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Benefits of dexamethasone usage in thyroid surgery: a prospective, randomized study

Предности примене дексаметазона код пацијената који се подвргавају операцијама штитасте жлезде: проспективно, рандомизовано истраживање

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SUMMARY

Introduction/Objective This study aimed to investigate the effects of preoperative dexamethasone usage on the incidence and severity of postoperative nausea and vomiting (PONV), postsurgical pain and vocal impairment after thyroid surgery.

Methods We performed a prospective, randomized, double blind study with 50 patients who underwent thyroid surgery. Group A patients (n = 25) received 0.9% NaCl solution (2 ml) before anesthesia, patients in Group B (n = 25) were administered dexamethasone 8mg. All patients received ondansetron 4 mg preoperatively. During the first 48 hours after surgery, postoperative complications were monitored in defined periods.

Results PONV rate and severity was significantly lower in Group B than in Group A (p < 0.05). Patients in Group B reported less pain in resting and in activity (p < 0.05) and lower vocal impairment (p < 0.05) than patients in Group A in each defined time period.

Conclusion Preoperatively adding dexamethasone to ondansetron is more effective than usage of ondansetron alone in the prevention of PONV. Dexamethasone significantly reduces the pain and improves voice function; therefore, we could advise the routine usage of single dose dexamethasone before thyroid surgery.

Keywords: PONV; postoperative pain; vocal impairment; thyroid surgery; dexamethasone; ondansetron

Сажетак

Увод/циљ Истраживање је спроведено са циљем да се испита утицај преоперативно примењеног дексаметазона на учесталост и интензитет постоперативне мучнине и повраћања, интензитет постоперативног бола и вокалну дисфункцију након операције штитасте жлезде.

Методе Проспективно, рандомизовано, двоструко слепо истраживање обухватило је 50 пацијената код којих је изведена операција штитасте жлезде. Пре увода у анестезију пацијенти Групе А (n = 25) су примили 0,9% NaCl (2 мл), а пацијенти Групе Б (n = 25) 8 мг дексаметазона (2 мл). Сви пацијенти су преоперативно примили и 4 мг ондансетрона. Постоперативне компликације су праћене 48 часова након операције у дефинисаним временским интервалима.

Резултати Постоперативна мучнина и повраћење је била значајно ређа и мањег интензитета (p < 0,05) код пацијената Групе Б у поређењу са пацијентима Групе А. Пацијенти групе Б су постоперативно осетили значајно слабији бол у миру и у напору (p < 0,05) и имали мање изражену вокалну дисфункцију (p < 0,05) у поређењу са пацијентима Групе А.

Закључак Преоперативна примена комбинације дексаметазона и ондансетрона је ефикаснија у превенцији постоперативне мучнине и повраћања у поређењу са применом само ондансетрона. Обзиром да дексаметазон значајно смањује и интензитет постоперативног бола и унапређује вокалну функцију, можемо предложити рутинску примену појединачне дозе дексаметазона пре операција штитасте жлезде.

Кључне речи: постоперативна мучнина и повраћање; постоперативни бол; вокална дисфункција; хирургија штитасте жлезде; дексаметазон; ондансетрон

INTRODUCTION

Common postoperative concerns for patients undergoing thyroid surgery consist of postoperative nausea and vomiting (usually summarized as PONV), acute postsurgical pain and vocal impairment. These concerns could, apart from reducing comfort, cause grave local and systemic complications. PONV is defined as nausea and/or vomiting during the first 24 hours after surgery with the incidence among all surgical patients between 20% and 30% [1].

The etiology of PONV is very complex. Many anesthetic, surgical and individual factors can have a significant impact on the frequency and severity of this complication [4, 5]. Individual risk factors include: female sex, young patients, non-smokers, patients with history of kinetosis and PONV. Apfel et al [6] developed a simplified risk score as a tool aiming to help the prediction of PONV, according to which there are 4 main risk factors: female sex, prior history of motion sickness and PONV, non-smoker and the use of postoperative opioids. According to his results PONV incidence was 10%, 21%, 39%, 60% and 78%, in the presence of none, one, two, three or all four of these risk factors respectively. Anesthetic risk factors include: older volatile anesthetics, nitrous oxide and opioids usage, as well as neostigmine in high doses [7, 8, 9]. Surgical risk factors mainly include duration and type of surgery [10].

PONV is not caused by a single stimulus or a single cause, so usage of single antiemetic in PONV prophylaxis is not effective enough. We should use the combination of antiemetic drugs [11–14]. It is not known yet how the combination of dexamethasone with 5-HT3 receptor antagonists works. Dexamethasone could actually inhibit seratonin central or peripheral production and/or secretion and enhance the antiemetic effects of a 5-HT3 receptor antagonists, or it could sensitize pharmacologic receptors which will lead to potentiating the main effects of other antiemetic drugs [15]. Furthermore, the usage of dexamethasone could be effective in prevention of acute postoperative pain and vocal impairment [16, 17, 18].

This study aimed to investigate the effects of adding dexamethasone to ondansetron prior to surgery on incidence and severity of PONV, and the effects of dexamethasone on pain and vocal impairment after thyroid surgery.

METHODS

We performed a prospective, randomized, double blind clinical study comprised 50 adult patients undergoing elective thyroid surgery (partial or total thyroidectomy) at Oncology Institute of Vojvodina in Sremska Kamenica, University of Novi Sad, Serbia. Institutional ethic boards approved the study. The inclusion criteria were: age ≥ 18 , patients

undergoing thyroid surgery, American Society of Anesthesiologists (ASA) physical status I or II. The exclusion criteria were: usage of antiemetic drugs 48 hours before surgery, known contraindication or hypersensitivity to study medications, abnormal levels of serum thyroid hormones, chronic pain, gastrointestinal diseases, BMI < 35, glaucoma, pregnancy, diabetes and severe cardiovascular, renal and respiratory diseases.

After admission into the hospital, patients underwent physical examination and were given explanation of the research and the purpose of the study. After the written informed consent has been obtained from patients, a random division into two groups of patients was done. Randomization was carried out by permuted-block randomization where the block size was six with gender as stratification factor.

The enrolling anesthesiologist prepared the group assignment was in sealed opaque envelopes. The treating and the enrolling anesthesiologist were different persons. Fifteen minutes before induction of anesthesia the envelopes were opened and an independent nurse, who was not participating in any other part of the study, prepared the drugs.

Ingestion of solid food is discontinued eight hours prior to the scheduled beginning of surgery, and ingestion of clear liquids is discontinued two hours prior to surgery. Both groups of patients received midazolam 2.5 mg IV 30 minutes prior to anesthesia and antiemetic drugs 10 minutes before anesthesia. The Group A patients (n = 25) received ondansetron 4 mg and placebo (2 mL of 0.9% NaCl solution), while patients in the Group B (n = 25) were administrated ondansetron 4 mg and dexamethasone 8 mg (2 mL).

The same team of surgeons performed all operations. Patients received standardized general anesthesia. For the induction we used propofol 2 mg/kg, fentanyl 2 μ g/kg and atracurium 0.5 mg/kg for tracheal intubation. All the intubations were conducted by experienced anesthesiologists using video laryngoscopy. After intubation, tracheal tube cuff pressure was measured with manometer and then adjusted to 20 to 30 cm H₂O. Anesthesia was maintained with sevoflurane titrated to achieve minimal alveolar concentration (MAC) 1 and nitrous oxide 50% in oxygen. Ventilation was mechanically controlled and adjusted to maintain the partial pressure of the end-tidal concentration of carbon dioxide between 35 and 40 mm Hg. Intermittent doses of atracurium were given during anesthesia to maintain adequate muscle relaxation throughout the procedure. Neuromuscular blockade was monitored using train-of-four monitoring and reversion were provided with atropine 0.01

mg/kg and neostigmine 0.02 mg/kg. Electrocardiography, heart frequency, blood pressure, blood oxygen saturation, and inspiratory and expiratory concentration of O₂, CO₂, nitrous oxide and sevoflurane were monitored during anesthesia.

Postoperative pain control was managed with ketorolac 30 mg IV every 8 hours. Paracetamole 1 g IV was administered when visual analogue scale was (VAS) \geq 5. Metoclopramide 10 mg IV was administered in to the patients who had more than 3 episodes of vomiting.

During the first 48 hours after surgery, postoperative complications were monitored in defined periods (first, sixth, 12th, 24th, 48th hour) by the third anesthesiologist. All the data were collected using anesthesia charts, a survey and observation.

The total PONV rate, incidence and severity of PONV in Group A and Group B, as well as the incidence of PONV among smokers were the primary end points of this study. The secondary end points were the acute postsurgical pain and vocal impairment. All data were collected within the first 48 hours following the anesthesia.

A 4-point scale was used to assess the presence and severity of PONV; Grade 1 - absence of nausea, Grade 2 - very mild nausea, Grade 3 - moderate nausea and retching (a retroperistalsis of the stomach and esophagus without vomiting), Grade 4 - vomiting (a forceful discharge of stomach contents).

Postsurgical pain was assessed using a 10-point visual analogue scale VAS (0 - no pain to 10 - the worst pain that could be imagine). Pain scores were measured at state of rest (no coughing) and with activity (coughing).

Analysis of voice quality included patient's own subjective evaluation of voice according to the Voice Visual Analog Scale (VVAS, 10 - normal voice, 0 - worst voice that could be imagine).

Statistical evaluation was carried out using the SPSS® statistical package, version 16.0 (SPSS Inc., Chicago, IL, USA) for Windows®. Statistical significance was defined for p value less than 0.05.

RESULTS

Our study involved 6 (12%) male and 44 (88%) female patients. Statistically significant differences between the groups were not found in patients' demographic characteristics, ASA score, indications for surgery and type of thyroid surgery (Table 1).

The mean duration of anesthesia was 84.5 minutes. No significant difference was found between the groups in the mean duration of anesthesia which could influence on PONV incidence (Group A = 88 min, Group B = 81 min, p = 0.124). All patients were hemodynamically stable in perioperative period.

The total PONV (including very mild nausea) incidence in both groups up to 48 hours after anesthesia was 52% (26/50 patients). In the Group A 72% of patients reported PONV. In the Group B the PONV rate was significantly lower (32% of patients, p < 0.05). There were no significant differences in metoclopramide dose administered (80 mg in Group A for four patients, in Group B 20 mg for two patients).

PONV severity was also significantly lower in the Group B compared with the Group A (p < 0.001, Fig 1). Very mild nausea (Grade 2) was reported by 16% of patients in Group B and in 36% of patients in Group A. Moderate nausea and retching (Grade 3) were reported by 8% of patients in Group B and in 20% of patients in Group A. Only 8% of patients in Group B had vomiting (Grade 4), compared with 16% of patients in Group A.

During the first hour following surgery, intense vomiting (Grade 4) occurred among 8% (2/25) of patients in Group A, whilst not a single patient in Group B reported intense vomiting, which is statistically lower (p = 0.034). In following defined periods there was no statistically significant difference between the groups regarding severity of the PONV (Table 2).

Twenty patients were smokers and 30 nonsmokers. Significant difference in PONV incidence between smokers and nonsmokers was found in the period between the 1st and the 6th hour (p = 0.004) and the 6th and the 12th hour (p = 0.013), while there was no difference in other defined time intervals.

Regarding intensity of acute postoperative pain, we found significant difference between the groups in each determined time period following surgery. Patients in Group B reported significantly less pain at the state of rest and on coughing in all periods than patients in Group A (Table 3). In accordance to this, 5 patients in Group A received paracetamole (8 g in total) while in Group B paracetamole was administered only in one patient (1g) (p < 0.05).

Our research showed that development of vocal impairment was significantly lower in Group B compared with Group A (p < 0.05) in each defined time period during the first 48 hours after the surgery (Table 3).

DISCUSSION

The most prominent perioperative concerns from the patients' point of view are the ones causing him the biggest discomfort – pain, nausea and vomiting. PONV happens to be one of the most common causes of dissatisfaction among patients after undergoing anesthesia. Despite the fact that serious complications caused by PONV are rare, nausea and vomiting are still a disagreeable and common complications following the surgery [1]. Fortunately, this unpleasant complication could be effectively managed [4].

In our study, demographic and clinical characteristics, duration of anesthesia, type of surgical interventions, anesthetic and perioperative analgesic usage were similar between the two groups. None of the patients in both groups required opioids in postoperative period. In addition, the patients with obesity and previous postoperative emesis and history of sickness while driving had been excluded from the study. There were no difficult intubations. Therefore, the difference in incidence of PONV between the groups could be explain only by different antiemetic drugs administered before surgery. One of the main causes of PONV, especially during the early postsurgical recovery period is, for sure, the use of inhalational drugs [6, 7, 19]. Nitrous oxide is well-known and recognized as the risk factor for PONV. Myles et al. [20] concluded that usage of antiemetic drugs before surgery could eliminate the risk of severe PONV caused by nitrous oxide. We designed our study to show prophylactic effectiveness of dexamethasone and ondansetron on PONV in case of anesthesia with nitrous oxide.

Among 50 patients in the study 26 of them had PONV including very mild nausea, moderate nausea and vomiting, that presents 52% of patients.

We found that the total incidence of PONV after preoperative usage of dexamethasone in combination with ondansetron (32% of patient) was significantly lower in comparison to ondansetron alone pretreatment (72% of patients). This is confirmed in some other studies [21–24]. The PONV incidence in our study was higher compared with mentioned studies, probably because we considered very mild nausea (Grade 2), which patients have described more as an inconvenience. Excluding very mild nausea, the total PONV incidence was 26% (36% in the ondansetron alone group, 16% in the dexamethasone with ondasetron group). Dexamethasone combined with others drugs could significantly reduce the incidence of PONV in postoperative 24 h [25]. Ahsan et al. [22] and Song et al. [23] compared ondansetron and dexamethasone combination effectiveness with ondasetron alone in preventing postoperative nausea and vomiting. Their results showed that the combination therapy was more effective.

The commonly used dexamethasone doses were 8–10 mg iv. No side effect related to single dose of 8 mg dexamethasone was found in our study and there was no prolonged hospital treatment due to use of dexamethasone. Our results suggest that the combination of ondansetron and dexamethasone is more effective for control of nausea and vomiting.

Severity of PONV was in our study lower in patients who were pretreated with dexamethasone and ondansetron than with ondansetron only. We found out that the difference in the severity of the PONV between the groups is significant only in first hour following surgery. Although this difference failed to maintain significant during overall period (0–48 h), the combination of medications is more beneficial than individual ondansetron usage according to the trend of 95% confidence intervals.

Although the fact that smoking has antiemetic effect is confirmed by many studies [26, 27], the etiology of its action is not completely known yet. There is a possibility that people who smoke have a lower incidence of PONV because they are more tolerant to anesthetic gases and other toxins than nonsmokers. According to our results PONV was more frequent in smokers; we found a marked difference in the incidence of PONV in the smokers compared with nonsmokers in the period between the 1st and the 12th hour after anesthesia. The small number of patients included in the study could be the cause of this result.

Postsurgical pain and PONV are two separate outcomes, but it is known that pain causes anxiety, which could be associated with nausea [16].

The results of meta-analysis conducted by De Oliveira et al. [28] support the fact that steroids have an analgesic effect. Since numerous effects of corticosteroids require gene expression and protein production, it is expected for them to have a delayed onset, which is uncommon for most analgesics. Expectedly, preoperative dosing turned out more effective than intraoperative administration. In the present study we found that patients receiving prophylactic dexamethasone rated postoperative pain significantly lower on the VAS scale at state of rest and on coughing than patients who were not pretreated with dexamethasone throughout the observation period.

Doksrod et al. [24] concluded that the incidence of PONV could be reduced effectively with dexamethasone; there were no differences in effectiveness between the medium (0,15 mg/kg) and the higher dose (0.30mg/kg). According to their results dexamethasone had no opioid sparing or analgesic effect after thyroid surgery. The similar were the results of metaanalysis performed by Li et al. [29].

Worni et al. [17] have been studying the effects of corticosteroids on voice impairment related to thyroidectomy, and have shown improved postoperative voice function, reduced nausea, vomiting and pain during the first 48 hours after surgery in the group of patients who were pretreated with dexamethasone. Our results also confirmed the benefits from the usage of dexamethasone regard to voice function. We found significantly lower rate of vocal impairment in dexamethasone and ondansetron group in each defined time period within the first 48 hours after surgery.

In a study conducted by Lee et al. [30] effects of ramosetron and dexamethasone usage were compared with ramosetron alone in patients who undergo thyroid surgery. The PONV incidence, need for additional antiemetics, intensity of postsurgical pain and incidence of shivering were the primary end points of the study. They concluded that combining ramosetron with dexamethasone significantly decreases the incidence of PONV, need for additional antiemetic treatment, pain intensity immediately after surgery, ketorolac consumption, as well as the incidence of shivering.

In spite of the fact that currently used antiemetics, such as ondansetron and granisetron, showed their effectiveness [23, 24], the solution is in better prevention.

The second generations of 5-HT3 antagonists' price is very high and that limits clinical application especially in low economy countries. On the other hand, dexamethasone has common clinical use due to its low price.

CONCLUSION

According to our findings, preoperatively adding dexamethasone to ondansetron provides much better prevention of PONV than ondansetron alone usage. Significant reduction of pain intensity and improvement of the voice function within the first 48 hours after thyroid surgery may be achieved by applying a single dose of dexamethasone prior to surgery.

Using dexamethasone is a safe and simple method for reduction the incidence and severity of PONV, pain and vocal impairment, so dexamethasone usage could reduce the total treatment costs. Therefore, we advise routine usage of single dose dexamethasone before thyroid surgery.

Conflict of interest: None declared.

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Table 1. Patient characteristics and surgical treatment	
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Patient characteristics	Group A $(n = 25)$	Group B (n = 25)	р
Mean age, y	53.3	48.9	0.575
ASA status, no. (%)			
Ι	0 (0)	3 (12)	0.067
II	25 (100)	22 (88)	0.077
Smokers, no.	11	9	0.564
Type of surgery			
Subtotal thyroidectomy	9	11	0.564
Lobectomy	9	7	0.544
Lobectomy with resection of	Λ	2	0.682
the isthmus	4	3	0.082
Total thyroidectomy	3	4	0.682

Table 2. Mean values of postoperative nausea and vomiting (PONV) severity in Group A and Group B; the presence and severity of PONV were assessed using a 4-point scale; Grade 1 - no nausea, Grade 2 - very mild nausea, Grade 3 - moderate nausea and retching, Grade 4 - vomiting

Time periods	Group A	Group B	PONV severity		
	(n = 25)	(n = 25)	р		
0–1h	1.2	0.5	0.034		
1-6h	0.3	0.1	0.214		
6–12h	0.3	0.1	0.18		
12–24h	0.4	0.12	0.138		
24–48h	0.1	0.1	1		

Table 3. Mean values of visual analogue scale (VAS) at rest and on coughing and voice visual analog scale (VVRS) in Group A and Group B; VAS – 10-point scale: from 0 – no pain to 10 – the worst pain imaginable; VVAS: from 10 – normal voice to 0 – worst voice imaginable

Time	V	AS at rest	at rest VAS on coughing VVAS						
periods	Group A (n = 25)	Group B (n = 25)	р	Group A (n = 25)	Group B (n = 25)	р	Group A (n = 25)	Group B (n = 25)	р
0–1 h	3	1.75	0.002	4	3	0.027	7.5	9	0.000
1–6 h	1.75	0.8	0.002	3.2	2	0.001	8.7	9.3	0.025
6–12 h	1.9	0.75	0.003	3.5	1.75	0.000	8.5	9.5	0.001
12–24 h	0.5	1.25	0.009	2.6	1.5	0.002	8.7	9.8	0.000
24–48 h	0.25	0.9	0.001	1.9	0.9	0.001	9	10	0.000





Figure 1. The presence and severity of postoperative nausea and vomiting in Group A and Group B during the period of 48 hours

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