Effect of Intraoperative Dexmedetomidine Infusion on Early Postoperative Cognitive Dysfunction (POCD) in Geriatric Patients Undergoing Hip Surgery Under Spinal Anaesthesia

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Material and Methods

Study area and institution: This study was conducted in the Department of Anaesthesiology, Tata Main Hospital, Jamshedpur, which is 914 bedded multidisciplinary teaching hospital.

Study population: Geriatric patients posted for elective hip surgeries in the department of orthopedics, Tata Main Hospital, Jamshedpur.

Study design: Prospective, randomized, placebo-controlled & double-blind study.

Approval: Approval by the ethics committee of Tata Main Hospital Jamshedpur was taken and written & informed consent of patients were obtained to conduct the study.

Sample size: A total of 120 patients with 60 patients in each group.

Sample size justification: Studies by Li Y et al [52] have demonstrated that the incidence of POCD was 20% in the dexmedetomidine group as compared to 42% in the control group in patients between 65 to 75 years of age undergoing laparoscopic cholecystectomy. Sample size for the simulated treatment to decrease the incidence of POCD from 42% to 20% assuming normal distribution of the outcome variable as well as using a conventional, with an Alpha Error of 0.05 and power of the study as 80% showed that the required sample size would be 54 in each Group.

The formula for calculated sample size is given below

$$n = \frac{[z1\text{-}\alpha/2.\sqrt{2P(1-P)} + z1\text{-}\beta.\sqrt{\{P1(1-P1) + P2(1-P2)\}}]^2}{(P1-P2)2}$$

$$= \frac{[1.645*0.654 + 0.842*0.635]^2}{(0.22*0.22)}$$

$$= (1.610)\ 2/0.0484$$

$$= 2.595/0.0484$$

$$= 53.61$$

where Zα/2 is the critical value of the Normal distribution at α/2 (e.g. for a confidence level of 95%, α is 0.05 and the critical value is 1.96), Zβ is the critical value of the Normal distribution at β (e.g. for a power of 80%, β is 0.2) and p1 and p2 are the expected sample proportions of the two groups.

The total sample size required for the study was 108, each group carry 54 patients. Considering few dropouts and to be on safer side, we decided to include 60 patients in each group i.e. a total of 120 patients.

Inclusion Criteria:

Patients with

1. American society of Anaesthesiology (ASA) status of I-III.
2. Age between 60-75 years scheduled for elective hip surgery under spinal anaesthesia.

Exclusion Criteria:

1. Patient not willing to be a part of the study.
2. Patients aged <60 or >75 years.
3. Contraindication to spinal anaesthesia.
4. Patients with accompanying medical conditions that may affect the level of consciousness, such as stroke, stupor or dementia, or patients with abnormalities in hepatic or renal function, electrolyte imbalance.
5. Patients suffering from preoperative bradycardia [heart rate (HR) <60 bpm] or hypotension [mean arterial blood pressure (MAP) <70 mmHg].
6. Patients who had recently received a sedative or opioid drug.
7. Patients with a MoCA (Montreal Cognitive Assessment) score <26.
8. Patients with persistent hypotension and bradycardia intra-operatively even after giving Mephentermine were excluded from the study.

Randomization and Grouping:

Blinding:

This is a prospective, randomized, placebo-controlled, double-blind clinical trial. The patients were recruited according to the inclusion criteria and were distributed to one of the groups according to computer-generated random assignment. The personnel involved in the study, including statisticians, investigators, anaesthesiologists, surgeons and the patients were blinded to the study.

Patients were randomized into one of the two groups using a computer based random number generator. https://www.randomizer.org. All recordings were performed by an anaesthesiologist blinded to the group allocation.

DEX Group: Received Dexmedetomidine at a dose of 1 mcg/kg over 10 min, after Spinal Anaesthesia and before start of surgery, followed by a continuous infusion at a rate of 0.4 mcg/kg/h until the end of surgery.

CONTROL Group: The Control Group received an equal volume placebo infusion of 0.9% normal saline.

METHODOLOGY

Pre-Anaesthetic check-up:

A detailed history was elicited including history of any major illness or disease in the past and a general physical examination and systemic examination of each patient was performed to check the general wellbeing and to exclude any major medical disorders including psychiatric illness.

Appropriate biochemical, hematological, and radiological investigations were done as per hospital protocol. Elective patients meeting the inclusion criteria were evaluated preoperatively at least one day prior to surgery. Patients cognition was assessed by using Montreal Cognitive Assessment (MoCA) test one day prior to surgery (M0) during PAC, on 1st Postoperative Day (M1), on 3rd Postoperative Day (M2) and 7th postoperative day (M3)

All patients had a fasting state for a minimum of 6 hours prior to surgery. All patients were uniformly pre-medicated with Tab. Ranitidine 150mg and Tab. Metoclopramide 10mg on the night before surgery and Tab. Ranitidine 150mg and Tab. Metoclopramide 10mg on morning of surgery with clear water 2 hours before anaesthesia.

Monitoring:

Baseline / pre-spinal vital parameters (T0) of patients including heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP); mean arterial pressure (MAP), respiratory rate (RR) and peripheral oxygen saturation (SpO2) were recorded every 10 minutes (T1,T2 & so on) in the operation theatre till the end of surgery.

In operation room patients were identified. WHO surgical checklist was done as per hospital protocol. Patients were allowed to lie supine on the operating table, standard monitors (pulse oximeter, 5 lead electrocardiograph and automated non-invasive blood pressure) were connected and baseline parameters were recorded. Intravenous access secured.

Sub-arachnoid block: Under all aseptic precautions, lumbar puncture was done in sitting position with midline approach with disposable 25-gauge Quincke spinal needle. After confirming the free flow of cerebrospinal fluid 2.5 ml of 0.5% bupivacaine heavy deposited in the subarachnoid space at the rate of 1 ml over 10 seconds. Patients were made supine after sealing the lumbar puncture site with antiseptic dressing. Time of intra-thecal drug deposition noted & haemodynamic parameters recorded.

The DEX Group patients received dexmedetomidine at a dose of 1 mcg/kg diluted in 10ml of normal saline over 10 mins after Spinal Anaesthesia and before starting of surgery, followed by a

continuous infusion at a rate of 0.4 mcg/kg/h until the end of surgery. The CONTROL Group received an equal volume of placebo infusion of 0.9 % normal saline.

Patients needing Intraoperative sedation were given intravenous midazolam in initial dose of 0.5-1 mg given over 2 minutes (not to exceed 2.5 mg)

Intraoperatively all patients received 2-3 liters/min. oxygen through nasal cannula to maintain SPO2 above ≥ 94%. Heart rate, blood pressure, respiratory rate, sedation level and oxygen saturation were monitored throughout the operation and recorded at 10-minute intervals. A decrease of more than 20% from the baseline in the mean arterial pressure (MAP) or less than 70mm Hg was considered as hypotension and treated with intravenous Mephentermine in aliquots of 6mg. Decrease in the heart rate below 50 beats/min was considered bradycardia and treated with atropine in aliquots of 0.6mg.

For post-operative analgesia, Injection Paracetamol infusion 1 gm 8 hourly and 1mg/kg Intravenous Tramadol 8 hourly was administered on the 1st postoperative day. Intravenous Pethidine was used as rescue analgesic if VAS Scores raised above 4 in an initial dose of 0.5mg/kg followed by increments of 0.25mg/kg every 10 minutes till VAS was below 4 (up to a maximum of 1.5 mg/kg/8 hours). From the 2nd postoperative day, the patient was given oral Paracetamol 1 gm 8 hourly and 1mg/kg Intravenous Tramadol as the rescue analgesic for the remaining duration of stay.

Montreal Cognitive Assessment (MoCA) test was assessed one day prior to surgery (M0), on 1st Postoperative Day (M1), on 3rd Postoperative Day (M2) and 7th postoperative day (M3) (Study Proforma 1.6.4 in English & Hindi).

STATISTICAL ANALYSIS:

- Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0.
- Continuous variables are presented as mean ± standard deviation, and categorical variables are presented as absolute numbers and percentage.
- The comparison of normally distributed continuous variables between the groups was performed using Student's t test.
- Nominal categorical data between the groups were compared using Chi-square test or Fisher's exact test as appropriate.
- A p value <0.05 was considered statistically significant.