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Effect of intraoperative dexmedetomidine on postoperative cognitive functions of elderly patients undergoing total laryngectomy

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Abstract

Background: Postoperative cognitive dysfunction is commonly encountered after major surgical operations. This study was conducted to evaluate the effect of dexmedetomidine on neurocognitive dysfunction and postoperative recovery after total laryngectomy in the elderly population.

Results: Preoperative characteristics were comparable between the two groups. However, both sevoflurane consumption and recovery time were significantly decreased in the Dex group. Also, the time to first analgesic request and sedation level showed a significant improvement in the same group. The Dex group showed its superiority regarding most of the used cognitive tests. Although there was no significant difference between the two study groups regarding basal S100B, postoperative levels significantly decreased in the Dex group.

Conclusions: Dexmedetomidine administration is associated with a significant improvement of cognitive function after surgery in the elderly population. It is associated with a better analgesic and sedative profile along with decreased neurological inflammatory markers. However, the patient must be closely monitored for side effects like bradycardia and hypotension.

Keywords: Dexmedetomidine, Post-operative cognitive dysfunction, Sedation, Pain

Background

Postoperative cognitive dysfunction (POCD) is one of the most severe morbidities commonly encountered in daily anesthetic practice, especially after major surgeries (Pappa et al. 2017; Skvarc et al. 2018). It was previously reported that about 80% of patients could develop that complication after surgery under general anesthesia (Sabol et al. 2015).

A is a common form of POCD, and it represents an acute complex neuropsychiatric syndrome that entails confusion and abnormal behavior. It occurs in 15–20% of hospital admissions (Ryan 2001). Not only is the prevalence of POCD and delirium high, but also its diagnosis and management are challenging due to the wide range of symptoms and limited diagnostic tools (Yap and Joyner 2014; Funder KS and Steinmetz 2012).

POCD has a significant negative impact on patient health. It is associated with increased morbidity, prolonged recovery, delayed restoration of function, impaired quality of life, and even increased mortality (Chen et al. 2001). Thus, the prevention of such problems is crucial for the anesthetic community (Pappa et al. 2017).

Dexmedetomidine is a highly selective α2 agonist which causes a reduction of norepinephrine release leading to decreased sympathetic outflow (Flükiger et al. 2018; Pereira et al. 2020). It has sedative, analgesic, and

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sympatholytic properties without significant adverse effects on respiration (Carollo et al. 2008; Wunsch et al. 2010).

Many studies have discussed the protective role of dexmedetomidine against 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 (Ma et al. 2004; Wang et al. 2019; Degos et al. 2013).

The current study aims to assess whether dexmedetomidine reduces neurocognitive dysfunction after total laryngectomy in the elderly population using a multimodal approach of clinical, psychiatric, and investigational tools.

Methods

The sample size was calculated using Power Analysis and Sample Size software program (PASS) version 15.0.5 for windows (2017) using the results published by (Su et al. 2016) with the incidence of postoperative delirium in the first 5 days after surgery as the primary outcome. Su et al. reported that postoperative delirium in the Dexmedetomidine group was 9% compared to 23% in the control group. A sample size of 82 patients in each group was needed to achieve 80% power (β= 20%) to detect a difference in the incidence of postoperative delirium between both groups of 14% using the two-sided Fisher's exact test with a significance level (α) of 0.05. The expected number of dropouts is nine patients, so 91 patients were enrolled in each group.

We included elderly patients (aged more than 60 years) over a period of 2 years from May 2019 till April 2021, from either gender, prepared for total laryngectomy and classified as American Society of Anesthesiologists (ASA) score I, II, or III. On the other hand, we excluded cases with BMI> 35 kg/m^2, uncontrolled systemic comorbidities, patients with bradycardia, hypotension, and heart failure as dexmedetomidine may exacerbate these conditions, pre-existing neurological or psychiatric disease and visual or hearing impairment. Also, cases with major intraoperative events, like major bleeding or allergy to the study medications, were excluded.

Patient preparation included detailed history taking, thorough physical examination and routine preoperative laboratory investigations. Evaluation of the basal presence of delirium was performed by The Confusion Assessment Method (CAM) developed by Jackson and Ely (2003). Basal executive function was assessed via Continuous Performance Test (PCPT) (Conners et al. 2003), Berg's "Wisconsin" Card Sorting Test (BCST) (Berg 1948), Tower of London (TOL) by (Shallice 1982; Ahonen et al. 2012), and Visual-Response Memory Span task using staircase method (Croschere et al. 2012).

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 facilitated 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.

The included 182 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 min, 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.

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 or 300 min which was sooner. The total volume of sevoflurane used was calculated using the formula published by Biro in 2014 (Biro 2014).

Intraoperative hypertension was defined as a drop of mean blood pressure below 65 mmHg (Scheeren and Saugel 2018). It was managed by decreasing the dose of inhaled sevoflurane down to a minimum of 1%, intravenous fluid bolus, and IV ephedrine increments (5–10 mg). Intraoperative bradycardia was defined as the presence of a pulse rate of less than 50 bpm (Spodick 1996), and it was managed by atropine increments (1 mg). The incidence of hypotension, bradycardia, need for vasopressor or fluid intake were recorded.

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 (Sessler et al. 2002).

Assessment of development of postoperative delirium was done by CAM starting 24 h after surgery every 12 h for 5 days postoperatively (Su et al. 2016). Patients were initially evaluated using the RASS. If the patient was too deeply sedated or unarousable (RASS −4 or −5), delirium assessment was aborted, and the patient was recorded as comatose. If RASS was greater than −4, delirium was assessed by use of the CAM.

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.

Statistical analysis of data

Data collection, tabulation, and analysis were conducted by using the statistical package of social science (SPSS, IBM, Inc., Chicago; USA) version 26 for windows. Quantitative data were tested for normality using Kolmogrov-Smirnov test and expressed as mean ± standard deviation (SD). Categorical data were expressed in percentage and frequency. Independent sample T and Mann-Whitney tests were used for inter-group comparison of parametric and non-parametric continuous data, respectively. Chi-square test or Fisher's exact test was used for comparing two or more groups of categorical data. Probability ($P< 0.05$) was considered to be statistically significant.

Results

Starting with demographic data, the mean age of the included cases was 67.98 and 69.02 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 27.43 kg/m^2 in the two groups, respectively. Smoking was reported in 89 and 82.4% of cases in the same groups, respectively. Generally, no significant difference was detected between the two groups regarding either of the previous parameters. Also, the prevalence of systemic comorbidities was comparable between the two groups. The previous data are shown in Table 1.

Although no significant difference was noted between the two study groups at baseline and induction regarding both heart rate and mean arterial pressure (MAP), the

Table 1 Demographic characteristics, medical history, operative duration, sevoflurane consumption, recovery time, intra-operative adverse events, first request of analgesia, incidence of delirium, and hospital stay

		Dexmedetomidine group ($n= 91$)	Control group ($n= 91$)	95% CI	*P*
Age (years)		67.98 ± 3.370	69.02 ± 4.412	−2.19, 0.10	0.075
Gender	**Male**	100.0% (91)	98.9% (90)	−0.03, 0.01	0.316
	Female	0.0% (0)	1.1% (1)		
BMI (kg/m^2)		28.11 ± 3.174	27.43 ± 3.836	−0.35, 1.71	0.194
History of DM		28.6% (26)	24.2% (22)	−0.17, 0.08	0.501
History of HTN		35.2% (32)	28.6% (26)	−0.2, 0.07	0.340
History of IHD		11.0% (10)	8.8% (8)	−0.11, 0.07	0.619
History of smoking		89.0% (81)	82.4% (75)	−0.17, 0.04	0.204
Duration of surgery (minutes)		329.3 ± 39.2	331.3 ± 43.7	−14, 10	0.749
Sevoflurane consumption (ml)		135.9 ± 39.2	166.5 ± 32.4	−41, −20	< **0.001**
Recovery time (minutes)		5.00 ± 1.789	8.85 ± 3.130	−4.59, −3.10	< **0.001**
Bradycardia		24.2% (22)	7.7% (7)	−0.27, −0.06	**0.002**
Hypotension		40.7% (37)	12.1% (11)	−0.41, −0.17	< **0.001**
Use of fluid bolus		36.3% (33)	8.8% (8)	−0.39, −0.16	< **0.001**
Use of ephedrine		27.5% (25)	5.5% (5)	−0.32, −0.12	< **0.001**
Time to first request of analgesia (hours)		3.73 ± 1.820	2.34 ± 1.708	0.87, 1.90	< **0.001**
Delirium		9.9% (9)	25.3% (23)	3.083	**0.006**
Total hospital stay (days)		6.11 ± 1.187	6.12 ± 1.163	−0.35, 0.33	0.950

Dex group expressed significantly lower values compared to controls throughout the subsequently recorded readings till 300-min follow-up ($P > 0.001$) (Fig. 1).

The duration of operation was comparable between the two groups ($P = 0.749$), as it had mean values of 329.3 and 331.3 min in the Dex and control groups, respectively. However, sevoflurane consumption significantly decreased in the Dex group (135.9 vs. 166.5 ml in controls—$P < 0.001$). Also, recovery time showed a significant decrease in the same group (5 vs. 8.85 min in controls—$P < 0.001$).

The incidence of cardiovascular (CV) side effects was significantly higher with Dex administration. Brady cardia was encountered in 24.2 and 7.7% of cases, while hypotension was encountered in 40.7 and 12.1% 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 36.3 and 8.8% of cases, whereas ephedrine intake was needed in 27.5 and 5.5% of cases in the same two groups, respectively.

The time to first analgesic request showed a significant prolongation in the Dex group (3.73 vs. 2.34 h in controls—$P < 0.001$). The duration of hospitalization showed no significant difference between the two groups (6.11 and 6.12 days in the two groups, respectively—$P = 0.950$). The overall incidence of delirium showed a significant decrease in the Dex group compared to controls (9.9 vs. 25.3%, respectively—$P = 0.006$). The previous data are summarized in Table 1.

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. Table 2 illustrates these data.

As shown in Fig. 2, although there was no significant difference between the two study groups regarding basal S100B protein levels (77.1 and 84.58 ng/l in the Dex and control groups, respectively—P 0.114), postoperative levels showed a significant decrease in the Dex group (111.41 vs. 474.99 ng/l in controls—$P < 0.001$).

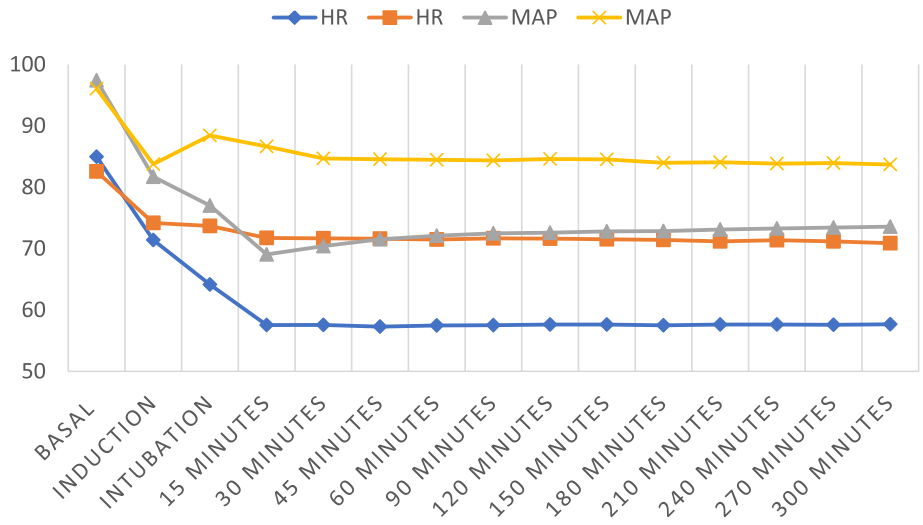

Fig. 1 Intra-operative follow-up of heart rate and mean arterial pressure of the studied groups

Table 2 Postoperative RASS score follow-up in the studied groups

RASS	Dexmedetomidine group ($n = 91$)	Control group ($n = 91$)	95% CI	*P*
At PACU	−1.62 ± 0.727	0.22 ± 0.879	−2.07, −1.60	**˂0.001**
24 h	0.00 ± 0.000	0.23 ± 0.700	− 0.38, −0.09	**0.002**
36 h	0.08 ± 0.372	0.32 ± 0.787	−0.42, −0.06	**0.009**
48 h	0.09 ± 0.354	0.24 ± 0.689	−0.31, 0.01	0.060
72 h	0.03 ± 0.233	0.18 ± 0.660	−0.29, 0.00	0.053
96 h	0.01 ± 0.105	0.10 ± 0.423	−0.18, 0.00	0.056
120 h	0.01 ± 0.105	0.03 ± 0.233	−0.07, 0.03	0.414

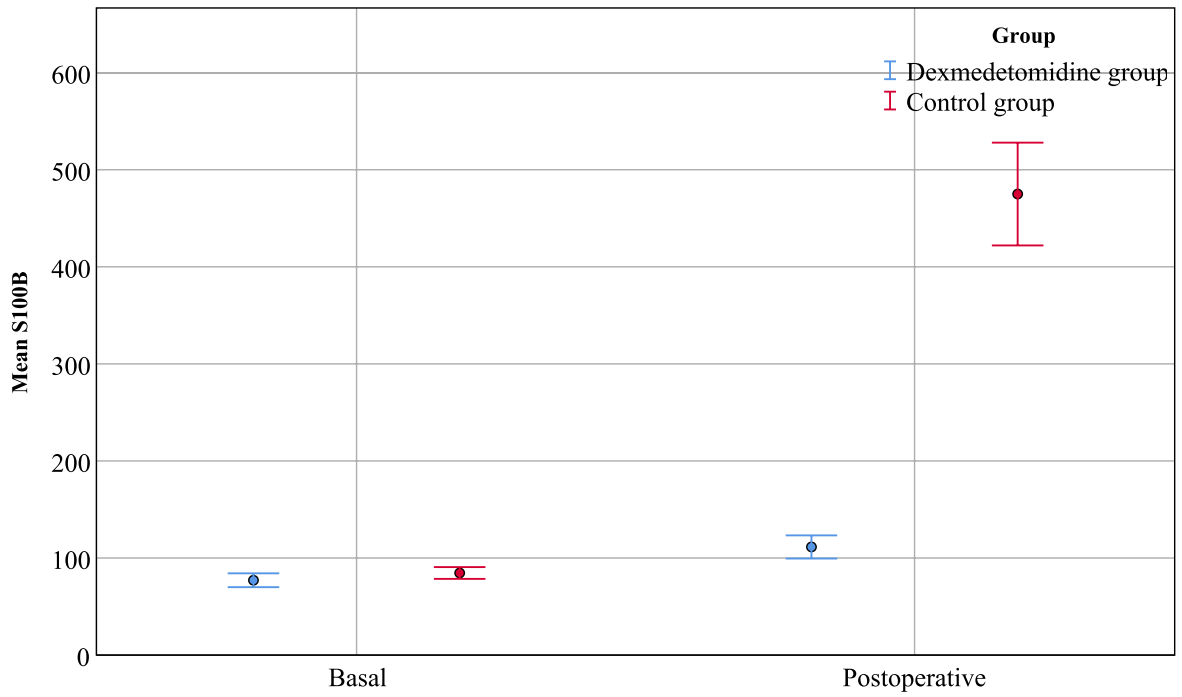

Fig. 2 Pre-and postoperative S100B (ng/l) assessment in the studied groups

PCPT parameters showed no significant difference between the two groups at baseline. However, correct detection, correct reaction time, and omission error showed a significant improvement with Dex administration compared to controls ($P < 0.05$) (Table 3).

Tower of London test showed no significant difference between the study groups at the baseline level. Nevertheless, the Dex group showed significantly lower total score and test time compared to controls after the operation ($P = 0.001$ and 0.004, respectively) (Table 3).

Table 3 Pre-and postoperative PCPT, TOL, and memory span assessment in the studied groups

Test	Domain	Time	Dexmedetomidine group ($n = 91$)	Control group ($n = 91$)	*P*
PCPT	**Correct detection**	**Basal**	305.02 ± 30.881	298.42 ± 31.180	0.153
		Postoperative	301.97 ± 32.598	292.29 ± 31.050	**0.042**
	Correct reaction time	**Basal**	434.90 ± 78.538	452.46 ± 80.568	0.138
		Postoperative	450.65 ± 83.821	486.59 ± 93.632	**0.007**
	Error reaction time	**Basal**	403.99 ± 68.897	388.77 ± 74.730	0.155
		Postoperative	415.19 ± 69.919	413.43 ± 92.773	0.885
	Omission error	**Basal**	23.57 ± 14.292	25.48 ± 14.497	0.371
		Postoperative	24.78 ± 14.175	29.42 ± 13.999	**0.044**
	Commission error	**Basal**	13.90 ± 7.250	15.57 ± 7.193	0.120
		Postoperative	14.59 ± 7.374	16.63 ± 7.580	0.068
TOL	**Total score moves**	**Basal**	170.85 ± 26.039	178.37 ± 26.303	0.054
		Postoperative	171.34 ± 33.640	192.36 ± 45.558	**0.001**
	Total test time	**Basal**	688.26 ± 225.986	749.62 ± 213.515	0.061
		Postoperative	677.33 ± 240.868	787.88 ± 265.850	**0.004**
Memory Span	-	**Basal**	4.00 ± 0.368	3.98 ± 0.422	0.729
	-	**Postoperative**	3.96 ± 0.370	3.88 ± 0.414	**0.033**

Table 4 Pre-and postoperative Berg's "Wisconsin" Card Sorting Test (BCST) assessment in the studied groups

BCST		Dexmedetomidine group (*n*= 91)	Control group (*n*= 91)	*P*
Correct responses	**Basal**	89.45 ± 13.663	85.68 ± 12.451	0.053
	Postoperative	86.40 ± 12.294	84.32 ± 10.880	0.229
Total errors	**Basal**	35.92 ± 13.049	39.20 ± 12.514	0.086
	Postoperative	35.85 ± 12.967	39.03 ± 12.473	0.093
Completed categories	**Basal**	6.95 ± 1.336	6.59 ± 1.316	0.075
	Postoperative	6.34 ± 1.470	5.88 ± 1.541	**0.040**
Perseverative response	**Basal**	43.69 ± 5.563	42.34 ± 5.281	0.095
	Postoperative	44.88 ± 6.734	43.62 ± 6.013	0.183
Perseverative errors	**Basal**	18.45 ± 2.222	17.97 ± 2.420	0.162
	Postoperative	18.64 ± 2.244	18.58 ± 2.539	0.877
Non-perseverative errors	**Basal**	18.52 ± 2.377	18.01 ± 2.248	0.142
	Postoperative	19.70 ± 2.889	19.42 ± 2.667	0.489
Trials to 1st cat	**Basal**	8.31 ± 5.940	10.02 ± 6.143	0.057
	Postoperative	8.91 ± 6.482	10.89 ± 6.634	**0.043**
Failure to maintain set	**Basal**	1.71 ± 1.642	2.08 ± 1.621	0.136
	Postoperative	1.79 ± 1.786	2.41 ± 1.972	**0.029**
Conceptual level response	**Basal**	76.41 ± 20.259	74.37 ± 20.438	0.501
	Postoperative	76.01 ± 19.806	70.55 ± 20.628	**0.042**
Reaction time	**Basal**	12835 ± 3889	13812 ± 4197	0.105
	Postoperative	13623 ± 4195	15110 ± 4865	**0.029**
Abstraction time	**Basal**	250097 ± 88819	239503 ± 86460	0.416
	Postoperative	242445 ± 94594	212507 ± 98560	**0.038**

BCST showed no significant difference regarding all of its subcomponents before surgery. However, the Dex group showed significant improvement regarding some of these components after surgery, compared to controls. These parameters included completed categories, trials to the first cat, failure to maintain set, conceptual level response, reaction time, and abstraction time (Table 4).

The preoperative visual-response Memory Span task showed no significant difference between the study groups ($P = 0.729$). However, postoperative values showed a significant increase in the Dex group compared to controls (3.96 vs. 3.88—$P = 0.033$) (Table 3).

Discussion

Patients with laryngeal cancer who undergo tumor resection can suffer from severe trauma, long-term artificial airway, prolonged operative time, and postoperative intensive care unit (ICU) stay (Obid et al. 2019). Keeping in mind that old age itself is an independent risk factor of POCD (Monk et al. 2008), and under such previous stressful conditions, POCD is commonly encountered in elderly laryngeal cancer patients (Chen et al. 2001). The prevention of POCD is of great importance to ensure patient safety (Skvarc et al. 2018; Kotekar et al. 2018).

The current study was conducted to study the effect of dexmedetomidine administration on neurocognitive dysfunction, hemodynamics, sedation, and postoperative recovery after total laryngectomy in the elderly population.

Based on the previously mentioned preoperative data (in the "Results" section), one can notice that there was no significant difference between all the previous parameters between the two groups. This indicates proper randomization, which should also nullify any bias that might have skewed the results in favor of one group rather than the other.

Our findings showed that the Dex group expressed significantly lower heart rates and MAP than controls throughout the subsequent recorded readings until the 300-min follow-up ($P > 0.001$). Dexmedetomidine can decrease norepinephrine release, reducing catecholamine release from nerve endings, leading to a decrease in heart rate and blood pressure (Tobias 2007). Guo and his coworkers reported a significant decrease in MAP and heart rate with Dex administration compared to controls ($P < 0.05$). This effect was evident 3 h after drug administration till 12-h assessment (Guo et al. 2015).

Other authors confirmed the previous findings, as the heart rate had mean values of 66.4 and 78.6 bpm, while

MAP had mean values of 76.4 and 85.3 mmHg in the Dex and control groups, respectively, with a significant difference between the two groups ($P = 0.009$ and 0.015, respectively) (Chen et al. 2013). This observation has also been documented in other studies (Jin and Chung 2001; Honkavaara et al. 2011; Ehara et al. 2012; Iirola et al. 2011). On the other hand, another study confirmed the safety of dexmedetomidine. The authors reported an excellent hemodynamic and recovery profile, with a better preservation MAP preservation (Ali et al. 2018).

In the current study, sevoflurane consumption significantly decreased in the Dex group (135.9 vs. 166.5 ml in controls—$P < 0.001$). In agreement with our findings, another study reported that dexmedetomidine was associated with significantly decreased inhaled anesthetic requirements during traumatic phases of surgeries (Volkov et al. 2015). Besides, other authors reported a 41% reduction in sevoflurane consumption in patients receiving IV dexmedetomidine as an adjuvant in patients undergoing laparoscopic cholecystectomy under general anesthesia (Sharma et al. 2017).

Our study showed a significant decrease in the recovery time with Dex administration (5 vs. 8.85 min in controls—$P < 0.001$). Likewise, Gong et al. reported a significant decrease in the same parameter with Dex administration ($P < 0.001$). It had mean values of 6.2 and 9.9 min in the intervention and control groups, respectively (Gong et al. 2018).

In our study, the time to first analgesic request showed a significant prolongation in the Dex group (3.73 vs. 2.34 h in controls—$P < 0.001$). This could be explained by the analgesic effect of dexmedetomidine, which is mediated through inhibition of nociceptive impulse transmission through the posterior horn of the spinal cord (Grewal 2011). In addition, it promotes acetylcholine release from spinal interneurons, leading to the overproduction of nitric oxide that acts as a mediator for analgesia (Liang et al. 2017).

One study reported that dexmedetomidine led to a decreased requirement for opioid analgesics (Volkov et al. 2015). In an additional study, forty-six thoracic surgery patients given dexmedetomidine reported a significant decrease in resting and coughing numerical rating scale scores. Dexmedetomidine use had a sufentanil-sparing effect during the early 24 h following surgery (Cai et al. 2016).

In our study, the Ramsay sedation scale showed better results in the Dex group during the early 36 h following the operation. However, the subsequent readings were comparable between the two groups. Dexmedetomidine produces unique sedative effects like normal sleep via its high specificity for α2 vs. α1 receptors (Tobias 2007). Multiple studies have shown that it can decrease body stress and inflammation and inhibit oxidation reactions (Naguib et al. 2013; Wagner et al. 2013). Dexmedetomidine has been used for long-term sedation during mechanical ventilation in critically ill patients at the intensive care unit and for decreasing patient agitation in the PACU (Fraser et al. 2013).

In agreement with our findings, Ding and his associates reported a significant improvement of Ramsay's sedation scale after Dex administration compared to controls ($P < 0.05$). It had mean values of 2 and 1.3 in the Dex and control groups, respectively (Ding et al. 2015).

Regarding our primary outcome (cognitive function), one should mention that the two groups had a comparable cognitive function before the operation. Nevertheless, the Dex group showed its superiority compared to controls regarding postoperative sustained and selective attention (measured by continuous performance test), cognitive flexibility (measured by Berg card scoring test), executive function (measured by Tower of London test), and visual memory (measured by visual response memory span task).

Surgical trauma could mediate hyperactivity of the hypothalamic-pituitary-adrenal axis as well as an immune response (Kohl and Deutschman 2006). Both of these inflammatory and hormonal changes could result in many dreadful complications, including atrial fibrillation, postoperative fatigue, and cognitive dysfunction (LI et al. 2012). Sato et al. demonstrated that dexmedetomidine had a neuroprotective effect by decreasing hippocampal neuronal damage in animal experiments (Sato et al. 2010). This was also confirmed by an in vivo experiment (Sanders et al. 2009). This has also been reported in several other previous studies (Goyagi et al. 2009; Kuhmonen et al. 2001; Kuhmonen et al. 1997).

In the same context, other authors used the Mini-Mental State Examination (MMSE) score to assess postoperative cognitive impairment. No significant difference was noted between the two groups regarding baseline MMSE values. However, the same score showed a significant improvement with Dex administration compared to controls throughout the first 3 days after the operation ($P < 0.001$) (Guo et al. 2015).

Likewise, other authors reported that MMSE scores in the observation group were significantly higher than those in the control group at the three-time points ($P < 0.001$). In the same study, cognitive impairment was diagnosed in 2.5 and 25% of cases in the Dex and control groups, respectively, with a significant difference between the two groups (Gong et al. 2018). The previous findings regarding MMSE were also confirmed by Chen et al., who reported a significant improvement of cognitive function in the Dex group compared to controls within one week after operation ($P = 0.005$) (Chen et al. 2013).

Xu and his associates reported a significant increase in the incidence of postoperative cognitive dysfunction in the control group (20.9%) compared to only 6.3% of cases in the Dex group (Xu et al. 2017). We suggest that the postoperative use of dexmedetomidine could still suppress excessive inflammation and the stress response, resulting in a lower incidence of postoperative neurological dysfunction.

Our results showed that the overall incidence of delirium showed a significant decrease in the Dex group compared to controls (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 (Zhang et al. 2019; Kang et al. 2019). Ding and his associates reported a significant decrease in the delirium score with Dex administration (P < 0.05). Delirium score had mean values of 13.2 and 17.4 in the Dex and control groups, respectively (Ding et al. 2015). Additionally, Zhang and his associates reported a significant decrease in the incidence of postoperative delirium in the Dex group (P = 0.015). Delirium was encountered in 16.7 and 30% of cases in the Dex and control groups, respectively (Zhang et al. 2020).

In the current study, although there was no significant difference between the two study groups regarding basal S100B protein levels (77.1 and 84.58 ng/l in the Dex and control groups, respectively—P 0.114), postoperative levels showed a significant reduction in the Dex group compared to controls (111.41 vs. 474.99 ng/l in controls—P < 0.001). S100 β is an acidic calcium-binding protein, a biomarker of central nervous system injury (Kleissner et al. 2021; Arrais et al. 2020). The elevated levels of S100 β in the brain are often associated with severe brain injury (Linstedt et al. 2002; Heyer and Connolly 2003). Accordingly, the S100 β protein could act as a surrogate biomarker for neuronal insult and POCD. The decreased serum levels of that marker in our study could be explained by the anti-inflammatory effects of dexmedetomidine mediated via α2 receptors (Kawasaki et al. 2013; Wu et al. 2013).

In another study, plasma S100 β protein concentration was significantly higher in controls compared to the Dex group at all postoperative time points (P < 0.05) (Zhang et al. 2018). Bindra et al. also 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, while the latter had mean values of 37.63 and 61.46 ng/ml in the Dex and control groups, respectively (Bindra et al. 2019). Another analysis showed that the serum concentrations of S100B were significantly lower in patients treated with dexmedetomidine than in those who received common sedation both on the day when delirium was diagnosed and on the third day after delirium was diagnosed (Li et al. 2019).

We suggest that the postoperative use of dexmedetomidine could still suppress excessive inflammation and the stress response, resulting in a lower incidence of postoperative neurological dysfunction.

In the current study, the incidence of CV side effects was significantly higher with Dex administration. Bradycardia was encountered in 24.2 and 7.7% of cases, while hypotension was encountered in 40.7 and 12.1% of cases in the Dex and control groups, respectively. Consequently, both fluid and ephedrine intake increased with Dex administration. In the same context, another study reported that dexmedetomidine also has some disadvantages, including inducing the increased risk for bradycardia and hypotension in old patients (Xu et al. 2020). On the other hand, other authors reported no significant difference between the two groups regarding the incidence of hypotension (P = 0.714) or bradycardia (P = 0.472). Hypotension complication was encountered in 5.26 and 2.74% of cases, while bradycardia was detected in 6.58 and 2.74% of cases in the Dex and control groups, respectively (Guo et al. 2015). Another recent study also confirmed these comparable findings (Zhang et al. 2020).

Our study has some limitations; First of all, it is a single-center study. Also, the included sample size was relatively small. Hence, more studies, including more cases from different surgical centers, should be conducted shortly.

Conclusions

Based on the previous findings, Dexmedetomidine administration is associated with a significant improvement of cognitive function after surgery in the elderly population. It is associated with a better analgesic and sedative profile and decreased neurological inflammatory markers (S100B). However, the patient must be closely monitored for side effects like bradycardia and hypotension.

Abbreviations

ASA: American Society of Anesthesiologists; BCST: Berg's "Wisconsin" Card Sorting Test; BMI: Body mass index; CAM: Confusion Assessment Method; CV: Cardiovascular; ECG: Electrocardiogram; ELISA: Enzyme-linked immunosorbent assay; ICU: Intensive care unit; MAP: Mean arterial pressure; MMSE: Mini-Mental State Examination; NIBP: Non-invasive blood pressure; PACU: Post-anesthesia care unit; PASS: Power Analysis and Sample Size software program; PCPT: Continuous Performance Test; POCD: Postoperative cognitive dysfunction; RASS: Richmond Agitation–Sedation Scale; SD: Standard deviation; SPSS: Statistical package of social science; TOL: Tower of London.

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Authors' contributions
AS: Main investigator, data collection and analysis. AZ: Manuscript writing. MG: Contributed data and analysis tools SR: Performed the analysis of the collected samples. GT: Conceived and designed the study. The authors read and approved the final manuscript.

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Availability of data and materials
All relevant data and materials are available on request.

Declarations

Ethics approval and consent to participate
The study was conducted at Mansoura University Hospitals after gaining approval from the local ethical committee (Proposal Code: MD.19.03.151) and getting informed written consent from all patients.

Consent for publication
Details, images, or videos relating to individual participants, written informed consent for the publication of these were obtained from the participants.

Competing interests
The authors declare that they have no competing interests.

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