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Research Article

OUTCOME OF INTRAOPERATIVE DEXMEDETOMIDINE ON POST-OPERATIVE COGNITIVE DYSFUNCTION OF AGED PATIENTS UNDER GOING LARYNX SURGERY.

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ABSTRACT

Postoperative Cognitive Dysfunction (POCD) is one of the most common complications affecting the central nervous system after general anaesthesia and surgery especially in elderly patients. It's characterized by short-term cognitive decline and includes memory, mood, confusion, and sleep disorders. Its medical manifestations include cognitive disorder, personality exchange and memory loss, intellectual problems and social impairment. Starting with demographic data, the mean age of the included cases was 69.98 and 70.02 years in the Dex and control groups, respectively. Males represented the majority of the included cases, as they formed 100 and 98.9% of cases in the same groups, respectively. Body mass index (BMI) had mean values of 28.11 and 27.43kg/m2 in the two groups, respectively. Dexmedetomidine administration is related with a considerable development of cognitive function after surgery in the elderly patients. It is linked with a better analgesic and sedative profile and decreased neurological inflammatory markers (S100B). Conversely, we should closely monitor for the side effects like bradycardia and hypotension in these patients.

Keywords: - Post-operative cognitive dysfunction, Dexmedetomidine, Sedation, Sevoflurane.

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INTRODUCTION

POCD (Postoperative cognitive dysfunction) is one of the most common complications affecting the central nervous system after general anaesthesia and surgery especially in elderly patients. It's characterized by short-term cognitive decline and includes memory, mood, confusion, and sleep disorders.1 Its clinical manifestations include cognitive dysfunction, personality change and memory loss, mental disorders and social impairment.

2 For the reason that long anesthesia duration and the severe surgical stress, the risk of POCD in elderly patients is incredibly increased.3 The incidence of POCD is ranging from 10% to 60% and varies with clinical, demographic and surgical variables, as well as the interval between surgery and assessment in older patients.

POCD has an important negative impact on the affected person's health. It is associated with increased morbidity, prolonged recovery, delayed restoration of function, impaired quality of life, and even increased mortality.5 Thus, the prevention of such problems is crucial for the anaesthetic community.6

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Dexmedetomidine (DEX) is an efficient and greatly selective α2-adrenergic receptor agonist and acts as a multifunctional drug in the treatment of various human diseases.[7] A previous study has suggested that DEX is efficient in the treatment of nerve diseases through the beneficial effects of decreasing central nervous system sympathetic outflow and providing sedation and analgesia.[8] DEX treatment may improve behavioral disturbances, including aggression, agitation and cognitive dysfunction.[9] In addition, some clinical studies have indicated that DEX has analgesic, anxiolytic and anti-delirium effects without respiratory depression. These properties make it an appropriate option for sedation in the intensive care unit and in perioperative period.[10]

Many researches have discussed the protective position of dexmedetomidine towards perioperative delirium. This effect is thought to be mediated by enhancing the expression of brain-derived neurotrophic factors, regulation of N-methyl N-aspartate receptors, and regulation of excitatory amino acid transport.[11] The current study aims to assess intraoperative dexmedetomidine on postoperative cognitive dysfunction of aged patients under taken total larynx ablation.

Material and Method:

The study was designed as a prospective, inpatient, double-blind trial carried out at the Department of Anesthesia of the Swamy Vivekanandha Medical College Hospital and Research Institute, Elayampalayam, Tiruchengode. Under the observation of experienced anesthetists, the evaluations performed and the examination completed. All the128 patients who had undergone total laryngectomy are classified as American Society of Anesthesiologists (ASA) score I, II, or III.

Patients underwent detailed history taking, thorough physical examination and routine preoperative laboratory investigations. The included 128 cases were randomly divided into two equal groups, the Dex and control groups, using the closed envelope method. In the Dex group, patients received dexmedetomidine infusion before the induction. One μg/kg was infused over 10 minutes, then infusion was maintained at 0.2–1.4 μg/kg/h. Controls were managed via the standard anesthetic protocol without any addictive drugs. For both groups, anesthesia was maintained using sevoflurane 1–3% according to patients' response and hemodynamic stability.

In contrast, we expelled cases with BMI> 35 kg/m2, uncontrolled systemic comorbidities, patients with bradycardia, hypotension, and heart failure as dexmedetomidine may exacerbate these conditions, pre-existing neurological or psychiatric problems and visual or hearing impairment. Also, cases with major intraoperative events, like major bleeding or allergy to the study medications, were excluded in this study. On arrival at the operative theater, the patient was placed supine, and then, an intravenous cannula was inserted into a suitable peripheral vein. Basic hemodynamic monitoring was established, including non-invasive blood pressure (NIBP), pulse oximeter, five-lead ECG, end-tidal capnography, and axillary temperature. A 5-ml blood sample was obtained before induction of anesthesia. The sample was centrifuged, and the plasma was used to measure the level of S100 protein by enzyme-linked immunosorbent assay (ELISA).

Fentanyl was administered intravenously at doses of 1–2 μg/kg and 2–3 min before induction. Propofol was used to induce anesthesia by 0.5–2 mg/kg according to clinical response and hemodynamic stability. If possible, tracheal intubation with an appropriately sized cuffed endotracheal tube was inserted using 0.5 mg/ kg atracurium. Otherwise, a tracheostomy was done by the operating surgeon. Increments of 0.1 mg/kg of atracurium were used to maintain muscle relaxation every 20–30 min throughout the intra-operative period.

Heart rate, mean arterial pressure, and pulse oximetry were monitored continuously and recorded by a different anesthetist, other than the investigator, before and immediately after induction, after intubation, every 15 min during the 1st hour and then every 30 min until the end of surgery. After the operation, patients were discharged from the operative room after fulfilling the criteria of discharge. The duration of operation was defined as the time from the skin incision to the last skin suture, whereas recovery time was defined as the time from the last skin suture until discharge from the operating room. Patients were transferred to the post-anesthesia care unit (PACU), and the Richmond Agitation–Sedation Scale (RASS) was used to assess the patients' sedation score 1 h after extubation before discharge from PACU. Assessment of neurocognitive function was repeated on the fifth postoperative day using the same tests used pre-operatively. The time to first analgesic request and the total duration of hospitalization were recorded. The effect of dexmedetomidine on neurocognitive function was our primary outcome. Secondary outcomes included intraoperative hemodynamic stability, postoperative recovery profile and agitation-sedation scores.

Representative experiments from at least three independent experiments are shown. Statistical analysis was performed using the SPSS 19.0 for Windows (SPSS, IBM, USA). All data were expressed as means ± SDs. Significant differences were assessed using Student's *t*-tests or Tukey's test and least significant difference with oneway analysis of variance (ANOVA), when appropriate. $P < 0.05$ was considered statistically significant.

Results:

Starting with demographic data, the mean age of the included cases was 69.98 and 70.02 years in the Dex and control groups, respectively. Males represented the majority of the included cases, as they formed 100 and 98.9% of cases in the same groups, respectively. Body mass index (BMI) had mean values of 28.11 and 27.43kg/m2 in the two groups, respectively. Smoking was reported in 90 and 85.4% of cases in the Dex group and control group respectively. The Dex group expressed significantly lower values in both heart rate and mean arterial pressure (MAP) compared to controls throughout the subsequently recorded readings till 300-min follow-up ($P > 0.001$).

The duration of operation was equivalent among the two groups ($P = 0.749$), as it had Dex group mean values of 331.3 and 342.3 min in the control groups, respectively. Sevoflurane consumption significantly decreased in the Dex group 135.9 compared of 166.5 ml in controls—$P < 0.001$). And also, time showed a significant decrease in the same group (5 vs. 8.85 min in controls—$P < 0.001$). Dex administration showed that highest prevalence of cardiovascular (CV) side effects. Bradycardia was encountered in 26.2%Dex cases and 9.7% of control cases, while hypotension was encountered in 48.7 and 15.1% of cases in the Dex and control groups, respectively. Additionally, both fluid and ephedrine intake showed a significant increase in the Dex group. Fluid bolus was commenced for 46.5% and 9.9% of cases, whereas ephedrine intake was needed in 29.5 and 6.5% of cases in the same two groups, respectively. The time to first analgesic request showed a significant persistence in the Dex group in 4.73 vs. 2.34h in controls—$P < 0.00$ and also duration of hospitalization observed no significant difference between the two groups 7.11 and 7.12 days in the two groups, respectively—$P = 0.950$). Prevalence of delirium showed a significant decrease in the Dex group compared to controls (9.9 vs. 25.3%, respectively—$P =0.006$).

The postoperative sedation scale showed better results in the Dex group during the early 36 hours following the operation. However, the subsequent readings were comparable between the two groups. Even though, Basal S100B protein levels 88.1 in the Dex and 94.58 ng/l control groups, P 0.116 has no significant difference between both the study groups. Postoperative levels showed a significant decrease in the Dex group than control.

Discussion:

In present study was conducted to the effect of dexmedetomidine administration on neurocognitive dysfunction, hemodynamics, sedation and postoperative recovery after total laryngectomy in the elderly individuals. Our result showed that the Dex group expressed significantly lower heart rates and MAP than controls until the 300-min follow-up ($P > 0.001$). Dexmedetomidine can decrease norepinephrine release, reducing catecholamine release from nerve endings which leading to a decrease in heart rate and blood pressure. This correlates with the findings of Tobias et al and Guo et al [12-13] who reported a significant decrease in MAP and heart rate with Dex administration compared to controls ($P < 0.05$). This consequence was evident in 3 h after drug administration till 12-h assessment. Volkov et al.[14] reported that dexmedetomidine was connected with noticeably decreased inhaled anesthetic requirements during traumatic phases of surgeries. which is correlated with sevoflurane consumption significantly decreased in the Dex group 135.9 compared of 166.5 ml ($P < 0.001$). Sharma et al.[15] reported a 41% reduction in sevoflurane consumption in patients receiving IV dexmedetomidine as an adjuvant in patients undergoing laparoscopic cholecystectomy under general anesthesia.

In the current study, the incidence of CV side effects was significantly higher with Dex administration. Bradycardia was encountered in 26.2 and 9.7% of cases, while hypotension was encountered in 48.7 in the Dex and control groups15.1% of cases respectively. Accordingly, both fluid and ephedrine intake increased with Dex administration. In Xu et al[16] study reported that dexmedetomidine also has some disadvantages, high risk of bradycardia and hypotension in old patients. In present study, the time for first analgesic request showed a significant prolongation in the Dex group 4.73 vs. 2.34h in controls—$P < 0.001$ which similar to the Liang et al[17] report this may be due to analgesic effect of dexmedetomidine, which is mediated through inhibition of nociceptive impulse transmission through the posterior horn of the spinal column and also it promotes acetylcholine release from spinal interneurons, leading to the overproduction of nitric oxide that acts as a mediator for analgesia. Zhang et al.[18] results showed that the overall incidence of delirium showed a significant decrease in the Dex group compared to controls. Delirium score had mean values of 13.2 and 17.4 in the Dex and control groups which correlated with present study 9.9 vs. 25.3%, respectively—$P =0.006$. In agreement with our results, recent studies also noted that dexmedetomidine decreased emergence agitation after surgery. The observation is that the dexmedetomidine decreased emergence of agitation after surgery.

In the present study, there was no significant difference between the two study groups about basal S100B protein levels (Basal S100B protein levels 88.1 in the Dex and 94.58 ng/l in the control groups, P 0.116), when postoperative levels showed a significant reduction in the Dex group compared to controls (122.41 vs. 587.99 ng/l in controls—$P< 0.001$). It is an acidic calcium-binding protein; a biomarker of central nervous system

injury which is similar to Bindra et al.[19] reported that the Dex group was associated with a significant decrease in serum S100B protein at 24- and 8-h readings. The former had mean values of 52.55 and 99.34 ng/ml.

Conclusion:

Dexmedetomidine administration is related with a considerable development of cognitive function after surgery in the elderly individuals. It is linked with a better analgesic and sedative profile and decreased neurological inflammatory markers (S100B). Conversely, the patient must be closely monitored for side effects like bradycardia and hypotension. These findings in this study are in correlation with the results of different authors.

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