A small dose of dexmedetomidine decreased the postoperative bleeding by reducing cough and emergence agitation after thyroidectomy – A randomized, double-blind, controlled study

Sang Hun Kim
Department of Anesthesiology and Pain Medicine, College of Medicine and Medical School, Chosun University

Yoo Seok Kim
Department of Surgery, Chosun University College of Medicine, Chosun University Hospital

Seongcheol Kim
Department of Anesthesiology and Pain Medicine, Chosun University Hospital

Ki Tae Jung (mdmole@chosun.ac.kr)
Department of Anesthesiology and Pain Medicine, College of Medicine and Medical School, Chosun University

Research Article

Keywords: cough, dexmedetomidine, hemorrhage, Ramsey sedation scale, recovery, thyroidectomy

DOI: https://doi.org/10.21203/rs.3.rs-163702/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License
Abstract

Background: Bleeding after a thyroidectomy occurs due to violent cough during the emergence. Dexmedetomidine is helpful for smooth emergence and suppressing the cough. The purpose of the present study was to compare the effect of dexmedetomidine on postoperative bleeding after thyroidectomy. Methods: Randomized, double-blind, controlled trial in female patients (ASA I–II, aged 20 to 60 years) were conducted. Patients were randomly allocated into two groups. About fifteen minutes before the end of the surgery, dexmedetomidine was administered (0.6 µg/kg/hr) without a loading dose in group D (n=69), and normal saline was administered in group S (n=70) at the same infusion rate. Hemodynamic data, coughing reflex, extubation time, Ramsay sedation scale (RSS), recovery time were assessed during the administration of study drugs and recovery from anesthesia. Amounts of postoperative hemorrhage were measured for 3 days. Results: A total of 139 patients were analyzed. The incidence of severe cough was significantly decreased in group D compared to group S (4.3% vs. 11.5%, P = 0.022). Emergence agitation in the postanesthetic care unit was significantly decreased in group D compared to group S (P = 0.01). Postoperative bleeding showed a significant decrease in group D compared to group S until the second postoperative day (P = 0.015). Conclusions: Dexmedetomidine can decrease postoperative bleeding by reducing coughing and emergence agitation after thyroidectomy. Trial registration: This study was registered at http://clinicaltrials.gov (registration number NCT02412150, 09/04/2015).

Background

Bleeding after a thyroidectomy, although its incidence is relatively low from 0% to 4.2%, is regarded as a severe complication that can be life-threatening and requires immediate treatment [1]. Many cases of post-thyroidectomy bleeding occur due to violent cough which develops during the awake from the anesthesia and extubation, especially [2]. There have been various trials such as administration of remifentanil or dexmedetomidine to suppress the cough during the extubation period and emergence [3, 4].

Dexmedetomidine, a highly selective α₂-receptor agonist, is focused as an intraoperative adjuvant for various situations recently. Dexmedetomidine helps decrease the emergence agitation which keeps a patient in a calm state after surgery [5, 6]. Moreover, a small dose of dexmedetomidine is effective in suppressing the cough during emergence from anesthesia without respiratory depression [4]. Thus, a small dose of dexmedetomidine may also reduce the postoperative bleeding after thyroidectomy by reducing the cough and emergence agitation. However, no studies have shown a result of whether the effects of dexmedetomidine on reducing emergence agitation and cough can reduce postoperative bleeding after the thyroidectomy.

The purpose of the present study was to find out the effect of dexmedetomidine which is administered during emergence without a loading dose in the female patients undergoing elective thyroidectomy on the postoperative bleeding by reducing coughing and emergence agitation.
Methods

This randomized, double-blind, controlled study was conducted after approval of the Institutional Review Board of Chosun University Hospital (2014-04-004) and was registered at http://clinicaltrials.gov (registration number NCT02412150, 09/04/2015).

A total of 139 female patients who are undergoing elective total thyroidectomy under general anesthesia (ASA class 1-2, aged over 20-60 years) in our hospital were enrolled for the study. Patients with conditions as follows were excluded: risk of a difficult airway, history of respiratory disease, chronic cough, or cardiovascular disease, pregnant or breast-feeding woman. All patients agreed to participate in the study after careful explanation and written informed consent for the participation of the study was obtained. Random allocation of the recruited patients in a 1:1 ratio was done according to the computer-generated random numbers, and the sealed envelopes were prepared by an independent anesthesiologist. When the patients agreed to participate in the study, the envelopes were opened in sequential order and the patients were allocated according to the number into two groups: Group D (n=69), Dexmedetomidine (Precedex®, Pfizer, New York, NY) was administered (0.6 μg/kg/hr) after stopping the administration of remifentanil 15 minutes before the end of surgery; Group C (n=70): Normal saline was administered as a control in the same way. For the blindness, an independent nurse and anesthesiologist who does not participate in the anesthetic procedure prepared the study drugs and assessed outcomes. Dexmedetomidine which was diluted to a 50 mL volume (diluted as 0.2 μg/mL) and normal saline were prepared in a code labeled 50 mL syringe according to the coded number of the patients.

Patients were advised for the overnight fasting and premedicated intramuscular midazolam (0.05 mg/kg) before transfer to the operating room (OR). When the patients have arrived at the OR, a monitoring device (Carescape; GE Healthcare, USA) such as electrocardiogram, non-invasive blood pressure, pulse oximetry, neuromuscular monitoring sensor, and bispectral index (BIS) was applied. Induction of anesthesia was performed by the skilled anesthesiologist who was blinded to the allocation of the patient. For the induction, propofol 2.0 mg/kg was administered and targeted effect-site concentration (Ce) of remifentanil was adjusted as 2.0 ng/ml using a target-controlled infusion device (Orchestra® Base Primea, Fresenius-Vial, France) based on a Minto pharmacokinetic models. When the consciousness of the patient was lost, rocuronium bromide (0.8 mg/kg) was administered and endotracheal intubation with armored tube (internal diameter: 7.0 mm) was done after confirming the adequate neuromuscular blockade by train-of-four (TOF) ratio which became 0, and no neuromuscular blocker was used during the surgery. For the maintenance of anesthesia, desflurane with a 50% O₂-air mixture was used and the end-tidal concentration of desflurane and the Ce of remifentanil were adjusted according to the BIS score (between 40–60) and vital signs (within 20% of baseline values). The initial tidal volume was set at 8 ml/kg with respiratory rates of 12 breaths per minute which were adjusted to maintain the end-tidal CO₂ between 35-40 mmHg and peak inspiratory pressure below 28 mmHg.

When the surgeon informed the subcutaneous suture, which was about fifteen minutes before the end of the surgery, infusion of remifentanil is discontinued, and code labeled syringe was prepared and infused...
at a rate of 3 ml/kg/hr until the patient wakes up fully and transferred to the postanesthetic care unit (PACU). When the surgeon ended the suture, about five minutes before the end of the surgery, desflurane is discontinued and the patient was ventilated with 100% \( O_2 \) (5 L/min) and fentanyl for the control of postoperative pain was administered with a patient-controlled analgesia instrument according to the hospital protocol (basal infusion, 0.625 \( \mu g/kg/hr \) without a loading dose; intermittent bolus, 1.0 \( \mu g/kg/hr \); lockout time, 15min). After the use of reversal agents (pyridostigmine 0.15 mg/kg with glycopyrrolate 0.2 mg/5 mg of pyridostigmine), the recovery from the neuromuscular blockade was confirmed using a neuromuscular monitor (TOF ratio >99%). During the recovery, the patients were asked to open their eyes by the verbal request without any other stimulation or disturbance. When the patient restored spontaneous ventilation and consciousness (BIS score became over 90), careful extubation was done while avoiding irritation and the patient was transferred to the PACU.

The primary outcome of the study was measuring the amount of postoperative bleeding for 3 consecutive days. The amount of postoperative bleeding which is collected in the drainage system was measured by an independent nurse before leaving the PACU and also measured at the ward per 24 hours of time interval. Secondary outcomes such as vital signs, extubation time, recovery time, cough reflex, Ramsay Sedation Scale (RSS), 11-point numeric rating scale (NRS, 0 = no pain and 10 = worst pain imaginable) for the pain measurement, etc. were assessed by independent anesthesiologist and surgeon. The patient’s characteristics, duration of surgery, duration of infusion of study drugs, and the amount of fluid administration during the surgery were recorded. Vital signs such as mean blood pressure (MBP) and heart rate (HR) are measured according to the time interval as follows: T0, before administration of study drugs; T1, 5 minutes after administration of study drugs; T2, 10 minutes after administration of study drugs; T3, 5 minutes after administration of study drugs; T4, just before extubation; T5, 5 min after extubation; T6, after arrival at PACU. During the recovery from the anesthesia (time interval from discontinuing the desflurane to transfer to PACU), coughing reflex was measured and graded according to the severity (Grade 0, no cough; Grade 1, single cough with mild severity; Grade 2, cough persistence less than 5 s with moderate severity; Grade 3, severe, persistent cough for more than 5) [7]. Extubation time (time interval from discontinuing the desflurane to extubate) and recovery time (time interval from discontinuing the desflurane to transferred to the ward) were assessed. About 5 minutes after arrival at the PACU, RSS of the patient is measured as follows: 1, patient anxious and agitated or restless or both; 2, patient cooperative, oriented and tranquil; 3, the patient responds to commands only; 4, asleep or a brisk response to a light glabellar tap or loud auditory stimulus; 5, sluggish response to a light glabellar tap or loud auditory stimulus; 6, no response to a light glabellar tap or loud auditory stimulus [8]. Then, the patients were also classified according to the RSS as follows: agitated, RSS 1; Calm, RSS 2-3; Sedated, RSS 4-6 [9]. In the PACU, the incidence of desaturation (<90%) was assessed as an adverse effect of dexmedetomidine. After the patient was transferred to the ward, the amount of postoperative bleeding and pain score using NRS were assessed daily until the third postoperative day (POD). The duration of the drainage catheter placement after surgery was recorded.
The sample size was calculated using "G*Power3" free software. The effect size was calculated based on a previous study in which the incidence of cough was 55% after a single use of dexmedetomidine infusion [4]. The total sample size was calculated as 136 with the calculated effect size of 0.441, $\alpha = 0.05$, and a power of 80%. The drop-out rate was assumed as 10% and 70 patients were allocated to each group.

Statistical analyses were performed using SPSS 21.0 (IBM Corporation, Somers, NY, USA). The normality test was done using the Kolmogorov-Smirnov test and the Shapiro-Wilk test. Values are expressed as the mean (SD), median [interquartile range], or the number of patients (%) with exact P values. Normally distributed data (age, height, weight, and BMI) were analyzed with Student’s t-test. Non-normal distributed data (duration of surgery, amount of intraoperative fluid, infusion duration of study drug, extubation time, recovery time, and duration of the drainage catheter placement) were analyzed using Mann–Whitney U-test. Categorical variables (ASA class, coexisting disease, grades of cough response, the incidence of severe cough, and RSS) were analyzed by the Chi-square or Fisher's exact test. The change in vital signs, NRS score, and amount of postoperative bleeding according to the time sequence were analyzed by repeated-measures two-way ANOVA, and post-hoc testing was performed using the Mann–Whitney U-test. A P value less than 0.05 was considered statistically significant between the two groups.

**Results**

A total of 140 female patients who scheduled for the elective thyroidectomy were assessed for eligibility. Among the 140 patients, there were no patient who are not meet inclusion criteria or refused to participate. A total of 140 patients were enrolled, but one patient in group D was excluded because of re-operation according to the biopsy results. Finally, 139 patients (Group D, n=69; Group S, n=70) were analyzed (Fig. 1).

There were no significant differences in the patient's characteristics, duration of surgery, amount of intraoperative fluid, and infusion duration of study drugs between the two groups (Table 1). The MBP and HR of both groups showed little changes during the infusion of study drugs and which were increased during the periods of extubation (Fig. 2). There were no significant differences in MBP between the two groups ($P = 0.143$), but the HR showed significant differences between the two groups ($P = 0.001$.) The HR of group D was significantly lower just before extubation compared to group S ($P = 0.015$, Fig. 2A).

Emergence profiles are presented in table 2. There were no significant differences in the extubation time ($P = 0.728$) and recovery time ($P=0.604$). Cough reflex showed significant differences between the two groups ($P = 0.015$) and the incidence of severe cough (grade 3) was significantly decreased in group D compared to group S ($P = 0.022$). The RSS also showed significant differences between the groups ($P < 0.022$). According to the classification using RSS, patients in group D maintained a calmer state (36.0% in group D vs. 29.5% in group S, $P = 0.01$) in the PACU. Especially, patients in group D showed a lower incidence of the agitated state compared to the control in the PACU (7.9% in group D vs. 20.1% in group S). There was no event of oxygen desaturation in the PACU in both groups.
The amount of postoperative bleeding showed significant differences between the two groups (P = 0.015, Fig. 3A). The amount of drained blood during the emergence and PACU staying was significantly decreased in the group D compared to group S (19.0 ml vs. 33.1 ml, P = 0.001) and decrease of postoperative bleeding in the group D has lasted at the first and second POD (P = 0.016 and 0.003, respectively). However, there were no significant differences in the duration of drainage catheter placement between the groups (group D: 3.7 days vs. group S: 4.0 days, P = 0.103).

The pain score using NRS also showed significant differences between two group S (P < 0.001, Fig. 3B). The NRS was significantly decreased in the group D compared to group S at the PACU (P < 0.001), but there were no significant differences during POD.

**Discussion**

In this study, dexmedetomidine infusion during the emergence from anesthesia significantly decreased the incidence of severe cough, emergence agitation in the PACU, and the amount of bleeding which was measured by the drainage system. To our knowledge, the current study is the first to report that administration of dexmedetomidine (0.6 μg/kg/hr) without a loading dose during the recovery from anesthesia is significantly associated with the decrease of postoperative bleeding after thyroidectomy.

As the thyroid gland is an organ with high blood flow, severe bleeding after thyroidectomy is related to the major complication which is life-threatening and requires treatments including intensive care although the incidence of significant bleeding after thyroidectomy as low as 2.0% [1, 2]. Moreover, thyroidectomy itself is associated with postoperative cough, especially in female patients [10]. Thus, bleeding after thyroid surgery should be observed. Even though there are numerous risk factors associated with postoperative bleeding after thyroidectomy such as male gender, older age, postoperative hypertension, etc. those bleeding frequently occurs with suddenly violent cough during extubation and emergence [2]. Cough after thyroidectomy would lift the thyroid cartilage and loosening the ligation, and lead to bleeding after thyroidectomy [2]. Therefore, we hypothesized that the effect of dexmedetomidine which reduces the cough and emergence agitation during the awake period would decrease the postoperative bleeding after thyroidectomy.

There were various efforts to reduce coughing during the awake period, such as intravenous or topical lidocaine, sub-hypnotic propofol, and remifentanil [11-13]. Dexmedetomidine has sedative and analgesic effects without significant respiratory depression which can be used during the stressful procedure such as awake intubation [14]. Moreover, dexmedetomidine is focused as an adjuvant drug during the emergence from anesthesia, recently. We were focused on such effects of dexmedetomidine and conducted this study. However, we omitted a loading dose as previous studies of dexmedetomidine because of the possibility of sudden hemodynamic changes [4, 6].

Lee et al. reported that a single dose of dexmedetomidine (0.5 μg/kg for 10 minutes) with a low-dose remifentanil infusion (Ce of 1.0 ng/mL) at the end of thyroid surgery showed effective suppression of cough during emergence and hemodynamic stability. However, only dexmedetomidine infusion with the
rate of 0.4 μg/kg/hr did not reduce the cough grade during the emergence [6]. Unlike previous studies, dexmedetomidine alone (0.6 μg/kg/hr) without a loading dose during the emergence from anesthesia showed a significant decrease of cough reflex in our study. The incidence of cough was significantly lower in group D (69.7%) than group S (82.9%). In particular, the incidence of severe cough as a grade 3 in Group D decreased significantly compared to Group S (4.3% in Group D and 11.5% in Group S, respectively). We considered the cause of these differences as the differences of gender. A previous study revealed that there are gender differences in the estimated EC50 of remifentanil for reducing cough during emergence, and which was significantly lower in females than males (1.30 ng/mL in female vs. 2.57 ng/mL in male) [15]. Unlike previous studies, all of our subjects were female. Therefore, these gender differences were as one of the factors that dexmedetomidine alone (0.6 μg/kg/hr) used in this study had sufficient effect on reducing the cough reflex. However, further research about dexmedetomidine sensitivity according to gender is needed.

It is well known that the sedative effect of dexmedetomidine is associated with the decrease of incidence of emergence agitation. Dexmedetomidine administration (0.4 μg/kg/hr during the anesthesia) without a loading dose also provided smooth emergence after surgery and reduced emergence agitation [5, 6]. In the current study, we measured RSS score to compare the emergence profile, which revealed that dexmedetomidine provided calm awake in the PACU (36.0% in group D vs. 29.5% in group S, P = 0.01). Particularly, we classified RSS to compare the incidence of emergence agitation [9], and the results showed that dexmedetomidine decreased agitation (7.9% in group D vs. 20.1% in group S, P = 0.01) during the emergence period in the PACU. Despite the sedative effects, there were no significant differences in the extubation time (P = 0.728) and recovery time (P=0.604) and no event of desaturation after administration of dexmedetomidine.

The unique result of this study was an assessment of postoperative bleeding and this study identified a decrease in the amount of bleeding after thyroidectomy along with the above results that the reduction of the cough reflex and emergence agitation, although the duration of drainage catheter placement showed no significant difference. Still, there is disagreement over the studies on the effect of dexmedetomidine on perioperative bleeding. Dexmedetomidine decreased perioperative bleeding by maintaining stable hemodynamic response during the tympanoplasty or septoplasty when administered as an adjuvant drug for the maintenance of anesthesia [16]. However, dexmedetomidine slightly increased perioperative bleeding after thyroidectomy in the pediatric patients when administered before the induction of anesthesia (0.5 μg/kg) due to the vasodilative effect as an α2 adrenergic agonist [17]. Moreover, continuous infusion of dexmedetomidine attenuated the activation of coagulation in the patients who are undergoing radical gastrectomy according to the thromboelastography by reducing the intraoperative stress response and an anti-inflammatory effect, paradoxically [18]. Nevertheless, in the current study, we administered a small dose of dexmedetomidine at the end of surgery when the vascular ligation and bleeding control were ended. The previous study also showed a low dose of dexmedetomidine similar to our study does not affect the clotting profiles [17]. We assessed the amount of postoperative bleeding for 3 days which revealed a significant decrease of bleeding during the emergence and PACU staying (19.0 ml vs. 33.1 ml, P = 0.001), and the decrease of bleeding was confirmed until the second POD.
results appear to be because of the effects of dexmedetomidine which reduce the cough reflex and emergence agitation.

Additionally, dexmedetomidine decreased postoperative pain at the PACU in our study although there were no significant differences in NRS after the second POD. The analgesic effect of dexmedetomidine is well-known and intraoperative dexmedetomidine can decrease postoperative pain effectively [19]. Even low dose dexmedetomidine (0.4 μg/kg/hr infusion during laparoscopic surgery) showed a reduction in postoperative analgesic requirements [20]. According to the study of Yoo et al. [21], the intensity of postoperative pain after thyroidectomy was greatest at 30 minutes after surgery in the PACU and decreased by one-third after 24 hours. As postoperative pain is identified as an independent risk factor for post-thyroidectomy hemorrhage [22], the analgesic effect of dexmedetomidine may also contribute to the reduction of postoperative bleeding. However, we only measured the intensity of postoperative pain on the first day in the PACU and this is considered a limitation point of our study.

Administration of dexmedetomidine without a loading dose showed no significant differences in MBP between the two groups (P = 0.143), but the HR in our study significantly lower before extubation compared to the control (P = 0.015). Infusion of a loading dose of dexmedetomidine can increase blood pressure and decreased heart rate significantly [23]. We omitted a loading dose to avoid sudden hemodynamic fluctuations. Hemodynamic changes after administration of dexmedetomidine vary according to the individual variability and the infusion methods. Lee et al. [4] showed no differences in the MBP and HR compared to the control with a small dose of dexmedetomidine without a loading dose. However, the infusion rate (0.6 μg/kg/hr vs. 0.5 μg/kg/hr) and duration of infusion (median 34 minutes vs. 10 minutes) of dexmedetomidine were higher and longer than the previous study. This difference in methods may have resulted in only a decrease in heart rate without a difference in blood pressure.

There are several limitations in this study. First, we selected only female patients as subjects of the study. This was because most of the patients with thyroid cancer were women in our hospital since thyroid cancer is 2.9-times more common in female than male [24]. And post-thyroidectomy cough is associated with the female as mentioned above. Therefore, we restrict the subjects to women. However, the sensitivity of drugs might be different according to the gender, and the results of the current study are applicable only to women. Second, we did not evaluate postoperative nausea and vomiting (PONV). After thyroidectomy, PONV is a common complication and related to postoperative bleeding [2]. Adjuvant dexmedetomidine was effective for the prevention of PONV [25]. Dexmedetomidine used in our study may have reduced PONV and be related to the outcome of our study that reduced postoperative bleeding. We only focused on cough reflex and emergence agitation with dexmedetomidine administration, therefore further evaluation about PONV is required. Third, the optimal dosing method of dexmedetomidine should be evaluated. We used only a low dose of dexmedetomidine for a relatively short time without a loading dose of dexmedetomidine. Both previous studies and this study had different infusion rates and duration of dexmedetomidine [5, 6]. There are no guidelines yet for the appropriate infusion dose and rate of dexmedetomidine administration to reduce coughing or emergence agitation. In the end, the effects of dexmedetomidine may vary depending on the blood concentration of
the dexmedetomidine, further research on the exact plasma concentration, infusion rate, and dosage are required.

**Conclusions**

In conclusion, the administration of dexmedetomidine (0.6 μg/kg/hr) without loading dose during the recovery from anesthesia significantly reduced the amount of bleeding after thyroidectomy by decreasing the incidence of severe cough and emergence agitation in the PACU. These results suggest that dexmedetomidine can be an effective method for the prevention of severe postoperative bleeding after thyroidectomy.

**List Of Abbreviations**

ASA: American Society of Anesthesiologist.

BIS: bispectral index

Ce: effect-site concentration

HR: heart rate

MBP: mean blood pressure

NRS, numeric rating scale

PACU: postanesthetic care unit

POD: postoperative day

RSS: Ramsay Sedation Scale

TOF: train-of-four

**Declarations**

**Ethics approval and consent to participate**

This study was conducted after approval of the Institutional Review Board of Chosun University Hospital (2014-04-004) and was registered at http://clinicaltrials.gov (registration number NCT02412150, 09/04/2015).

Written informed consent for the participation of the study was obtained from all patients after careful explanation in accordance with the Declaration of Helsinki in order to report and publish the individual patient data obtained.
Consent for publication

Not applicable

Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare no conflict of interest.

Funding

Clinical Medicine Research Institute at Chosun University Hospital (2020)

Authors' contributions

Conceptualization: Ki Tae Jung. Experiment conduction: Sang Hun Kim, Yoo Seok Kim, Seongcheol Kim, Ki Tae Jung. Data acquisition: Yoo Seok Kim, Seongcheol Kim. Formal analysis: Sang Hun Kim, Ki Tae Jung. Funding: Ki Tae Jung. Supervision: Ki Tae Jung. Writing—original draft: Ki Tae Jung. Writing—review & editing: Sang Hun Kim, Ki Tae Jung.

Acknowledgements

The present study was supported by grants from the Clinical Medicine Research Institute at Chosun University Hospital (2020).

References

1. Wojtczak B, Aporowicz M, Kaliszewski K, Bolanowski M: Consequences of bleeding after thyroid surgery - analysis of 7805 operations performed in a single center. Arch Med Sci 2018, 14(2):329-335.
2. Chen E, Cai Y, Li Q, Cheng P, Ni C, Jin L, Ji Q, Zhang X, Jin C: Risk factors target in patients with post-thyroidectomy bleeding. Int J Clin Exp Med 2014, 7(7):1837-1844.
3. Lee B, Lee JR, Na S: Targeting smooth emergence: the effect site concentration of remifentanil for preventing cough during emergence during propofol-remifentanil anaesthesia for thyroid surgery. Br J Anaesth 2009, 102(6):775-778.
4. Lee JS, Choi SH, Kang YR, Kim Y, Shim YH: Efficacy of a single dose of dexmedetomidine for cough suppression during anesthetic emergence: a randomized controlled trial. Can J Anaesth 2015, 62(4):392-398.
5. Kim DJ, Kim SH, So KY, Jung KT: Effects of dexmedetomidine on smooth emergence from anaesthesia in elderly patients undergoing orthopaedic surgery. *BMC Anesthesiol* 2015, 15:139.

6. Kim SY, Kim JM, Lee JH, Song BM, Koo BN: Efficacy of intraoperative dexmedetomidine infusion on emergence agitation and quality of recovery after nasal surgery. *Br J Anaesth* 2013, 111(2):222-228.

7. Kim JY, Kim JY, Park SY, Jung WS, Kwak HJ: Effect of low dose ketamine to prevent remifentanil-induced cough: a randomized, double-blind, placebo controlled trial. *Korean J Anesthesiol* 2009, 56(6):624-627.

8. Ramsay MA, Savege TM, Simpson BR, Goodwin R: Controlled sedation with alphaxalone-alphadolone. *Br Med J* 1974, 2(5920):656-659.

9. Namigar T, Serap K, Esra AT, Ozgul O, Can OA, Aysel A, Achmet A: [The correlation among the Ramsay sedation scale, Richmond agitation sedation scale and Riker sedation agitation scale during midazolam-remifentanil sedation]. *Rev Bras Anestesiol* 2017, 67(4):347-354.

10. Wu Y, Fang Q, Xu C, Li H: Association between postoperative cough and thyroidectomy: a prospective study. *BMC Cancer* 2019, 19(1):754.

11. Shroff PP, Patil V: Efficacy of cuff inflation media to prevent postintubation-related emergence phenomenon: air, saline and alkalinated lignocaine. *Eur J Anaesthesiol* 2009, 26(6):458-462.

12. Jung SY, Park HB, Kim JD: The effect of a subhypnotic dose of propofol for the prevention of coughing in adults during emergence from anesthesia with sevoflurane and remifentanil. *Korean J Anesthesiol* 2014, 66(2):120-126.

13. Kang DH, Kim YW, Choi SW, Lee SE, Lim SH, Lee JH, Lee KM, Cheong SH, Choe YK, Kim YJ et al: A comparison of the suppression of cough reflex by intravenous lidocaine and remifentanil prior to extubation of the endotracheal tube. *Korean J Anesthesiol* 2008, 55(4):452-457.

14. Gerlach AT, Murphy CV, Dasta JF: An updated focused review of dexmedetomidine in adults. *Ann Pharmacother* 2009, 43(12):2064-2074.

15. Soh S, Park WK, Kang SW, Lee BR, Lee JR: Sex differences in remifentanil requirements for preventing cough during anesthetic emergence. *Yonsei Med J* 2014, 55(3):807-814.

16. Durmus M, But AK, Dogan Z, Yucel A, Miman MC, Ersoy MO: Effect of dexmedetomidine on bleeding during tympanoplasty or septorhinoplasty. *Eur J Anaesthesiol* 2007, 24(5):447-453.

17. Mizrak A, Karatas E, Saruhan R, Kara F, Oner U, Saricicek V, Baysal E: Does dexmedetomidine affect intraoperative blood loss and clotting tests in pediatric adenotonsillectomy patients? *J Surg Res* 2013, 179(1):94-98.

18. Chen Z, Shao DH, Mao ZM, Shi LL, Ma XD, Zhang DP: Effect of dexmedetomidine on blood coagulation in patients undergoing radical gastrectomy under general anesthesia: A prospective, randomized controlled clinical trial. *Medicine (Baltimore)* 2018, 97(27):e11444.

19. Schnabel A, Meyer-Friessem CH, Reichl SU, Zahn PK, Pogatzki-Zahn EM: Is intraoperative dexmedetomidine a new option for postoperative pain treatment? A meta-analysis of randomized controlled trials. *Pain* 2013, 154(7):1140-1149.
20. Manne GR, Upadhyay MR, Swadia V: Effects of low dose dexmedetomidine infusion on haemodynamic stress response, sedation and post-operative analgesia requirement in patients undergoing laparoscopic cholecystectomy. *Indian J Anaesth* 2014, **58**(6):726-731.

21. Yoo B, Kwon JY, Hwang BY, Hong JM, Kim TK, Kim HK: Postoperative pain and side effects after thyroidectomy: randomized double blind study comparing nefopam and ketorolac. *Anesth Pain Med* 2014, **9**(2):110-114.

22. Lee M, Rhee J, Kim Y, Jung YH, Ahn SH, Jeong WJ: Perioperative risk factors for post-thyroidectomy hematoma: Significance of pain and ketorolac usage. *Head Neck* 2019, **41**(10):3656-3660.

23. Han Y, Han L, Dong MM, Sun QC, Ding K, Zhang ZF, Cao JL, Zhang YY: Comparison of a loading dose of dexmedetomidine combined with propofol or sevoflurane for hemodynamic changes during anesthesia maintenance: a prospective, randomized, double-blind, controlled clinical trial. *Bmc Anesthesiol* 2018, **18**.

24. Rahbari R, Zhang L, Kebebew E: Thyroid cancer gender disparity. *Future Oncol* 2010, **6**(11):1771-1779.

25. Choi EK, Seo Y, Lim DG, Park S: Postoperative nausea and vomiting after thyroidectomy: a comparison between dexmedetomidine and remifentanil as part of balanced anesthesia. *Korean J Anesthesiol* 2017, **70**(3):299-304.

Tables
### Table 1.

Patient’s characteristics and intraoperative variables

|                      | Group D ($n = 69$) | Group S ($n = 70$) | P-value |
|----------------------|--------------------|--------------------|---------|
| Age (yr)             | 44.2 (1.4)         | 45.0 (4.9)         | 0.646   |
| Height (cm)          | 158.8 (5.7)        | 159.5 (1.4)        | 0.444   |
| Weight (kg)          | 61.7 (7.8)         | 61.4 (6.4)         | 0.909   |
| BMI                  | 24.1 (5.2)         | 23.8 (2.1)         | 0.652   |
| ASA class (I/II)     | 49/20              | 51/19              | 0.852   |
| Coexisting disease   |                    |                    |         |
| Hypertension         | 9 (13.0)           | 11 (15.7)          | 0.810   |
| Diabetes             | 3 (4.3)            | 4 (5.7)            | 1.000   |
| Renal disease        | 0 (0)              | 1 (1.4)            | 1.000   |
| Duration of surgery (min) | 115.0 [45.0]      | 115.0 [35.0]       | 0.947   |
| Amount of intraoperative fluid (ml) | 300.0 [100.0]  | 300.0 [50.0]       | 0.779   |
| Infusion duration of study drug (min) | 34.0 [8.0]   | 32.0 [22.0]        | 0.539   |

Values are the mean (standard deviation), median [interquartile range], or number (%). Group D, administered dexmedetomidine (0.6 ug/kg/hr); Group S, administered normal saline as a control; BMI, body mass index; ASA. American Society of Anesthesiologist.

### Table 2.

Emergence profile during awake and in the postanesthetic care unit.

|                      | Group D ($n = 69$) | Group S ($n = 70$) | P-value |
|----------------------|--------------------|--------------------|---------|
| Extubation time (min)| 10.0 [8.0]         | 8.0 [5.25]         | 0.728   |
| Recovery time (min)  | 41.0 [16.0]        | 42.0 [13.0]        | 0.604   |
| Cough reflex (grade 0/1/2/3) | 21/29/13/6      | 12/20/22/16       | 0.015   |
| Incidence of severe cough (grade 3) | 6 (4.3)            | 16 (11.5)          | 0.022   |
| RSS at PACU          | 2.3 (0.7)          | 1.7 (1.4)          | 0.002   |
| Agitated (RSS 1)     | 11 (7.9)           | 28 (20.1)          |         |
| Calm (RSS 2-3)       | 50 (36.0)          | 41 (29.5)          | 0.01    |
| Sedated (RSS 4-7)    | 8 (5.8)            | 1 (0.7)            |         |
| Desaturation         | 0 (0)              | 0(0)               | -       |
Values are the mean (standard deviation), median [interquartile range], or number (%). Group D, administered dexmedetomidine (0.6 \( \mu \text{g/kg/hr} \)); Group S, administered normal saline as a control. Extubation time, the time interval from discontinuing the desflurane to extubate; recovery time, time interval from discontinuing the desflurane to transferred to the ward; RSS, Ramsay Sedation Scale; PCAU, postanesthetic care unit. Patients were classified as agitated, RSS 1; Calm, RSS 2-3; Sedated, RSS 4-6.