirium in elderly patients undergoing hip surgery was reported as 4% in the DEX group and 17% in the NSS group. The calculated sample size of 86 patients per treatment group would be required to achieve a statistical power of 0.80 with a two-tailed significance level of 0.05 in order to detect a difference. Therefore, we decided to increase the sample size to 100 patients per treatment in order to account for potential dropouts after randomization.

All analyses were performed on an intention-to-treat basis, including all patients in the groups to which they were randomized. The normal distribution of data was assessed using the Shapiro-Wilk test. Primary outcomes, which consisted of categorical data, were reported as frequencies and percentages for each group. Other outcomes, including continuous data, were presented as means ± standard deviations (SDs) or median (Q1, Q3), depending on the normality of the data. Categorical data were also reported as frequencies and percentages. The analyses were conducted using STATA version 16.0 (StataCorp, College Station, TX, USA) with two-sided significance tests at a p-value < 0.05. Fisher's exact test was used to analyse categorical data, while the Student t-test or Mann-Whitney U test, as appropriate, were employed for continuous data. Regression analysis was employed to access differences in hypothesis testing.

RESULTS

A total of 249 patients were eligible for this study from October 2022 to June 2023. Among them, 49 patients were excluded as they met the exclusion criteria. Eight patients declined to participate and 24 patients had a history of delirium or dementia before the operation. Additionally, three patients had a history of head injury and still had neurological deficits, nine patients refused spinal anesthesia, and five patients had failed spinal anesthesia and were converted to general anesthesia before the operation. No delirium assessments were terminated due to deep sedation (Richmond agitation sedation scale less than -2) or coma and no emergency unblinding was necessary. The final intention-to-treat analysis included 100 patients in each group: the DEX and the NSS (Fig 1).

There were no significant differences between the two groups in terms of demographic data. The mean estimated dose of DEX was 0.43±0.1 μg/kg in the DEX group (Table 1).

The preoperative MMSE indicated normal cognitive function within our population, and the preoperative screening using the CAM did not detect any signs of delirium. The overall incidence of POD, defined as the occurrence of any delirium assessed at any time using the CAM, was significantly lower in the DEX compared to the NSS, with a p-value of less than 0.001 and a relative risk of 0.45 (95% CI 0.28, 0.73), and this difference remained significant at each postoperative assessment time point (Table 2).

All patients underwent the CAM screening for POD, except for three patients in the DEX and two patients in the NSS, who were intubated at 24-48 hours postoperatively, and they were assessed using the CAM-ICU for indicated POD.

There was no statistical difference between the treatment groups in terms of sedation score (Table 2), which used a cut-off point of less than -2 to indicate deep sedation requiring intervention, as well as perioperative hemodynamics values (Table 3). However, there were some notable differences in certain parameters were observed. The intraoperative heart rate (HR) of patients in the DEX was 75.9 (70, 85) bpm, whereas it was 80.8 (70, 90) bpm in the NSS. Additionally, the systolic blood

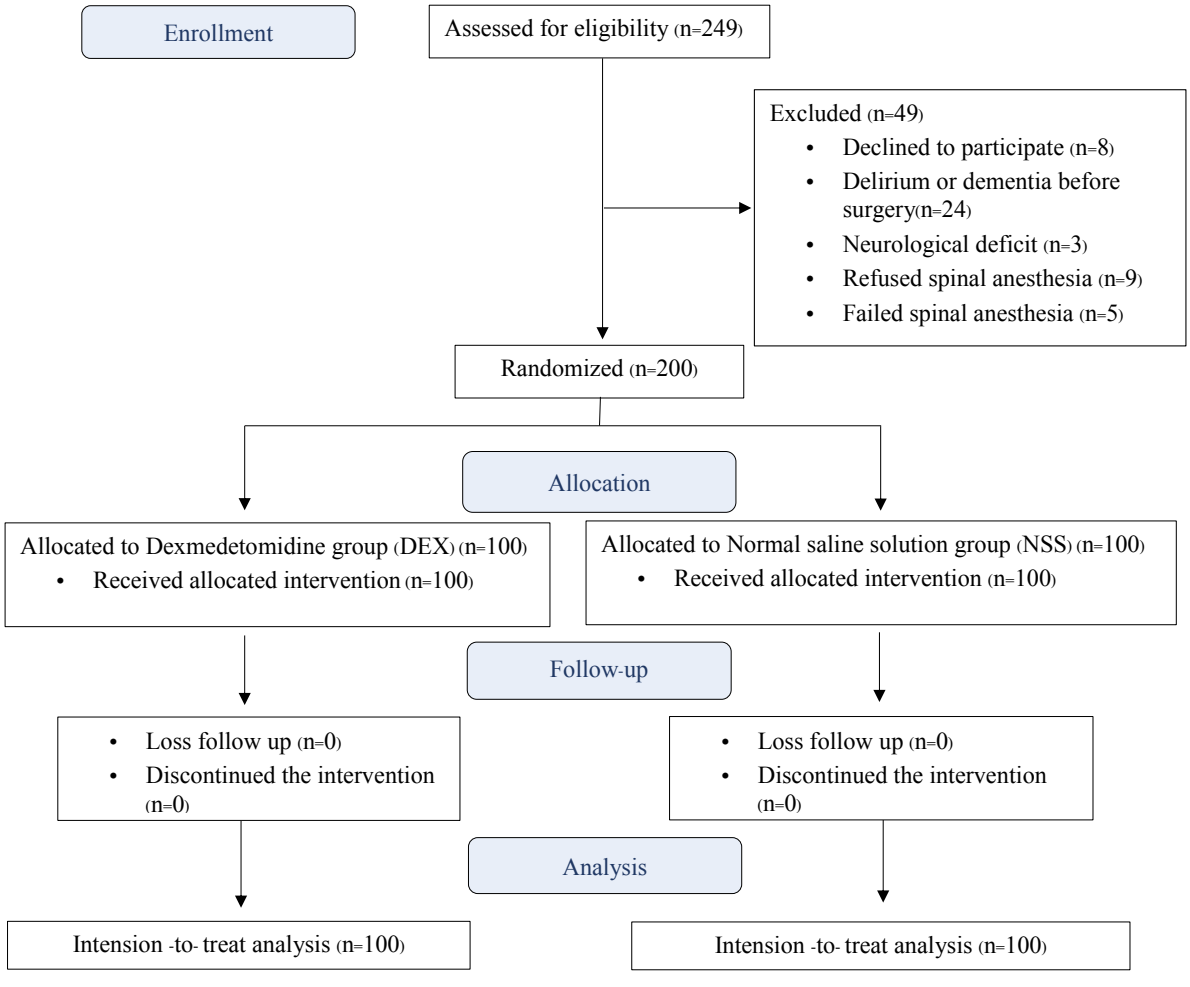


Fig. 1 CONSORT-Study Flow Diagram

TABLE 1. Baseline patients characteristic.

Variables	DEX group	NSS group	P value
Age (yr.)	78.8±8.8	80.4±7.8	0.053
Gender (M/F)	29/71	18/82	0.095
BMI (kg/m^2)	21.0±3.7	20.9±4.2	0.792
ASA physical status			
II/III/IV	5/95/0	1/95/4	0.051
Diagnosis			
Intertrochanteric fracture	66	63	0.177
Neck of femur fracture	29	36	
Subtrochanteric fracture	5	1	
Operations			
Cephalomedullary nail	69	65	0.543
Dynamic hip screw	0	1	
Multiple screws	2	0	
Hemiarthroplasty	22	27	
Total hip arthroplasty	7	7	
Co-morbidities			
HT	59	66	0.381
CAD, Valvular heart	7	10	0.613
Asthma/COPD/interstitial lung	6	6	1.000
Stroke with full recovery	8	8	1.000
DM	39	28	0.134
Thyroid disease	4	2	0.683
Chronic kidney disease (stage III-IV)	4	6	0.748
Liver cirrhosis (Child–Pugh grade A-B)	4	1	0.369
Medication			
Antihypertensives	60	65	0.557
Antihistamines	22	30	0.259
Diuretics	15	24	0.153
Opioids	18	23	0.484
NSAIDs	35	29	0.449
Benzodiazepines	30	22	0.259
Pre-operative lab values			
Hb (g/dl)	10.2 (9.1, 11.6)	10.2 (9, 11.3)	0.501
Sodium < 135 or > 145 mM/L	19	19	1.000
Potassium < 3.5 or > 5.5 mM/L	4	3	1.000
Perioperative Data			
Operative time (min)	115.5 (90, 135)	108.5 (90, 120)	0.073
Estimate intraoperative blood loss (ml)	131.7 (50, 1150)	118.4 (50, 150)	0.966
Intraoperative infusion (ml)	1081.7 (850, 1300)	961.6 (750, 1125)	0.051
Allogenic blood transfusion(ml)	95.7 (0, 235)	72.7 (0, 198)	0.255

TABLE 2. Incidence of post-operative delirium & sedation score.

Timing	DEX group n (%)	NSS group n (%)	RR (95% CI)	P value
Overall-Delirium	18 (18)	40 (40)	0.45 (0.28, 0.73)	***< 0.001****
PACU	1 (1)	11 (11)	0.09 (0.01, 0.69)	***0.020****
24 h	13 (13)	33 (33)	0.39 (0.22, 0.70)	***0.002****
48 h	11 (11)	34 (34)	0.32 (0.17, 0.60)	***< 0.001****
72 h	15 (15)	29 (29)	0.52 (0.30, 0.90)	***0.021****
Over all-Sedation score	6 (6)	9 (9)	0.67 (0.25, 1.8)	0.425
PACU	0	0	-	-
24 h	2 (2)	7 (7)	0.29 (0.06, 1.32)	0.112
48 h	2 (2)	1 (1)	0.50 (0.05, 5.43)	0.569
72 h	0	3 (3)	-	-

*A p value < 0.05 indicates statistical significance

TABLE 3. Perioperative hemodynamic values.

Parameters	DEX group n (Q1, Q3)	NSS group n (Q1, Q3)	P value
HR (/min)			
Preoperative	87.9 (80, 96)	88.9 (79, 99)	0.579
Intraoperative	75.9 (70, 85)	80.8 (70, 90)	***0.015****
PACU	80.0 (70, 87.5)	82.1 (70, 90)	0.190
SBP (mmHg)			
Preoperative	146.9 (131, 160)	142 (130.5, 154.5)	0.260
Intraoperative	105.9 (100, 120)	107.3 (100, 120)	0.570
PACU	115.8 (105, 122.5)	120.6 (110, 130)	***0.029****
DBP (mmHg)			
Preoperative	79.9 (71, 90)	77.9 (68, 86.5)	0.082
Intraoperative	62.1 (60, 70)	63.5 (60, 70)	0.084
PACU	68.5 (60, 70)	68.9 (60, 75)	0.604
SpO_2 (%)			
Preoperative	96.1 (95, 98)	96.4 (95, 98)	0.350
Intraoperative	97.9 (98, 100)	98.1 (97, 100)	0.215
PACU	98.8 (98, 100)	98.5 (98, 100)	0.311

*A p value < 0.05 indicates statistical significance

pressure (SBP) observed at the PACU in the DEX was 115.8 (105, 122.5) mmHg, compared to 120.6 (110, 130) mmHg in the NSS. Both of these hemodynamic changes were significantly lower in the DEX compared to the NSS, with p-values of 0.015 and 0.029 for intraoperative HR and SBP observed at the PACU, respectively.

The opioid consumption within the initial 72 hours postoperatively was evaluated, with a protocol in place to minimize opioid use by specifically choosing intravenous morphine. Consequently, no significant differences were observed in the dose of morphine between the two groups during this period.

For the safety outcome, there was no statistical difference between the treatment groups. (Table 4) None of the patients received additional anesthetic, sedative agents or pain relief medication during the operation. For postoperative pain control, patients received acetaminophen, or NSAIDs, with opioids such as morphine (0.1-0.2 mg/kg) administered as needed only during the first 24 hours postoperatively. None of the patients received benzodiazepines or other sedative drugs postoperatively, except for the patients diagnosed with delirium, for whom they were prescribed by a psychiatrist.

There was also no statistical difference between the treatment groups for postoperative outcomes, including the total length of stay and in-hospital complications. However, the length of stay after the operation in the DEX was significantly shorter compare to the NSS (4.9 [3, 6] vs. 6[4, 6.5] days) with a p-value of 0.006 (Table 5).

DISCUSSION

This study has provided evidence that dexmedetomidine effectively reduces the incidence of postoperative delirium within 72 hours after surgery, consistent with numerous prior studies.[14,16,18,19,25–28] According to our findings, both groups demonstrated a higher incidence of delirium compared to previous studies[17,18], including the study conducted by Xie S and Xie M, which was employed for samples size calculation.[25] The higher incidence can be attributed to the enrollment of older patients, with ages of 78.8±8.8 and 80.4±7.8 years in the two treatment groups. besides, these patients experienced pain from hip fractures and may have been in a dehydrated status due to the restrictions on food and drink before the operation.

To ensure outcome accuracy, we made efforts to adjust controllable confounding factors, that have been identified in previous studies[29,30] as contributing to postoperative delirium in elderly patients with hip fracture. These factors include screening and preventing infection, maintaining adequate volume status during admission, screening and treating abnormal electrolyte levels, avoiding multiple drug used, ensuring adequate pain control and selecting neuraxial techniques with peripheral nerve blocks.

This trial stands out as the only one that utilized a different technique for administering DEX, specifically a small single-dose infusion. We opted for this technique considering the pharmacokinetic and pharmacodynamic

TABLE 4. Safety outcomes.

Parameters	Intraoperative periods				PACU			
	DEX group n (%)	NSS group n (%)	RR (95% CI)	P value	DEX group n (%)	NSS group n (%)	RR (95%CI)	P value
Bradycardia	18 (18)	13 (13)	1.38 (0.72, 2.67)	0.332	10 (10)	10 (10)	1.00 (0.44, 2.30)	1.000
with intervention	8 (8)	7 (7)	1.14 (0.43, 3.03)	0.789	2 (2)	1 (1)	2(0.18, 21.70)	0.563
Tachycardia	3 (3)	3 (3)	1.00 (0.21, 4.84)	1.000	0	1 (1)	-	-
with intervention	0	0	-	-	0	0	-	-
Hypotension	48 (48)	35 (35)	1.37 (0.98, 1.92)	0.065	16 (16)	11 (11)	1.45 (0.71, 2.98)	0.305
with intervention	28 (28)	25 (25)	1.12 (0.71, 1.78)	0.631	6 (6)	3 (3)	2.00 (0.51, 7.78)	0.317
Hypertension	0	0	-	-	0	1 (1)	-	-
with intervention	0	0	-	-	0	0	-	-
Hypoxia	2 (2)	1 (1)	2.43 (0.18, 21.70)	0.569	0	0	-	-
with intervention	0	0	-	-	0	0	-	-

TABLE 5. Postoperative outcomes.

Parameters	DEX group n (Q1, Q3)	NSS group n (Q1, Q3)	P value
Total length of stay (day)	12.5 (8.5, 14)	13.9 (9, 15.5)	0.341
Length of stay after operation (day)	4.9 (3, 6)	6.0 (4, 6.5)	***0.006****
Intraoperative complications			
vasopressors	40	35	0.468
convert to general anesthesia	3	0	0.082
shivering	1	2	0.563
arrythmia	1	0	0.319
In-hospital complications			
death	1	0	0.319
pulmonary embolism	1	0	0.319
myocardial infarction	2	1	0.563
respiratory failure	1	0	0.319
sepsis	1	1	1.000
pneumonia	2	1	0.563
acute kidney injury	1	0	0.319
urinary tract infection	3	7	0.196
volume overload	1	1	1.000
lung atelectasis	1	0	0.319
Total complications	8	13	0.251

*A p value < 0.05 indicates statistical significance

of DEX in elderly patients. It is important to note that the distribution phase of DEX is rapid, with a distribution half-life of approximately six minutes and an elimination half-life of two hours in a healthy population[10], which may be longer in the elderly population. Moreover; the operative time of hip surgery at our institute was relatively short, with a mean duration of 115.5 (90, 135) and 108.4 (90, 120) minutes in the two treatment groups. Therefore, a single dose of DEX would be sufficient for elderly patients undergoing hip surgery.

Furthermore, considering the main concern, the infusion technique also involved potential adverse effects, such as hypotension and bradycardia, as shown in previous studies.[14,18,19,28] We hypothesized that a single small dose of DEX in this study would result in a lower incidence or no statistically significant difference between the treatments group for hypotension and bradycardia. Our results confirmed this hypothesis when comparing to previous studies[28,31] However, in our study, the DEX also exhibited statistically lower intraoperative heart rate and lower systolic blood pressure observed at the PACU. Nevertheless, these values did not show clinical significance nor required any intervention.

Another side effect of DEX is sedation, which was assessed using the Richmond agitation sedation scale. The desired sedation level ranged from 0 to -2, indicating patients' status were claim to light sedation. In our study, there was no significant difference in sedation between the two groups. Furthermore, no patients in the DEX, experienced deep sedation or coma at the PACU, which is believed to be within the elimination half-life of DEX. During the intraoperative periods, two patients in the DEX and one patient in the normal saline solution group experienced hypoxia with SpO_2 level below 90%. However, no intervention was required as these episodes of hypoxia were of short duration (less than ten minutes) and the patients' SpO_2 levels manually increased to above 90%.

Additionally, there was a significant difference

in the length of stay after the operation, excluding the waiting time for surgery, between the two groups. Specifically, the DEX had a slightly shorter duration of stay compared to the NSS. It is possible that patients in the DEX experienced less POD than those in the NSS, which might have allowed patients to return home more quickly. However, several factors affect the length of stay after the operation, so we cannot conclusively attribute the reduction in length of stay solely to DEX.

All perioperative complications showed no significant difference between the two groups, consistent with previous studies[14,19,28] Considering the most common complication, which is the need of vasopressors, it is expected that the DEX, which had more patients experiencing hypotension, would also have more patients requiring vasopressors. Three patients in the DEX requested a conversion to general anesthesia after realizing that spinal anesthesia alone was not sufficient for their comfort during the lengthy operation (lasting over four hours). An 85-year-old patient in the DEX developed hospital acquired pneumonia (HAP) with respiratory failure and sepsis from a Covid infection five days after surgery. Unfortunately, the patient's condition deteriorated and he passed away after twenty days of admission. Additionally, one patient in the DEX developed atrial fibrillation (AF) with a rapid ventricular response of 170 bpm within 24 hours after surgery. After receiving appropriate treatment and stabilization, the patient was diagnosed with a myocardial infarction by cardiologist. Finally, they were successfully treated and discharge from the hospital after a 15-day admission.

The strength of this study lies in its design as a randomized, double-blinded, placebo-controlled trial, which demonstrated the significant efficacy of DEX in reducing POD. Moreover, this trial introduced a difference administration technique of DEX in prevention of POD. We believe that this approach could greatly facilitate perioperative management for anesthesiologists and potentially encourage the wider utilization of this drug among the elderly population.

There were several limitations to this study. Firstly, it was conducted at a single-center, which could introduce selection and treatment biases. The uniformity of care provided by the same team and the influence of local practices and personal experience may limit the generalizability of the findings. In addition, the selection criteria limited the inclusion of a border range of elderly patients with hip fractures, thus reducing the applicability of the results. Secondly, the follow-up period was relatively short, spanning only 72 hours postoperatively. While we believed that most cases of POD would occur within this mentioned timeframe by the study of Whitlock et al.[6], there is a possibility that some patients may have experienced POD beyond this period. Thirdly, this study failed to include brain imaging, quantitative EEG information, sophisticated neurophysiologic testing and blood markers to determine and classify delirium. Fourthly, we were unable to defined all preoperative predictors for POD, such as preoperative cognitive function classified by other screening tools or preoperative functional impairment, due to missing data that cannot be corrected from medical records or patient information. Finally, delirium is a multifactorial condition, and despite our efforts to control confounding factors, there may still uncontrollable variables influencing its occurrence.

CONCLUSION

The administration of a single-dose dexmedetomidine demonstrated efficacy in reducing the incidence of postoperative delirium within 72 hours postoperatively in elderly patients undergoing hip surgery without affecting intraoperative hemodynamic stability. Further investigation into the long-term outcomes of dexmedetomidine in the elderly is warranted.

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