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Research Article

The effect of Dexmedetomidine on the incidence of postoperative cognitive dysfunction in elderly patients after prolonged abdominal surgery

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KEYWORDS

Dexmedetomidine;
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Abstract *Background:* Postoperative cognitive dysfunction (POCD) in elderly patients is a common complaint after prolonged surgeries. In the present study, we aimed to investigate the effect of intraoperative infusion of Dexmedetomidine on POCD.
Methods: 50 patients aged more than 60 years old undergoing elective abdominal surgery expected to last more than 2 hours were randomized into 2 groups of 25 patients each: those receiving Dexmedetomidine at a dose of 0.4 μg/kg/h, group (A) and those receiving 0.9% normal saline as placebo group (B). All patients underwent neuropsychometric tests (Montreal cognitive assessment and Stroop color word interference tests) the day before the surgery and 24 h after the surgery, and one week postoperatively.
Results: The use of Dexmedetomidine as an adjuvant during Sevoflurane anesthesia did not have significant effect on protection against POCD in one day and one week postoperatively. The anesthetic and analgesic sparing effect of Dexmedetomidine was significantly proved by lower Sevoflurane need and significant lesser amount of total 24 hours postoperative Fentanyl requirements, but with significant prolonged extubation and orientation times in Dexmedetomidine group than placebo group.
Conclusions: The findings of this pilot study suggest that intraoperative use of Dexmedetomidine as an adjuvant in major surgery in elderly patients was not associated with significant protection against POCD.

1. Introduction

Postoperative cognitive dysfunction (POCD) is a common and well known complication after prolonged surgery. Especially the elderly patients are at risk of cognitive dysfunction. But due to the subtle nature of POCD, this complication might be recognized only by the patient's relatives. Thus, neuropsychological testing is necessary for its detection [1]. Early

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cognitive dysfunction may affect the recovery period in several ways. Delayed physical and emotional rehabilitation may delay hospital discharge and return to work. Also, it can interfere with accelerated care programs, which encourage a shorter hospital stay and early independence. These problems may be wrongly attributed to drugs or complications of surgery and anesthesia [2].

Some neuro-pathophysiological studies have suggested that post-operative cognitive disorder (POCD) might even share some mechanisms with Alzheimer's disease through deposition of plasma β amyloid and Tau phosphorylation [3,4].

Dexmedetomidine is a potent and highly selective alpha 2 adrenergic receptor agonist. It provides sedation with modest analgesic and possible anti delirium effects, but with minimal respiratory depression. In addition, the use of alpha 2 agonists has been associated with lower cardiovascular complications in high-risk non-cardiac surgery [5,6]. Taken together, Dexmedetomidine could provide specific advantages over commonly used analgesic and sedative agents for prolonged surgeries.

Besides, Dexmedetomidine's well-established sedative effects on increasing of both in vitro and in vivo evidence indicate that Dexmedetomidine also has a cell-protective effect on nervous tissue under ischemic conditions [7]. Moreover, there is recent evidence suggesting that this effect is mediated by the binding to imidazoline 1-recepors, which are known to be important regulators for cell survival and mediators of neuroprotective effects of many drugs [7–9].

In this randomized double blind pilot study, we aimed to examine whether the intraoperative use of Dexmedetomidine was associated with a lower incidence of neurocognitive dysfunction in elderly patients undergoing elective prolonged abdominal surgery when compared to Placebo.

We also assume that Dexmedetomidine by its analgesic and sedative effect can be adjuvant to inhaled anesthetics and can help in lowering the concentration of inhaled anesthetics and analgesic consumption that added a role in protection from POCD.

2. Methods

This was a pilot, randomized, double-blinded, controlled clinical trial. It was conducted in a tertiary referral hospital (King Faisal Specialist Hospital and Research Center, Jeddah, Saudi Arabia). Ethics approval for this study was provided by the institutional Ethics Committee of the hospital on 18/04/2010. The study was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12613000378729).

Written informed consent was obtained from all patients. 50 patients men and women 25 patients per group, aged 60 years or older, American Society of Anesthesiologists (ASA) physical status classes I to III, scheduled for elective abdominal surgery (expected to be longer than 2 h), hospital stay >48 h, and educable, were included in this study.

All participants were given a written description of their involvement in the research, the neurocognitive test to be made, their rights and how their rights and interests will be protected, particularly in respect of confidentiality, privacy and safety. And all participants are made aware of their ability to withdraw consent and discontinue participation at any time exclusion criteria were patients with high vagal tone (heart rate <60), any arrhythmic disorders, severe ventricular dysfunction (EF $<35\%$), hypovolemic patients, patients with any psychological disorders, preexisting cognitive impairment, alcohol or drug abuse, patients with preexisting CNS deficit, or any neurological symptomatic disorder confirmed by MRI, patients who showed inability or unwillingness to abide by the protocol, inability to follow procedures, or poor comprehension of the language used in the study, and patients with severe visual or auditory handicap.

The patients were randomly allocated to one of two groups, Dexmedetomidine (A) group and a control (B) group, using a computer-generated sequence of random numbers and a sealed envelope technique. Study drugs were prepared by a pharmacist who did not participate in either the intraoperative management or the postoperative care. According to the randomization table, drugs were prepared in unlabeled 50 ml syringes. The unlabeled syringes were filled with normal saline or with Dexmedetomidine. Both the patients and the investigators were blinded to the study drug.

Our primary endpoint was the proportion of patients in each treatment group who was diagnosed to have POCD, while the secondary end points were included the estimation of intraoperative Sevoflurane consumption, Fentanyl consumption, depth of anesthesia, and emergence time. Participants were recruited from the outpatient clinic for anesthesia for preoperative evaluation. The preoperative interview included a medical and surgical history, current medications, alcohol consumption and substance use history, any neurological or psychological disorders, and ASA classification. Echo cardiography in addition to routine laboratory investigation and Electrocardiography was ordered.

2.1. Neuropsychometric evaluation

The baseline cognitive functions were conducted by a trained interviewer who was blinded to patient's allocation, for each patient, a day before surgery and repeated 24 h postoperatively and one week later. The tests used in this study were the following:

(A) Stroop color word interference test, which estimates the directed attention, mental speed and mental control using a booklet consists of 3 basic parts: (1) word page; the s patient reads words of color names (e.g., red, blue) printed in black ink. (2) Color page: the patient identifies colors (e.g., rectangles printed in red or blue). (3) Color-word page; the patient should name the color in which a word is written, while ignoring the printed word. Thus, incongruence between the word's color and identity (e.g., the word "red" presented in green). Lower score indicates higher performance [10,11].

(B) Montreal cognitive assessment test, which is a one page, 30 point test done in approximately 10 min for assessment of attention, memory, abstraction, delayed recall and orientation, with total score of 30, the short-term memory recall task (5 points) contains 2 learning trials of 5 nouns and delayed recall after approximately 5 min. Visuospatial abilities are assessed by a three-dimensional cube copy (1 point) and a clock-drawing task (3 points). Many ways of executive functions are evaluated using an alternation task adapted from the trail-making B task (1 point), a phonemic fluency task