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Research Article

Comparative Study of the Preemptive Dexmedetomidine Versus Ondansetron Effect in Post-Operative Nausea and Vomiting after Middle Ear Surgery

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ABSTRACT

Background: Nausea and vomiting after operation has high prevalence and cause adverse effect. The aim of this study was to compare the effect of dexmedetomidine with ondansetron in prevention of post-operative nausea and vomiting (PONV) after middle ear surgery under general anesthesia.and saliva gas in traumatic patients under mechanical ventilation.

Methods: This in this double-blinded clinical trial study, one hundred and sixty-two patients undergoing middle ear surgery under general anesthesia were randomly divided into three groups of 55 each: ondansetron (O), dexmedetomidine (D) and control (C). Group O received 0.1 mg/kg of ondansetron, Group D received 1 µg/kg/min of dexmedetomidine and Group C received 10 cc of normal saline 15 to 20 minutes before surgical incision. After that, the patients were examined in post-anesthesia care unit (PACU) and up to 24 hours after the operation in terms of PONV and other study variables.

Results: The severity of nausea after operation based on VAS (visual analog scale) was significantly different between Group O (2.2±0.7) and Group D (3.9± 0.7) and Group C (5.15±1.3) (P= 0.04). The incidence of vomiting in the first 24h postoperatively was 14.8% in Group O, 46.3% in Group D and 88.8% in Group C (P= 0.003).

Conclusion: Our study showed that ondansetron was better than dexmedetomidine for prevention of PONV after middle ear surgery.

Introduction

Trauma Postoperative nausea and vomiting (PONV) is one of the common causes of patients' dissatisfaction with the medical services received [1]. In previous studies, PONV was reported in 20-30% of patients, which increased to 62-80% after middle ear surgery [2-3]. PONV can increase the risk of visceral injuries and result in delayed wound healing, dehydration, prolonged hospitalization, delayed return to work, and increased risk of aspiration [4-5]. Several factors are known to increase the risk of PONV, including:

1) Patient-related factors, such as female sex, history of motion sickness and PONV, age below 50 years, delayed gastric emptying due to diabetes, hypothyroidism, pregnancy, and increased intracranial pressure [6-9].

2) Surgery-related factors, including the type of surgery (e.g., cholecystectomy, gynecological surgeries, and laparoscopy), duration of surgery, and type of anesthesia (PONV is more common in general anesthesia than regional anesthesia) [7, 9].

3) Postoperative factors, including pain, patient movement (e.g., sudden movements and transfer from the recovery room to the surgery room in patients receiving opioid compounds) [10-12], and opioid use [13-14].

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Ondansetron is a serotonin antagonist, used as an antiemetic drug. This drug exerts its effects by blocking central and peripheral 5HT3 receptors. It is widely used in procedures, such as laparoscopy, otolaryngology surgeries, thyroid surgeries, strabismus surgery, and chemotherapy [15-16]. Additionally, dexmedetomidine is a selective alpha-2 receptor agonist, which exhibits sedative, analgesic, anxiolytic, and antiemetic properties by affecting alpha-2 receptors in the central nervous system [17].

In a previous study, ondansetron reduced the incidence of nausea and vomiting from 53% to 20% following middle ear surgery [18]. Also, a meta-analysis indicated that dexmedetomidine significantly reduced PONV, although it increased the risk of complications, such as hypotension and bradycardia [19]. Considering the side effects of dexmedetomidine and the scarcity of research comparing the antiemetic effects of ondansetron and dexmedetomidine following middle ear surgery, the present study aimed to compare the effects of these two drugs in preventing nausea and vomiting after middle ear surgery.

Methods

This double-blind randomized clinical trial was performed after obtaining approval from the university's ethics committee, as well as informed consent from patients who were candidates for middle ear surgery. The inclusion criteria were (1) the American Society of Anesthesiologists (ASA) class I or II and (2) age range of 18-65 years. On the other hand, the exclusion criteria were as follows: any history of sensitivity to the medications used in this study; obesity (BMI >30 kg/m2); history of motion sickness or Parkinson's disease; and use of any antiemetic drug before surgery. Besides, any changes in the anesthesia method, as well as patient's death during surgery, were considered as the exclusion criteria.

The sample size, measured by the sample size formula, was calculated for mean comparisons at a confidence level of 95% and power of 80%, based on previous studies (10% and 33.4%). A sample size of 54 people per group was calculated for the three groups, with a total sample size of 162. The patients were randomly divided into three groups (n=54), using the random allocation software.

Preoperatively, the patients were given the necessary explanations about the visual analog scale (VAS), which is an objective tool for evaluating the severity of PONV. Additionally, the patients' age, sex, weight, and underlying diseases were recorded in a data collection form. In the operating room, the patients underwent cardiopulmonary monitoring with pulse oximetry, non-invasive blood pressure measurement, capnography, and electrocardiography. All patients underwent general anesthesia with fentanyl (2 µg/kg), lidocaine (1 mg/kg), thiopental (4-6 mg/kg), and finally, atracurium (0.15 mg/kg). Subsequently, they were intubated and subjected to mechanical ventilation with a ventilator (50% oxygen and 50% air). Anesthesia was maintained with 1% isoflurane without nitrous oxide (N2O).

During surgery, the anesthesiologist prescribed a sufficient amount of crystalloids by calculating the amount of fluid needed. Following general anesthesia and 15-20 minutes before the surgical incision, group O received 0.1 mg/kg of ondansetron (maximum dose, 4 mg), group D received dexmedetomidine at 1 µg/kg body weight per minute, and group C received 10 cc of normal saline. For the three groups, the drug volume received was 10 cc, injected within 10 minutes. The anesthesiologist who collected the data and the statistician who analyzed them were not familiar with the study groups. At the end of surgery, atropine (0.02 mg/kg) and neostigmine (0.04 mg/kg) were administered to reverse the effects of muscle relaxants. After the tracheal tube removal and stabilization of the vital signs, the patients were transferred to the recovery room.

The severity of nausea during recovery was measured using the VAS scale every 15 minutes for one hour and then, every six hours for 24 hours. Generally, VAS is a 10-cm ruler on which the respondent marks his/her health status. A VAS score of zero indicates the best status, whereas a score of 10 indicates the worst status. If the VAS score was >4, the patient received metoclopramide at a dose of 0.15 mg/kg. The frequency of vomiting was recorded up to 24 hours postoperatively. Other information, including the first time to tolerate liquid and solid food diets, length of stay in the recovery room, level of patient satisfaction, duration of extubation, and pain intensity, was also recorded.

The collected data are reported as mean±standard deviation (SD) or number and analyzed in SPSS. ANOVA and Tukey's tests were used to analyze quantitative data, and Chi-square and Fisher's exact tests were used to analyze qualitative data. The collected data were analyzed at a significance level of $P<0.05$.

Results

This study was conducted on 162 candidates for middle ear surgery. The patients were divided into three groups (n=54 per group) and received ondansetron, dexmedetomidine, and placebo (Figure 1).

The three groups showed no significant differences in terms of the demographic or general characteristics. Besides, there was no significant difference between the three groups regarding the hemodynamic parameters (Table 1).

The severity of postoperative nausea based on VAS was significantly lower in group O compared to the other two groups (P=0.04).

Postoperatively, eight subjects from group O, 25 subjects from group D, and 48 subjects from group C experienced vomiting, which was significantly different between the three groups (P=0.003) (Table 2).

Eight subjects from group O, 27 subjects from group D, and 51 subjects from group C received metoclopramide, and the difference between the three groups was statistically significant (P=0.01). The mean administered dose of metoclopramide was significantly lower in group O compared to the other two groups (P=0.02) (Table 3).

Also, based on the results, the first time to tolerate liquid and solid food diets in the first 24 hours after surgery was significantly different between the three groups (Table 4).

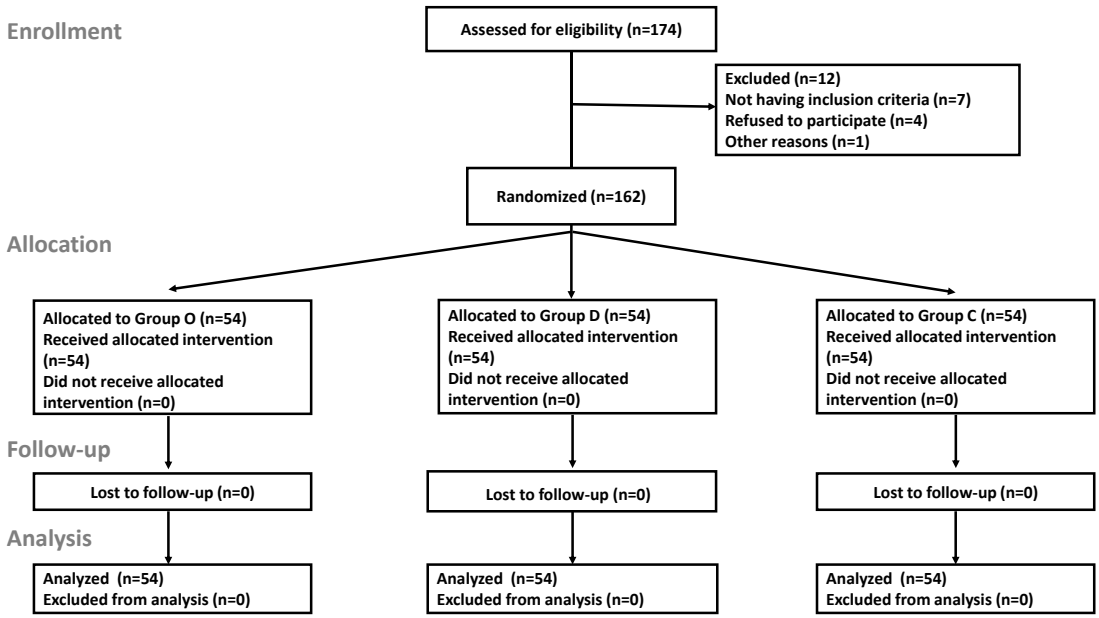

Figure 1- CONSORT flow diagram

Table 1- General and Demographic data of patients

Variable		Study groups			
		Group O (n=54)	Group D (n=54)	Group C (n=54)	P value
ASA (n, %)	I	32 (59.3)	32 (59.3)	(74) 40	0.42
	II	22 (40.7)	22 (40.7)	14(25.9)	
Sex (n, %)	Male	28 (51.9)	34(63)	)59.3 (32	0.605
	Female	26 (48.1)	20(37)	22(40.7)	
Age (years)		44.4±9.8	36.6 ±11.35	40.3 ±12.8	0.06
Weight (kg)		69.2 ± 5.4	70.4 ± 5.3	68.9 ± 6.6	0.31
Duration of anesthesia(min)		88.3 ±13.15	96.85 ±7.35	97.05 ±7.12	0.09
Duration of surgery (min)		77.14± 5.4	81.5±7.9	88.9 ± 8.17	0.17
PACU time (min)		74.3 ± 30.75	71.5 ± 20.5	69.55±14.3	0.775
Extubation time (min)		15.9± 7.0	17.0 ± 7.8	13.75 ±4.25	0.29
Patients satisfaction (cm)		7.5 ± 1.1*	5.5 ± 1.0 ↑	3.45 ± 1.4	0.02

Data are presented as number (percentage) or mean ± standard deviation. Group O received ondansetron 0.1 mg/kg, Group D received dexmedetomidine 1µg/kg/min, Group C received 10 cc of normal saline. P value < 0.05 was considered significant. * P<0.05 vs the other Groups. ↑ P<0.05 vs Group C.

Table 2- The incidence of vomiting and severity of nausea and pain up to 24 hours after operation

Variable	Study groups			
	Group O (n=54)	Group D (n=54)	Group C (n=54)	P value
VAS of nausea (cm)	2.2± 0.7*	3.9 ± 0.7 ↑	5.15 ±1.3	0.04
Incidence of vomiting (n,%)	8 (14.8)*	25(46.3) ↑	48(88.8)	0.003
VAS of pain (cm)	0.8 ±3.5	2.7± 0.8*	1.1±4.2	0.01

Data are presented as number (percentage) or mean ± standard deviation. Group O received ondansetron 0.1 mg/kg, Group D received dexmedetomidine 1µg/kg/min, Group C received 10 cc of normal saline. * P<0.05 vs the other Groups.
↑ P<0.05 vs Group C. VAS= visual analog scale

Table 3- The frequency and mean dose of requiring metoclopramide in three groups

Variable	Study Groups			
	Group O (n=54)	D Group (n=54)	Group C (n=54)	P value
Number of patients received metoclopramide (n,%)	8 (14.8)*	27(50)↑	51(94.4)	0.01
Dose of metoclopramide (mg)	10.4± 0.95*	1.12 ±14.3↑	16.7±1.2	0.02

Data are presented as number (percentage) or mean ± standard deviation. Group O received ondansetron 0.1 mg/kg, Group D received dexmedetomidine 1µg/kg/min, Group C received 10 cc of normal saline. * P<0.05 vs the other Groups. ↑ P<0.05 vs Group C.

Table 4- The fisrt time to tolerate liquid and solid diet

	Time / Groups	S1	S2	S3	S4
The first time to tolerate liquid diet	Group O (n=54) (n,%)	19(35.2)*	35(64.8)*	0*	0*
	Group D (n=54) (n,%)	10(18.5)↑	21(38.8)↑	23(42.6)↑	0↑
	Group C (n=54) (n,%)	4(7.4)	12(22.2)	14(25.9)	24(44.4)
	P value	0.03	0.05	0.02	0.001
The first time to tolerate solid diet	Group O (n=54) (n,%)	9(16.6)*	21(38.8)*	24(44.4)*	0*
	Group D (n=54) (n,%)	4(7.4) ↑	12(22.2)↑	14(25.9)↑	24(44.4)↑
	Group C (n=54) (n,%)	0	6(11.1)	8(14.8)	38(70.3)
	P value	0.04	0.04	0.03	0.01

Data are presented as number (percentage). Group O received ondansetron 0.1 mg/kg, Group D received dexmedetomidine 1µg/kg/min, Group C received 10 cc of normal saline. * P<0.05 vs the other Groups. ↑ P<0.05 vs Group C. S1= the first 6 hours after operation, S2=the second 6 hours after operation, S3= the third 6 hours after operation, S4= the fourth 6 hours after operation.

Discussion

Traumatic in the present study, ondansetron, dexmedetomidine, and placebo were compared in terms of the antiemetic effects postoperatively. A total of 162 candidates for middle ear surgery were divided into three groups of 54 people. There were no significant differences between the three groups regarding the baseline and demographic variables. No severe hemodynamic disorder was reported in any of the patients.

The severity of nausea and pain and the frequency of vomiting were calculated in the three groups. Additionally, the frequency of administration and average dose of metoclopramide, which was used as an antiemetic drug, along with the first time to tolerate liquid and solid food diets, were recorded. The present results showed that the severity of nausea based on VAS, the frequency of vomiting, the number of patients requiring metoclopramide, and the average dose of drug used were lower in group O compared to the other two groups; there was also a significant difference between group D and group C.

Ondansetron is recognized as a 5HT3 receptor antagonist [20]. It inhibits these receptors in the chemoreceptor trigger zone (CTZ), which is located in the nucleus tractus solitarii in the brain stem and is effective in the vomiting reflex [18, 20]. According to a study by Kamali et al. in Taleghani Hospital of Arak, Iran, the effects of ondansetron, dexmedetomidine, and haloperidol were examined in 114 hysterectomy candidates, and the results revealed that ondansetron was more effective in relieving PONV and also reducing the need for antiemetic drugs after surgery compared to the other two medications [17]. Moreover, in a study by P. Scuderi, ondansetron doses <8 mg were more effective than the placebo in reducing PONV. They were also found to be safe, without causing any complications or hemodynamic changes [21].

Moreover, dexmedetomidine is a selective alpha 2-adrenoceptor agonist, with sedative, analgesic, and antisympathetic effects [22]. In a meta-analysis by Shenhui Jin, continuous infusion of dexmedetomidine reduced PONV and did not cause any complications, such as hypotension or bradycardia after general anesthesia [19]. Additionally, in a study by Islam M. Massad, it was found that the addition of dexmedetomidine to other anesthetic agents reduced the incidence of nausea and vomiting following laparoscopic gynecological surgeries [23]. Overall, the results of the mentioned studies are consistent with the findings of the present study.

Limitations

Considering the limitations of this study, such as the small sample size, multiple exclusion criteria, and age restriction, further relevant research is highly recommended.

Conclusion

The pain intensity is an important factor in increasing the incidence of PONV. Based on the current findings, the intensity of pain was significantly lower in group D compared to group O; however, the incidence of PONV was higher in group D compared to group O. Patient satisfaction after surgery was also higher in group O as

compared to the other two groups. Based on the present results, ondansetron was significantly more effective than dexmedetomidine and placebo in reducing PONV, decreasing the need for metoclopramide, and increasing tolerance for liquid and solid food diets. According to the abovementioned findings, since ondansetron exerts no effects on the hemodynamic status, it may be considered a more effective option than dexmedetomidine in reducing nausea and vomiting following middle ear surgery.

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