Ondansetron administration before transoesophageal echocardiography reduces the need for sedation and improves patient comfort during the procedure

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Aims

Transoesophageal echocardiography (TEE) is an uncomfortable procedure for the majority of patients. In the current double-blind randomized prospective study, we sought to assess whether ondansetron would improve patient comfort, reduce the need for sedation, and increase tolerance during TEE, and we compared ondansetron, metoclopramide, and placebo.

Methods and results

One hundred and fifty-six patients who underwent TEE were randomized into three groups receiving ondansetron HCl, metoclopramide, or placebo. Data concerning additional doses of midazolam, procedural time, recovery time in the outpatient ward, blood pressure values, percutaneous arterial oxygen saturation values, side effects of the medications used, and patient discomfort via a visual analogue scale (VAS) were collected and analysed. The ondansetron group received less additional midazolam than the metoclopramide and placebo groups (ondansetron group: 0.6 ± 0.7 mg; metoclopramide group: 1.9 ± 0.9 mg; and placebo group: 2.1 ± 0.8 mg; P < 0.001). VAS was significantly lower in the ondansetron group than in the metoclopramide and placebo groups (4.0 ± 1.6, 6.1 ± 1.8, and 6.6 ± 1.6, respectively; P < 0.001). Recovery time in the outpatient ward was shorter in the ondansetron group than in the metoclopramide and placebo groups (22.5 ± 4.8, 30.9 ± 6.6, and 30.4 ± 5.0 min, respectively; P < 0.001). No adverse reaction to ondansetron was observed, whereas one patient developed mild spontaneously resolving dystonia due to metoclopramide.

Conclusion

Ondansetron administration reduces the need for sedation during TEE and improves patient comfort.

Keywords

Transoesophageal echocardiography • Premedication • Ondansetron • Antiemetics

Introduction

Transoesophageal echocardiography (TEE) has become one of the major cornerstones of cardiovascular imaging since its first introduction in the late 1970s.1 TEE provides an unrestricted view of the heart via the oesophagus and it allows the employment of high-frequency transducers, which results in improved image quality. In addition, it has the ability to visualize posterior heart structures, which are difficult to detect by transthoracic echocardiography (TTE).

Despite those benefits, TEE is a semi-invasive and uncomfortable procedure for the majority of patients.2 Experiences in gastroenterology and upper digestive system endoscopy facilitated the application of topical anaesthesia in the oropharyngeal cavity.3 In addition, short-acting sedatives like midazolam were applied to improve patient comfort.4 However, side effects due to midazolam can occur in a significant proportion of patients undergoing TEE.5,6 Ondansetron, a 5-HT3 receptor antagonist, has been successfully used to control chemotherapy-induced nausea and vomiting.7 The purpose of our present study was to compare the efficacies of
ondansetron, metoclopramide, and placebo and to investigate whether ondansetron administration before TEE would improve patient comfort, reduce the need for sedation, and increase patient tolerance.

**Methods**

**Study design and patients**

This is a prospective, single-centre, and double-blind randomized study carried out between May 2005 and December 2007. Initially, 201 patients undergoing regular TEE examination were consecutively enrolled (Figure 1). Exclusion criteria were previous TEE or upper digestive system endoscopic examinations (former interventions could cause preconception in patients towards the procedure) \( n = 23 \), emergency examinations \( n = 5 \), pregnancy, and mechanical ventilation. Seventeen patients did not agree to participate in the study. Subsequently, 156 patients were included in the study groups. The study was approved by the local Ethics Committee and written informed consent was obtained from all patients. Randomization was done using a computer-generated random number table and patients were separated into three groups: ondansetron group \( n = 52 \) and metoclopramide group \( n = 52 \) received 4 mg ondansetron and 10 mg metoclopramide i.v., respectively, 5–10 min before the procedure. Placebo group \( n = 52 \) received saline intravenously as placebo. Study medications containing 10 mL of solution in identical syringes were prepared by a single nurse to ensure blinding.

**Transoesophageal echocardiography**

TEE examinations were performed by two skilled operators who were blinded to the antiemetic agent used. All patients were anaesthetized topically in the oropharynx with 10% aerosol solution of lidocaine until the gag reflex was suppressed, the appropriate antiemetic or placebo was administered intravenously, and they received 2 mg of midazolam before the procedure. Liberal usage of additional doses of midazolam by the operators was allowed (considering the patient’s anxiety status and operator’s comfort), after the introduction of the TEE probe into the oesophagus. Sedation level of the patients was assessed by using the Ramsay sedation score, which ranges from 1 to 6. Score 1 stands for inadequate sedation, scores 2–4 for adequate sedation, and scores 5 and 6 for excessive sedation. It monitors patients’ responses to commands and to different types of auditory or noxious stimuli. Details of this scoring system are described in detail elsewhere.

After the procedure, all the patients were observed for recovery in an outpatient ward until their ‘Postanesthetic Recovery Score of Aldrete and Kroulik’ was 8 or above, which was checked every 5 min by a nurse. This is a widely employed scoring system applied for recovery after anaesthesia.

During the whole procedure and afterwards until discharge, percutaneous arterial oxygen saturation level, pulse rate, blood pressure (Vital care 506DXN), and electrocardiogram (via the echocardiography machine during TEE and via a defibrillator in the ward) were monitored and recorded.

All TEE examinations were carried out on a ‘Vivid 7’ echocardiography machine (General Electric Vingmed Ultrasound, Horten, Norway) by the use of a ‘6T’ multipane adult TEE probe (General Electric Vingmed Ultrasound).

Before discharge, all the patients were requested to grade the intensity of their discomfort during the procedure by visual analogue scale (VAS) (scaling from 0 to 10; 0, no discomfort; 10, most discomfort).

Data concerning additional doses of midazolam, procedural time (defined as the time between introduction and withdrawal of the
probe into the oesophagus), recovery time in the outpatient ward, blood pressure values, percutaneous arterial oxygen saturation levels, and side effects of the medications used were collected and recorded by an experienced nurse who was not involved in the study.

**Statistical analysis**

Statistical analysis was performed with the SPSS 11.0 statistical package (SPSS, Chicago, IL, USA). Categorical variables were compared with the χ² test, followed by evaluation with the pairwise test for comparison of two proportions, corrected according to the Bonferroni method. The Kruskal–Wallis test was employed to assess the differences in continuous variables among groups, followed by evaluation with the Mann–Whitney U-test for multiple comparisons. Resulting P-values were corrected according to the Bonferroni method.

**Results**

**Patient characteristics and haemodynamic data**

TEE was performed for source of embolism in 37 (23%), atrial septal defect (ASD) and patent foramen ovale assessment in 33 (21%), congenital heart defect except ASD in 27 (17%), artificial heart valve assessment in 27 (17%), native valvular heart disease in 21 (13%), infective endocarditis in 8 (5%), and for miscellaneous reasons in 12 (7%). Demographic and haemodynamic variables are shown in Table 1. Although there were no significant differences between the groups, we observed a statistically significant fall within each group regarding arterial systolic and diastolic blood pressure and arterial oxygen saturation levels that were measured before and during the procedure.

**Transoesophageal echocardiography and recovery**

There were no unsuccessful intubation attempts. The mean (SD) midazolam dose was 2.6 (0.7) mg in the ondansetron group, 3.9 (0.9) mg in the metoclopramide group, and 4.1 (0.8) mg in the placebo group. Twenty-five patients required additional midazolam dose in the ondansetron group (18 patients 1 mg and 7 patients 2 mg), 48 patients in the metoclopramide group (12 patients 1 mg, 20 patients 2 mg, and 16 patients 3 mg), and 51 patients in the placebo group (11 patients 1 mg, 21 patients 2 mg, and 19 patients 3 mg). Total procedure time was longer in the ondansetron group than in the metoclopramide and placebo groups (mean (SD): 23 (5.2), 18.5 (2.7), and 18 (3.1) min, respectively) (P < 0.001). Recovery time was shorter and VAS scores were better in the ondansetron group compared with the metoclopramide and placebo groups [recovery times mean (SD) 22.5 (4.8), 30.9 (6.6), and 30.4 (5.0) min, respectively; and VAS: 4 (1.6), 6.1 (1.8), and 6.6 (1.6), respectively]. No adverse reaction to ondansetron was observed, whereas one patient developed mild spontaneously resolving dystonia due to metoclopramide.

**Discussion**

Improved resolution combined with the capability to visualize cardiac structures suboptimally visualized by TTE has widened the use of TEE.11–13 However, TEE is a semi-invasive procedure with some risks and patient discomfort as well, which occasionally does not allow a full detailed study.14,15 Experiences in gastroenterology and upper digestive system endoscopy facilitated the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic, haemodynamic, and procedural variables of patient groups</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Ondansetron</td>
</tr>
<tr>
<td>Age</td>
<td>44.4 ± 12</td>
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<tr>
<td>Male/female (n)</td>
<td>27/25</td>
</tr>
<tr>
<td>Weight</td>
<td>70.4 ± 9.9</td>
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<tr>
<td>SaO₂</td>
<td></td>
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<tr>
<td>Before procedure</td>
<td>96 ± 2.4</td>
</tr>
<tr>
<td>During procedure</td>
<td>94.2 ± 2.3</td>
</tr>
<tr>
<td>After procedure</td>
<td>95.1 ± 2.4</td>
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<tr>
<td>Diastolic blood pressure</td>
<td></td>
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<tr>
<td>Before procedure</td>
<td>80.6 ± 15.1</td>
</tr>
<tr>
<td>During procedure</td>
<td>72.9 ± 13.7</td>
</tr>
<tr>
<td>After procedure</td>
<td>77 ± 14.5</td>
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<tr>
<td>Systolic blood pressure</td>
<td></td>
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<tr>
<td>Before procedure</td>
<td>132.4 ± 17.1</td>
</tr>
<tr>
<td>During procedure</td>
<td>126.6 ± 17.4</td>
</tr>
<tr>
<td>After procedure</td>
<td>126.8 ± 16.3</td>
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<tr>
<td>Total midazolam dose (mg)</td>
<td>2.6</td>
</tr>
<tr>
<td>Number of patients requiring additional dose of midazolam</td>
<td>25</td>
</tr>
<tr>
<td>Total procedure time (min)</td>
<td>23</td>
</tr>
<tr>
<td>Recovery time (min)</td>
<td>22.5</td>
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<tr>
<td>VAS scores</td>
<td>4</td>
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</table>
application of topical anaesthesia in the oropharyngeal cavity. However, topical pharyngeal anaesthesia does not enhance patient tolerance; it only technically eases the procedure for the operator.3 To improve patient comfort, midazolam is widely given for conscious sedation before TEE procedures.2,4 However, the prevalence of side effects with midazolam has been reported in up to 17%.2 Premedication with midazolam before TEE causes more prominent tachycardia, a decrease in systolic blood pressure, and depression of oxygen saturation compared with the TEE probe insertion alone.5 Other common side effects vary from severe aggression to euphoria, depression, and hiccups.6

Such drawbacks of current medications have led to the research for alternative drugs to minimize nausea and vomiting during TEE examinations. Among them, serotonin antagonists such as ondansetron have gained increasing popularity owing to their reported effectiveness and low side effects and have become a gold standard in antiemetic therapy in cancer and surgery patients.16,17 The present study suggests that patients who received ondansetron before the procedure needed less doses of midazolam. High doses of midazolam sedation can cause tachycardia, decrease in blood pressure, and depression of SaO2.5 Ondansetron administration can be useful in haemodynamically unstable, advanced age, and respiratory depressed patients by reducing midazolam doses. Ondansetron reduced recovery times presumably as a result of reduced need for midazolam. In addition, ondansetron improved patient comfort during the study. Although procedure time was longer in the ondansetron group, VAS score was better when compared with the placebo and metoclopramide groups.

In summary, ondansetron administration before the TEE procedure improves patient comfort and reduces the need for sedation. Decreasing the midazolam dose can be important in patients with haemodynamic instability and depressed respiratory functions, which are commonly seen among TEE patients during daily practice.

Conflict of interest: none declared.

References