DEXMEDETOMIDINE USE IN DIRECT LARYNGOSCOPIC BIOPSY UNDER TIVA

Ayse Mizrak[*], Maruf Sanli[**], Semsettin Bozgeyik[*], Rauf Gul[*], Suleyman Ganidagli[*], Elif Baysal[***] and Unsal Oner[*]

Abstract

Background: The purpose of this study is to investigate the suitability of dexmedetomidine as a helpful sedative agent in direct laryngoscopic biopsy (DLB), under total intravenous anesthesia (TIVA).

Methods: In this double blind randomised study, patients were allocated to receive dexmedetomidine 0.5 μg/kg (group D, n = 20) or saline placebo (group P, n = 20) intravenously. Forty ASA I-III patients were infused propofol and administered rocuronium bromur. They were intubated and performed biopsy. Aldrete scores, intraoperative propofol and postoperative analgesic requirements, satisfaction scores, recovery time, Ramsay sedation scale (RSS), haemodynamic changes and side effects were recorded.

Results: Postoperative analgesic requirement in group D was significantly lower and satisfaction scores and RSS were significantly higher than in group P. Additionally, MAP (mean arterial blood pressure) significantly decreased at post-extubation time in group D.

Conclusion: The premedication with a single dose of dexmedetomidine decreases intraoperative propofol and postoperative analgesic requirements, increases the postoperative satisfaction and RSS considerably in patients undergoing DLB under TIVA.

Key words: Direct laryngoscopic biopsy (DLB), airway reflexes, dexmedetomidine, laryngeal tumor, TIVA (Total Intravenous Anesthesia).

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* Anesthesiology and Reanimation, Gaziantep University School of Medicine Gaziantep/TURKEY.
** Thoracic Surgery, Gaziantep University School of Medicine Gaziantep/TURKEY.
*** Ear Nose and Throat (ENT), Gaziantep University School of Medicine Gaziantep/TURKEY.
Corresponding author: Dr. Ayse Mizrak, Gaziantep University Medical Faculty, Department of Anesthesiology and Reanimation, 27310 Sahinbey, Gaziantep, TURKEY, E- mail: aysemizrak@mynet.com, Fax: 00903423602244, Tel: 00905337181025.

Introduction

The incidence of laryngeal CA is about 1% of all cancers. Squamous cell CA's are the most common laryngeal tumors in our patient population. Laryngeal tumors also include papillomas, cysts in the glottic area[1]. Before the anesthetic management of these patients, preoperative examination and evaluation by the ear, nose, and throat (ENT) surgeons are essential[2]. If the patient has difficulty opening the mouth, mallampati class is higher than grade 2 and airway categories are higher than grade 2b, generally, the next procedure is to proceed with fiberoptic intubation or tracheostomy. There are several advantages of DLB, along with a number of detrimental effects. Patients with laryngeal tumors can present a challenge to guarantee the airway for laryngeal biopsy. During DLB, there may be acute changes in systemic and pulmonary haemodynamics, together with blood gas changes such as increase in heart rate, blood pressure, airway and circulatory reflexes during surgical procedure[3]. Dexmedetomidine, an α-$_2$ agonist, has none to minimal respiratory depressant effects, which is clearly a great advantage in handling a critical airway while inducing sedation. Further, dexmedetomidine has anxiolytic, antisialagogue[4] and moderate analgesic[5] effects. It was demonstrated to be a useful agent for sedation during awake fiberoptic intubation in difficult airways[6]. Furthermore dexmedetomidine was demonstrated to attenuate the increase in heart rate and arterial blood pressure during intubation[7] and was shown to attenuate the airway and circulatory reflexes during extubation in ocular surgery[8]. Our patients consisted of more frequently elderly, ASA I-III patients who may have some latent respiratory and cardiovascular disease. Jorden et al.[9] concluded that, an accidental overdose in the perioperative setting with the administration of dexmedetomidine up to 0.5 µg/kg/min produced excessive sedation but stable haemodynamics.

As, DLB is a rather shortly procedure, it also needs a short time for general anesthesia. Therefore the action time of the induction and sedative agents should be short with minimum respiratory side effects. Propofol may be the ideal agent with these objectives for DLB. So far, no drug has been proposed for the attenuation of cardiovascular and airway responses during DLB under TIVA. To avoid the detrimental effects of DLB and benefit from these desirable effects, we preferred to use dexmedetomidine in the present study.

Thus, we aimed to investigate the effect of low dose of dexmedetomidine on airway reflexes, haemodynamics, patient comfort, sedation, and intraoperative anesthetic and postoperative analgesic requirements during and after DLB.

Methods

A. Selection and description of participants: The study group comprised 40 ASA I-III patients, aged 32-67 years. All participants were scheduled to undergo direct laryngoscopy and biopsy under TIVA. All procedures were performed by the same surgeon. The work presented was performed in accordance with the most recent version of the Helsinki Declaration. Following approval from the institutional review board, written informed consent was obtained from all participants.

All patients were in part of grade 1, which includes patients with fully visible vocal folds, grade 2a, which includes patients with clearly visible vocal folds with small or medium size tumors not obstructing the view of glottis, or grade 2b in which only parts of vocal folds are partly visible and large tumors involve 1 or both vocal folds. The evaluation was carried out by the ear, nose, and throat (ENT) surgeon by means of the preoperative indirect laryngoscopy. The patients with difficulty opening the mouth, Mallampati class higher than 2, airway categories higher than grade 2b (grade 3, grade 4), or ischemic heart disease, heart blocks, the use of premedication drugs such as β adrenergic blockers, and tricyclic antidepressant drugs, and a known or a family history of reactions to dexmedetomidine HCl (Precedex®, Abbott, North Chicago, IL, USA) or propofol (Propofol, 1%, Fresenius Kabi AB, Sweden) were excluded.

B. Technical information: Patients were assigned to one of two study groups using a computer generated random number table. After the patients had been taken to surgery room, standard monitors including electrocardiography, non invasive blood pressure (MAP) measurement and pulse oximetry were used throughout the procedure (Monitor; Siemens

SC 7000, Sweden). No patient was premedicated with another drug. The study medication consisted of dexmedetomidine (0.5 μg/kg) or normal saline in a total volume of 20 mL, which was prepared by an anesthesiologist not involved to measurements and evaluation, and was infused intravenously in 10 minutes before induction of anesthesia. After premedication with the study drugs, fentanyl 1 μg/kg and propofol were administered slowly (20 mg/10 sec) until the loss of eyelash reflex or the patient no longer responded to his name being called loudly. Propofol was continued to be given at a rate of 6 mg/kg/hour, followed by fentanyl (Fentanyl citrate, B. Braun Melsungen AG, Berlin, Germany) 1 μg/kg and rocuronium bromur (Esmeron, Organon, Oss Holland) 0.6 mg/kg because of the short duration of the procedure. Tracheal intubation with Miller blade (2-4 sizes) was attempted to expose the glottis for intubation using a polyvinyl tracheal tube of 5.5 to 6 mm ID in patients with grade 1, grade 2a and grade 2b. Ventilation was assisted with 70% oxygen and 30% air without inhalation anesthetic. At the end of the procedure, muscle relaxant effects were reversed using neostigmine and atropine and all patients were given oxygen after the operations.

When the patients were awake and cooperative, tracheal extubation was accomplished in the post anesthesia care unit. Intraoperative propofol requirement, Aldrete score, and recovery time were recorded. The recovery time was considered as the time from the time anesthetics are discontinued until verbal communication and the eyes being opened. Non invasive mean arterial blood pressure (MAP), heart rate (HR), and SPO2 values were recorded at baseline, 0, 5, 10, 15, 30, and 45, minutes. In addition, visual analog scale (VAS), anesthesia quality, and RSS of the groups were evaluated at 30 and 60 min in the postoperative period when the patients were fully awake. At the end of the operation, the assessment of pain related biopsy was performed using a 10 cm VAS, with anchors of 0 = no pain and 10 = worst pain imaginable. The quality of anesthesia was assessed according to the following numeric scale: 4 = Excellent (no complaint from patient); 3 = Good (minor complaint without any need for supplemental analgesics); 2 = Moderate (complaint which required supplemental analgesics); 1 = Unsuccessful (requiring general anesthesia). In addition, sedation was recorded on a numerical scale of Ramsay; 1 = Anxiety and completely awake, 2 = Completely awake, 3 = Awake but drowsy, 4 = Asleep but responsive to verbal commands, 5 = Asleep but responsive to tactile stimulus, and 6 = Asleep and not responsive to any stimulus. Postoperative analgesic (Diclomec, Diklofenak Sodyum, 75 mg/3 ml, amp, Topkapı Istanbul) requirement was ascertained during postoperative 24-hour-period.

All the evaluations were performed by a blinded observer who was different from the person who had performed the premedication. Pre-intra- postoperative hypertension, hypotension, bradycardia, tachycardia, nausea, vomiting, coughing, straining, dizziness, respiratory depression (defined as a respiratory rate <10 breaths/min), hypoxemia (defined as SPO2 ≤90%, tachycardia (HR >100 beat/min), bradycardia (HR <50 beat/min), hypotension (MAP <60 mmHg), hypertension (MAP >120 mmHg) were noted if present at 30 and 60 min in the preoperative and postoperative period.

C. Statistics: Data are presented as mean ± SD and median (interquartile ranges) values, and statistical significance was reported when the p value was <0.05. Between-groups, differences were evaluated by means of Mann Whitney-U test. Friedman and Wilcoxon sign tests were applied to evaluate the differences between repeated values in the groups. Data were presented as means ± SD. All data were analyzed using SPSS (version 14.0) for Windows (SPSS Inc.) with differences associated with $p< 0.05$ interpreted as statistically significant.

After the foremost calculation according to the t test, the total sample size that we need to detect the significant difference between the doses of propofol consumption of the groups was 17 (effect size w: 0.90: Alpha: 0.05, Power: 0.95, Critical Chi^2: 3.84).

Results

Demographic data was similar between the groups with regard to duration of anesthesia, surgery, Aldrete score activity >8, and recovery time ($p >0.05$, Table 1).

Table 1
Demographic Data, Aldrete Score, Recovery Time, Intraoperative Propofol and Postoperative Analgesic

Requirement (mean ± SD)

	Group D |(n = 20)	Group P (n = 20)
Age (year)	51 ± 17	49 ± 17
Weight (kg)	71 ± 14	70 ± 11
Gender (M/F)	15/5	17/3
Smoking (%)	95	90
Duration of Anesthesia(min)	16 ± 4	20 ± 4
Duration of surgery (min)	20 ± 5	13 ± 3
Aldrete Score Activity>8 (min)	6 ± 4	8 ± 7
Intraoperative Propofol Requirement	157 ± 15*	171 ± 17
Recovery time	5 ± 4	6 ± 5
Postoperative analgesic (Dicloron amp) requirement (mg)	15 ± 6*	52 ± 12

* p <0.05 when compared with placebo group.

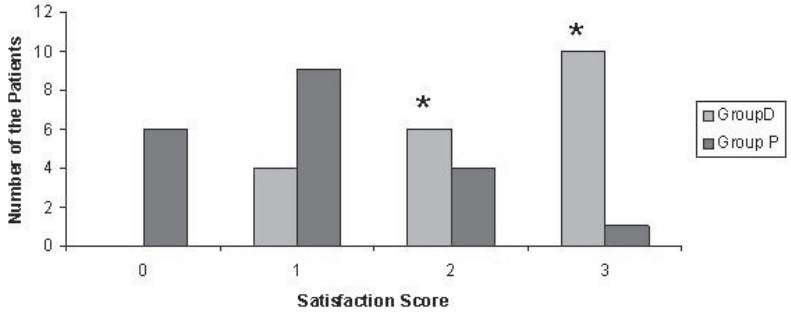
Table 2
The Number of Perioperative Side Effects

	Group D (n = 20)	Group P (n = 20)
Hypotension	3	2
Hypertension	1	2
Bradycardia	1	0
Tachycardia	2	5
Nausea	6	4
Vomiting	0	0
Caughing	4	4
Straining	3	6

P >0.05

Intraoperative propofol consumption and postoperative analgesic requirement (Dikloron amp, intramuscular) were significantly lower in group D than in group P (p <0.05, Table 1). The number of patients who experienced coughing, nausea, strain, tachycardia, hypotension and hypertension in group D were 4, 6, 3, 3, 2, 1, and in group P were 1, 4, 6, 5, 2, 2 during intraoperative and postoperative periods. The overall respiratory and haemodynamic side effects observed in both groups were; hypertension (n = 3), hypotension (n = 5), bradycardia (n = 1), tachycardia (n = 7), nausea (n = 10), coughing (n = 8), straining (n = 9). No patient experienced respiratory depression, hypoxemia and vomiting. Three patients in group D and 2 in group P received ephedrine (10 mg) for hypotension, and 1 patient in group D received atropine (0.5 mg) for bradycardia. Furthermore, 4 patients were administered atropine (0.5 mg) for decreasing the saliva in group P. Haemodynamic side effects were observed during the intubation, surgical procedure and extubation period but the respiratory side effects were observed in the preoperative and postoperative period especially during intubation and extubation period; however, there was no significant difference between the groups regarding the respiratory and haemodynamic side effects (p <0.05, Table 2). The number of the patients who had a postoperative satisfaction score of >1 in group D was significantly higher than in group P (p <0.05, Fig. 1). Moreover, the number of the patients who had a RSS of >2 in group D was significantly higher than in group P at postoperative 30 and 60 minute (p <0.05, Fig. 2). MAP

Fig. 1
Postoperative Satisfaction Scores of the groups. The number of the patients has a postoperative satisfaction scores reported to be >1 in group D was significantly higher than in group P (p <0.05)



n= 20, *p< 0,05 when compared with placebo group.

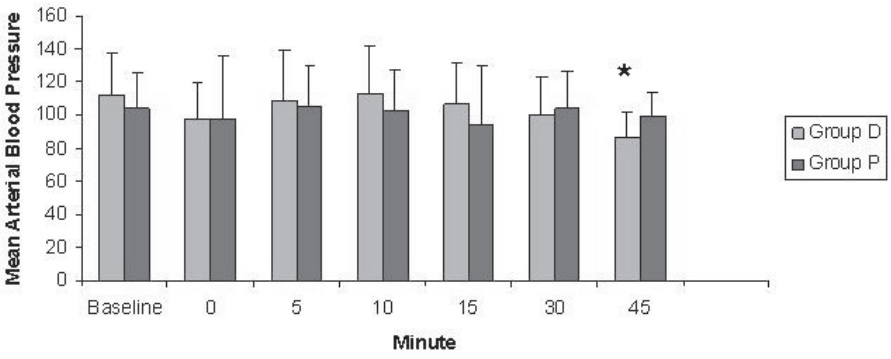


Fig. 3
Changes in mean arterial blood pressure between groups during perioperative period (Mean ± SD). MAP in group D was significantly lower than in group P at 45 minute in the postoperative period (p <0.05)

n= 20, *p< 0,05 when compared with placebo group.

in group D was significantly lower than in group P at 45 minute in the postoperative period (p <0.05, Fig. 3), and HR was similar in group D and group P (p >0.05, Fig. 4).

Discussion

It has been demonstrated that the low dose of i.v. dexmedetomidine administration before DLB under TIVA achieves gratifying patients' comfort, moderate sedation, dry airway, reduction of intraoperative propofol and postoperative analgesic consumption without serious airway problems and haemodynamic side effects.

This study includes the patients with larynx tumor by whom direct laryngoscopy and biopsy under TIVA are performed. The surgeons can evaluate the laryngeal tumor and its extent by means of DL[10]. During the procedure, the anesthesiologist and the surgeons are prepared for emergency interventions in case securing the airway presented a problem.

During DLB, some respiratory and haemodynamic side effects might be faced with. For example, the presence of the endotracheal tube leads to reflex responses, the most common of which is coughing[11]. The incidence of coughing was reported to be 76% during procedure. Coughing can cause hypertension, tachycardia, increased intraocular and intracranial pressure, myocardial ischaemia, bronchospasm, and surgical bleeding[12]. Although the mechanisms responsible for haemodynamic changes during extubation are not exactly known, possible factors may be; wound pain, and tracheal irritation[8,13].

Endotracheal intubation is associated with significant increases of MAP, HR, and plasma

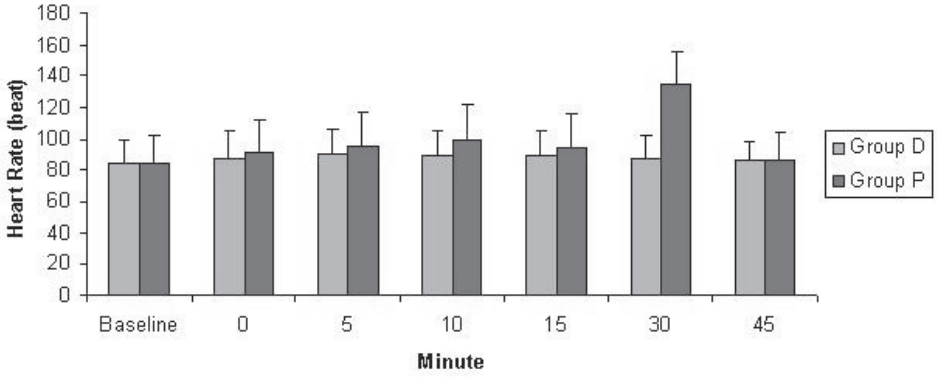


Fig. 4
Changes in heart rate between groups during perioperative period (Mean ± SD). HR was similar in group D and P (p >0.05)

n= 20, p> 0,05

catecholamine concentrations. Additionally, recovering from anesthesia often results in pain and elevating catecholamine concentrations. Hence, α-$_2$ adrenoceptor agonists may be beneficial in the postoperative period by their sympatholytic and analgesic effects without respiratory depression[14,15]. In addition, airway irritation leads to parasympathetically mediated reflex bronchoconstriction of airways of 1 mm and larger[15,16]. Dexmedetomidine may be a useful premedication agent for such undesirable side effects during DL and biopsy.

In the patients with laryngeal tumor, mechanical ventilation and weaning can be further complicated by airway irritation. It was reported that α-$_2$ adrenergic receptors inhibit bronchoconstriction in human airways[17,18]. Dexmedetomidine is an α-$_2$ adrenoreceptor agonist with several unique properties that make it an ideal agent for the management of difficult and critical airways. Dexmedetomidine causes minimal respiratory impairment, even when given in large doses[19]. It also can relax the airway even in the hyper-reactive state[20]. Thus, the efficacy of dexmedetomidine in DLB procedures for patients under TIVA were decided to investigate.

In this study, intraoperative propofol requirement and analgesic consumption during postoperative 24-hour-period were significantly lower in group D than in group P (Dikloron amp, group D: 15 ± 6 mg; group P: 52 ± 12 mg). In some cases, supplemental propofol was discontinued after dexmedetomidine initiation. Similarly, Venn et al. reported that dexmedetomidine provides intense analgesia during the postoperative period. Despite the lower doses of propofol, the higher satisfaction scores which were observed in group D may be dependent on the effect of dexmedetomidine. The need of midazolam for sedation was diminished by 80%, and postoperative analgesic requirement was reduced by 50% in cardiac patients[21]. Some of the difference in propofol use may be explained by the difference in case length.

As the mean age of the patients in this study was 51 years, and most of them were chronic smokers, they may have had latent cardiovascular and respiratory disorder. Therefore, dexmedetomidine may be useful for those generally old-patient-population during DLB. Talke et al.[22] reported that because of the decrease in HR and blood pressure, dexmedetomidine might lead to fewer ischemic events.

In this study, the course of Aldrete score activity >8 and recovery time was similar in both groups, and dexmedetomidine did not prolonge the recovery time. It activated the postsynaptic α-$_2$ receptors in the locus coeruleus, which is an important modulator of wakefulness.

Dexmedetomidine has analgesic, anxiolytic, and antisialogogue properties[7,21]. Avitsian et al.[23] concluded that less respiratory depressive effect and facilitation of post-intubation neurologic examination make dexmedetomidine a useful alternative for sedation in awake fiberoptic intubation. Similarly, it is an advantage during DLB. In group D, the patients who have a higher satisfaction scores felt comfortable and acted calmly. Dexmedetomidine provided moderate levels of sedation without causing respiratory distress. It was estimated that higher sedation scale and the analgesic effect of dexmedetomidine provided a better satisfaction score in the postoperative period.

As the half-life of dexmedetomidine is 40-47 min[24] and the time to complete all anesthetic and surgical procedure in our protocol (approximately 20 min) was less than 30 min, a continuous infusion of dexmedetomidine was not necessary in our study. The routine postoperative approach in our clinic is to observe the patients for an hour in the postoperative care unit, and then send them to their ward. The dexmedetomidine concentration used in this study was on the low level of the doses generally used for sedation in the intensive care unit, where the initial bolus was 2 µg/kg.

In this study, MAP in group D was significantly lower than in group P at 45 th. minute during postoperative period, whereas HR was similar in both groups. Ephedrine 10 mg was administered to the patients who experienced hypotension (Group D: n = 3, Group P: n = 2).

It was stated that dexmedetomidine should be administered over no less than 10 minutes, as because of sudden exogenous catecholamine release, the loading dose of up to 1 µg/kg and too rapid administration can lead to tachycardia, bradycardia, and hypertension[25]. With this in mind, dexmedetomidine 0.5 µg/kg was given over 10 minutes in this study. Furthermore,

dexmedetomidine has a mid range dose for preventing haemodynamic side effects.

Hyperdynamic side effects such as hypertension and tachycardia may have been suppressed by propofol during surgical procedure in both groups. The decrease in systemic pressure following an induction dose of propofol appears to be due to both vasodilation and myocardial depression, the leading cause of which may be a reduction in sympathetic activity[26]. Propofol, which provides hypnosis and amnesia is antiemetic[27] and induces bronchodilation in patients with chronic obstructive pulmonary disease[28].

Three patients in group D and 2 patients in group P received ephedrine (10 mg), and 1 patient in group D received atropine (0.5 mg). The possible reasons may first be the respiratory and haemodynamic effects of propofol as explained before. Secondly, the use of low and single dose of dexmedetomidine which may have not suppressed these airway reflexes and haemodynamic answers sufficiently. Thirdly, patients' chronic smoking, laryngeal irritation, postoperative pain because of biopsy and absence of local anesthetics injection to block the upper airway nerves may trigger especially respiratory side effects.

Additionally, the cost of dexmedetomidine is potentially higher than that of conventional anesthetics, but the advantage of dry airway, high satisfaction, moderate sedation, reduction of intraoperative propofol and postoperative analgesic consumption without serious airway and haemodynamic side effects may well justify this expense.

In conclusion, the use of low dose dexmedetomidine before TIVA carried out with propofol, could provide a safe and advantageous condition for DLB.

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