Intravenous Ondansetron as Antiemetic Prophylaxis for Postoperative Nausea and Vomiting after Shoulder Arthroscopy

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Background: Nausea and vomiting are common chief postoperative complaints. The clinical literature indicates that postoperative nausea and vomiting (PONV) is common after orthopedic surgery. This study examines the clinical therapeutic efficacy of Ondansetron injected intravenously before the end of shoulder arthroscopy as antiemetic prophylaxis to help reduce the incidence of PONV.

Methods: Participants were identified through retrospective chart review and patients undergoing shoulder arthroscopy performed by the same orthopedic surgeon at the same hospital from 2005 to 2009 were analyzed. Subjects were classified into two groups based on whether Ondansetron was given. Differences in the incidence of PONV among the two groups were compared. Basic patient information, anesthesia records, and surgical records were obtained, as well as records on PONV, postoperative pain intensity, and postoperative analgesic injections within 24 hours after surgery.

Results: The study involved 90 patients. The Group A contained 34 patients who did not receive Ondansetron, and the Group B contained 56 patients who were given Ondansetron. Analytical results for the postoperative 24 hour period showed a significant difference in the incidence of vomiting between the two groups, with a lower incidence (p < 0.05) for the Group B. However there was no significant difference in the incidence of nausea between the two groups in the same postoperative 24 hour period, although there was a trend of a lower incidence in the Group B (p = 0.17). The overall incidence of PONV during the 24-hour period was lower in the Group B (14%) than the Group A (32%), and the Group B demonstrated lower pain intensity and lower analgesic injection needs.

Conclusion: Routine intravenous injection of Ondansetron 30 minutes before completion of shoulder arthroscopy can reduce the incidence of vomiting and overall PONV in patients. Additionally, the patients using Ondansetron demonstrated lower pain intensity and lower analgesic injection needs than the control group.

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Key words: postoperative nausea and vomiting (PONV), shoulder arthroscopy, Ondansetron, prophylactic antiemetics
Postoperative nausea and vomiting (PONV) is a common, often unpleasant and exhausting complication, which frequently results in a longer observation period in the recovery room, higher likelihood of hospitalization and increased health care costs. The incidence of PONV under general anesthesia is 20-30% on average.\(^1\-\(^3\)\) Because nausea and vomiting can be extremely distressing, it is a major concern of patients.\(^4\)

The incidence of PONV varies with different surgical techniques and procedures.\(^5\) Surgeries in the fields of laryngology, obstetrics and gynecology, ophthalmology, and orthopedics have higher incidences of PONV than surgeries in other fields.\(^6\)

PONV is one of the most common complaints of surgical patients. Although PONV involves little immediate danger, its high rate of occurrence and difficult prophylaxis make it an important post-operative issue.\(^7\)-\(^8\) According to the clinical literature, orthopedic surgery has a PONV incidence rate between 25% and 34%.\(^9\) There is a higher incidence rate of PONV with general anesthesia than with regional anesthesia.\(^10\)

Many different drugs have been reported for PONV prophylaxis and treatment. Although there has been increased interest in the use of serotonin 5-HT3 receptor antagonists for the treatment of PONV in recent years, solid study results are scarce and inconclusive.

Recently, studies report that Ondansetron, a 5-HT3 receptor antagonist, is very effective in prophylaxis for PONV when taken orally or intravenously.\(^11\) Studies have shown that intravenous Ondansetron 4 mg was a better treatment than intravenous metoclopramide 10 mg, but higher doses of Ondansetron (16 mg) were no more effective than lower doses.\(^12\)

Since 2008 the Orthopedic Department of Chang Gung Memorial Hospital has included Ondansetron in an approved list of routine postoperative drugs to reduce the incidence of PONV. Our hospital has accumulated sufficient clinical data from cases of patients who received and did not receive Ondansetron to do group comparison studies and analyze the clinical results. However, this information has not been systematically investigated.

For our study, we targeted patients with a high incidence of PONV who underwent shoulder arthroscopy (under general anesthesia) and compared the difference in the incidence of PONV between those who did not receive (Group A) and those who received Ondansetron (Group B) during postoperative pre-recovery care.

A substantial number of reports in the literature indicate that the incidence of PONV is related to factors such as patient age, gender, smoking status, type and duration of anesthesia, and type of surgery involved.\(^13\) A higher incidence of PONV has also been reported in younger patients, with the incidence rate decreasing by 13% for every 10-year increase in age.\(^14\) Women are twice as likely to exhibit PONV as their male counterparts.\(^15\) The use of nasogastric tubes in orthopedic postoperative patients does not seem to affect the incidence of PONV, whether or not immediate refeeding has taken place.\(^16\)-\(^17\)

In this study, we attempted to control for the risk factors for PONV and to exclude any PONV-inducing factors caused by the surgery itself. We selected subjects from patients at the same hospital who were operated on by the same orthopedic surgeon from 2005 to 2009. We performed retrospective and statistical analyses on those patient records that met the inclusion requirements, and compared the incidence of PONV between the experimental group receiving Ondansetron before the end of surgery and the control group.

**METHODS**

**Subjects**

Using retrospective and purposive sampling methods, we collected postoperative statistical data from patients who had undergone orthopedic shoulder arthroscopy with the same orthopedic surgeon from the Taoyuan branch of Chang Gung Memorial Hospital. The patients’ postoperative medical records were accessed to conduct this study.

Upon receiving approval for the study from the Institutional Review Board/Ethics Committee (IRB/EC), we included 90 patients from 18 to 79 years old from the Taoyuan branch of Chang Gung Memorial Hospital. There were 28 men and 62 women.

We excluded patients who were concomitantly undergoing bilateral shoulder joint surgery or other joint surgeries.
Study design

We recorded age, gender, weight, height, duration of anesthesia, duration of stay in the postanesthesia care unit (PACU), quantity of fluid transfused intraoperatively, nausea and vomiting during the 24-hour period following surgery, pain intensity, and postoperative analgesic injections.

From 2008, Chang Gung Memorial Hospital guidelines included prophylactic injections of Ondansetron as a standardized procedure following orthopedic surgery. Subjects in this study were divided into 2 groups. Group A contained patients who had surgery from 2005 to 2007, who did not receive an Ondansetron injection before the end of shoulder arthroscopy. Group B contained patients who had surgery from 2008 to 2009, who received an Ondansetron 4 mg injection immediately before the end of shoulder arthroscopy. All patients had surgery under general anesthesia, with standard anesthesia procedures and care. Ondansetron was given to the experimental group intravenously by an anesthesiologist approximately 30 minutes before the end of the operation.

After surgery, patients were observed for a 24-hour period, and the incidence of nausea, incidence of vomiting, pain intensity, and analgesic injection requirements were assessed.

Nausea was defined as a queasy, unpleasant sensation in the stomach leading to the urge to vomit. Vomiting was defined as the ejection of stomach contents through the mouth. The level of pain was assessed with a 10 point-visual analog scale (VAS, 0 = no pain to 10 = most severe pain).

If the patient complained of severe pain and requested analgesics, injections of meperidine, nalbuphine, or ketorolac were administered. Single or combined usage of any of the 3 analgesics mentioned above was regarded as requiring pain-relief injections. If none were used, the patient was considered to have received no pain-relieving injections.

Statistical analysis

All data were analyzed using SPSS version 16.0. Statistical tests used included the t-test and the chi-square test. If more than 20% of the cells had expected values of less than 5 in the chi-square test, we performed Fisher’s exact test of the p-value as the basis for discrimination. When the p-value was less than 0.05, the result was considered statistically significant. Figures calculated are expressed as percentages and as mean ± standard deviation. Finally, logistic regression analysis was used for correction.

RESULTS

A total of 90 patients were involved in this study, 34 in the control group which did not use Ondansetron (Group A) and 56 in the experimental group which received Ondansetron (Group B). Table 1 details basic patient information, including age, gender, weight and height. Analysis revealed no significant difference (p > 0.05) in the distribution of age, gender, height and weight between the experimental and control groups, indicating valid comparisons can be established.

Table 1 shows there was no significant difference in smoking rates between the two groups, p > 0.05.

Table 1 also indicates the American Society of Anesthesiologists’ (ASA) physical status classification for the experimental and control groups. Although p > 0.05, 20% of the cells had expected values less than 5, so the chi-square analysis of the p value could not be trusted, and we performed corrections with logistic regression analysis.

Further analysis of the patients’ surgical data is also shown in Table 1. The experimental group had significantly shorter durations of anesthesia and surgery, a significantly shorter stay in the PACU, and significantly less fluid transfused than the control group (p < 0.05).

As shown in Table 2, the control group (Group A) had a significantly higher incidence of PONV than the experimental group (Group B), p < 0.05.

We found that the experimental group had a significantly lower incidence of vomiting (p < 0.05). The difference between groups was not statistically significant for nausea, but the experimental group showed a decreasing trend (p = 0.17).

Since some patients in the control group were missing records for 24 hour postoperative VAS pain assessment, only 18 patients were included. Nevertheless, the Ondansetron experimental group had significantly lower VAS scores than the control group (p < 0.05).

Analgesic injections during the 24 hour postoperative period in the experimental and control group are listed in Table 3. Although there was no signifi-
significant difference in the incidence of analgesic injections used, the $p$-value was borderline ($p = 0.0597$). However, the difference was found to be significant with Fisher’s exact test ($p = 0.0308$), which allows us to conclude that the experimental group required fewer injections for pain relief.

**DISCUSSION**

PONV is one of the most common chief complaints in surgical patients. Although PONV involves no immediate danger, its high incidence and difficulty in prophylaxis make it an important postoperative management issue.

Many different prophylactic and therapeutic drugs have been reported for PONV, such as droperidol, suprascapular nerve blocks, and dexamethasone. Although there has been increasing interest in serotonin 5-HT3 receptor antagonists in the treatment of PONV in recent years, solid study results are scarce and have often been inconclusive.

In recent years many studies have pointed to the 5 main neurotransmitter receptors that function in the vomiting center of the brainstem. They include the serotonin-5-HT3 receptor, substance P-NK1 receptor, acetylcholine- muscarinic receptor, cholinergic receptor, dopamine-D2 receptor and histamine-H1 receptor. Serotonin-5-HT3 receptor antagonists have thus been targeted for drug development in hopes of reducing the incidence of nausea and vomiting.

5-HT3 receptor antagonists given intravenously 30 minutes before chemotherapy were originally used to treat chemotherapy-induced nausea and vomiting. Clinicians are also starting to use drugs such as Ondansetron, which is a serotonin 5-HT3 receptor antagonist.
antagonists, for the treatment of postoperative and radiotherapy-induced nausea and vomiting. The effect of the drug comes from its influence on the peripheral and central nervous system. It acts by blocking serotonin receptors in the chemoreceptor trigger zone, thereby suppressing vagus nerve stimulation of the vomiting center in the medulla oblongata. However, this drug is not very effective against motion sickness-induced vomiting, and it has no influence on dopamine or muscarinic receptors.

Ondansetron is a well-tolerated drug, with reports commonly indicating its only side effects are constipation, dizziness or headaches.

No significant drug interactions have been reported with this drug. It is broken down by the hepatic cytochrome P450 system and it has little effect on the metabolism of other drugs broken down by this system.\(^{(25)}\)

The results of the study show that routine intravenous injection of Ondansetron 30 minutes before the completion of shoulder arthroscopy can significantly reduce the incidence of vomiting and analgesic injection requirements in postoperative orthopedic patients. In this study, we found that the incidence of PONV in the control group was 32%, and in the experimental group was 14%.

Although the cause of PONV is unknown, it is likely influenced by a variety of factors. Therefore, we controlled for surgically related factors in our study to accurately evaluate the effect of Ondansetron on PONV high risk groups. In this study, all patients were selected from the same hospital and had their shoulder arthroscopy performed by the same experienced orthopedic surgeon, with the cohort groups consisting of patients of similar gender, heights, weights and age. We can conclude that the incidence of PONV is influenced by Ondansetron use.

The experimental group had shorter anesthesia and operation times, and a shorter stay in the PACU, as well as less interoperative fluid transfused.

We speculated that the difference in the operative time might have been related to the different years in which the surgeries were performed. Surgeries in the experimental group were performed from 2008 to 2009, while the control group had operations before 2007. Although the same surgeon performed all procedures, advances in surgical equipment, technique and support may have reduced the time required for an operation (reduced by 19 minutes on average).

Frequently reported risk factors for PONV include young age, female gender, nonsmoking, general anesthesia, long duration of anesthesia, and surgeries in the fields of laryngology, obstetrics and gynecology, ophthalmology, and orthopedics. The experimental and control groups were similar in respect to gender, age and smoking status. They also had the same type of surgery and anesthesia, and the same surgeon. Thus the remaining factor, anesthesia time, was the extraneous variable that mostly likely influenced our results. Prolonged anesthesia may result in an increased incidence of PONV.\(^{(26)}\) In order to make sure that the difference in the incidence of PONV was due to Ondansetron, and not anesthesia time, we performed corrections with logistic regression analysis.

The results, as shown in Table 4, revealed that those with no Ondansetron had significantly higher odds ratios for vomiting and PONV than those who received Ondansetron. Those with no Ondansetron also had higher odds ratios for nausea, although the difference was not profound. With correction for the risk factors mentioned in the literature for nausea, vomiting and PONV, there was a higher odds ratio for vomiting in those with no Ondansetron, with a significant p-value. The odds ratio for PONV also increased, while the p-value remained borderline significant.

Therefore, we can conclude that overall, Ondansetron was effective in reducing the incidence of PONV, but it was more effective against vomiting than nausea. Because the inhibition effect on nausea was not significant, the reduction in the incidence of PONV was not due to nausea.

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Nausea</td>
<td>2.04 (0.48-8.60)</td>
<td>0.33</td>
</tr>
<tr>
<td>Vomiting</td>
<td>5.34 (1.55-18.37)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>PONV</td>
<td>2.96 (0.96-9.12)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

**Abbreviations:** OR: odds ratio; CI: confidence interval; PONV: postoperative nausea and vomiting; *: Corrected for gender, age, length of anesthesia; ASA status, and smoking.

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PONV overall was diluted, so that the $p$-value was only borderline.

**Limitations of the study**

Ondansetron may reduce overall postoperative discomfort, and even reduce VAS indicators. However, whether the differences in pain scores for the two groups occurred because of Ondansetron use, or were also connected to the duration of surgery and anesthesia cannot be readily determined from our study, especially given that the VAS data in the control group was incomplete.

This retrospective nature of this study limited the data collection, as did the lack of some VAS data. The effective sample could not be increased for a more accurate comparison, as we would have needed to include patients who had surgery before 2005 in the control group. This in turn would have meant even greater differences between groups in surgical variables such as the year of the operation, operating time and duration of anesthesia, resulting in more statistical variation and reducing the comparability of other indicators. Increasing the number in the experimental group could only be done by extending the time period later than 2009, further increasing the time difference with the same problems in comparing surgical variables.

Given these limitations, the adequacy of the sample size for the control group conflicted with comparability with the experimental group. So in consideration of the missing data, we decided to choose years as close as possible for the control and experimental groups for this study’s statistical analysis.

More precise research, or a future prospective study, could permit robust VAS data collection, to reduce the problem of missing data, and reduce variability in surgical data between the control and experimental groups, ensuring better comparison of the relative incidence of PONV.

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骨科肩關節鏡手術結束前常規靜脈注射奧曲他碇 (Ondansetron)
對於降低術後噁心嘔吐發生率的效果研究

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背景：噁心嘔吐為手術後常見主訴，文獻指出骨科手術是易發生術後噁心嘔吐之手術種類。本研究探討接受骨科肩關節鏡之病患，於手術結束前常規接受奧曲他碇 (Ondansetron) 靜脈注射，是否能夠降低術後噁心嘔吐的發生率。

方法：選定 2005-2009 年於長庚醫院桃園分院接受同一骨科專科醫師施行肩關節鏡手術的患者為樣本，進行病歷回溯與統計，根據奧曲他碇 (Ondansetron) 的使用有無，分成有使用與未使用的兩組，收集個案基本資料、麻醉資料、手術資料，及術後 24 小時內噁心嘔吐情形，術後 24 小時內疼痛指數、術後 24 小時內止痛藥使用情形等資料，比較有使用奧曲他碇 (Ondansetron) 及未使用奧曲他碇 (Ondansetron) 等兩組，在術後噁心嘔吐發生率上的差異。

結果：本研究共統計 90 位病患，其中未使用奧曲他碇 (Ondansetron) 的對照組 34 位，有使用奧曲他碇 (Ondansetron) 的實驗組 56 位。分析結果，術後 24 小時內，對照組與實驗組其噁心的發生率有顯著的差異，且實驗組較低 (p < 0.05)；術後 24 小時內，對照組與實驗組其噁心的發生率並沒有顯著的差異，但實驗組有較低的趨勢 (p = 0.17)；至於術後 24 小時內，整體嘔吐 (PONV) 的發生率，實驗組 (14%)，比起對照組 (32%) 較低，且達到統計上的顯著 (p < 0.05)。另外，有服用奧曲他碇 (Ondansetron) 的實驗組，其術後 24 小時內的疼痛指數較低；且術後 24 小時內止痛藥的需求較少。

結論：接受骨科肩關節鏡手術的患者，於手術結束前三十分鐘常規靜脈注射藥品奧曲他碇 (Ondansetron)，可顯著降低手術後嘔吐的發生率，對於整體術後噁心嘔吐的發生率，也有減少的趨勢；此外，統計發現，手術結束前三十分鐘常規靜脈注射奧曲他碇 (Ondansetron) 的組別，較未注射奧曲他碇 (Ondansetron) 的組別，手術後二十四小時內的疼痛指數較低，且術後 24 小時內止痛藥的需求較少。

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關鍵詞：術後噁心嘔吐，肩關節鏡，奧曲他碇，預防噁心嘔吐