Cost-efficacy of Rofecoxib versus Acetaminophen for Preventing Pain after Ambulatory Surgery

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Background: Nonsteroidal antiinflammatory drugs are commonly administered as part of a multimodal regimen for pain management in the ambulatory setting. This randomized, double-blinded, placebo-controlled study was designed to compare the analgesic effect of oral rofecoxib, a cyclooxygenase-2 inhibitor, and acetaminophen when administered alone or in combination prior to outpatient otolaryngologic surgery.

Methods: A total of 143 healthy outpatients undergoing elective otolaryngologic surgery were assigned to one of four study groups: group 1 = control (500 mg vitamin C); group 2 = 2 g acetaminophen; group 3 = 50 mg rofecoxib; or group 4 = 2 g acetaminophen and 50 mg rofecoxib. The first oral dose of the study medication was taken 15–45 min before surgery, and a second dose of the same medication was administered on the morning after surgery. Recovery times, side effects, and the need for rescue analgesics were recorded. Follow-up evaluations were performed at 24 and 48 h after surgery to assess postdischarge pain, analgesic requirements, nausea, and patient satisfaction with their postoperative pain management and quality of recovery. Peak pain scores and the need for rescue analgesic medication were used as the endpoints for estimating efficacy of the study drugs, while cost to achieve complete satisfaction with analgesia was used in the cost-effectiveness analysis.

Results: Premedication with rofecoxib (50 mg) was significantly more effective than either placebo or acetaminophen (2 g) in reducing the peak postoperative pain, the need for analgesic medication, and improving the quality of recovery and patient satisfaction. Moreover, the addition of acetaminophen failed to improve its analgesic efficacy. An expenditure for rofecoxib of $16.76 (95% confidence interval, $7.89 to 21.03) and $30.24 (95% confidence interval, $5.25 to 54.20) would be required to achieve complete satisfaction with analgesia at both the cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) sites, and their use has been associated with increased operative and postoperative bleeding.

Conclusions: Rofecoxib, 50 mg administered orally, decreased postoperative pain and the need for analgesic rescue medication after otolaryngologic surgery. The addition of 2 g oral acetaminophen failed to improve its analgesic efficacy. NONSTERoidal antiinflammatory drugs (NSAIDs) are commonly administered as part of a multimodal analgesic regimen for preventing pain after ambulatory surgery. Use of NSAIDs has been reported to be effective in reducing postoperative pain and opioid analgesic requirements, as well as in facilitating an earlier discharge. However, the nonselective NSAIDs block prostaglandin synthesis at both the cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) sites, and their use has been associated with increased operative and postoperative bleeding as a result of their well-known effect on platelet function.

The COX-2–specific drugs have recently been introduced as alternatives to the nonselective NSAIDs in the management of acute pain, with claims that they produce comparable analgesia without the COX-1 side effects of platelet and gastrointestinal dysfunction. While preliminary studies with celecoxib and rofecoxib have shown these drugs to be effective analgesics after dental and orthopedic surgery, a study in patients undergoing radical prostatectomy led to questions regarding the analgesic efficacy of rofecoxib in the perioperative period. Furthermore, the comparative analgesic efficacy of NSAIDs and acetaminophen is controversial.

This randomized, double-blinded, placebo-controlled study was designed to compare the analgesic efficacy of rofecoxib and acetaminophen when administered alone or in combination prior to outpatient surgery. The hypothesis being tested was that oral premedication with rofecoxib alone or in combination with acetaminophen would reduce postoperative pain and the need for opioid-containing analgesics after ENT surgery, and consequently improve patient satisfaction with their recovery.

Materials and Methods

After we obtained institutional review board approval at the University of Texas Southwestern Medical Center and written, informed consent, 143 healthy outpatients (aged 18–75 yr) undergoing ENT procedures were studied according to a randomized, double-blind, placebo-controlled protocol. Patients were excluded if they had received any analgesic medication within 12 h prior to the operation, were pregnant or breast-feeding, or had a history of drug abuse, clinically significant neurologic, cardiovascular, renal, hepatic, or gastrointestinal disease.
In the preoperative holding area, patients completed baseline verbal rating scales (VRS) for pain and nausea, with 0 = none to 10 = worst imaginable. The patients were randomly assigned to one of four treatment groups: group 1 = placebo (500 mg vitamin C); group 2 = 2 g acetaminophen; group 3 = 50 mg rofecoxib; and group 4 = 2 g acetaminophen and 50 mg rofecoxib. The drugs were prepared by the operating room pharmacist according to a computer-generated random number schedule and were administered by a day-surgery nurse with 10–20 ml of water 15–45 min prior to entering the operating room. The patients, observers, and those involved in direct patient care were blinded to the contents of the oral premedication.

Patients received 20 µg/kg intravenous midazolam in the holding area. On arrival in the operating room, anesthesia was induced with 2 mg/kg intravenous propofol and 0.5 µg/kg intravenous remifentanil, and tracheal intubation was facilitated with 0.6 mg/kg intravenous rocuronium. Anesthesia was maintained with desflurane, 4% end-tidal concentration, in combination with air (0.5 l/min) and oxygen (0.5 l/min). An infusion of remifentanil was administered at an initial rate of 0.1 µg·kg⁻¹·min⁻¹ and subsequently varied from 0.0625 to 0.125 µg·kg⁻¹·min⁻¹ to maintain heart rate and blood pressure values within 15% of the preoperative baseline values. Droperidol, 0.625–1.25 mg administered intravenously, and 4–8 mg intravenous dexamethasone were administered for antiemetic prophylaxis. At the end of the surgical procedure, residual neuromuscular block was antagonized with 50–80 mg intravenous edrophonium and 0.5–0.8 mg intravenous atropine, and the maintenance anesthetic drugs were discontinued.

A blinded observer (T.I.) determined recovery times to awakening (e.g., opening eyes in response to a verbal command) and orientation to person, date, and place at 1-min intervals following discontinuation of the maintenance anesthetics. Patients rated their pain and nausea on the 11-point VRS at 30-min intervals and immediately prior to receiving any rescue analgesic medication in the postanesthesia care unit (PACU). Patients with VRS pain scores of 6 or higher were considered to have severe pain. Patients complaining of moderate-to-severe pain (VRS > 3) were treated with 25-µg intravenous bolus doses of fentanyl until the patient no longer complained of pain. In keeping with our standard PACU nursing practice, the nurses were not required to titrate fentanyl to achieve a specific VRS pain score. Patients with pain scores of 2 to 3 in the phase II recovery unit received a combination of oral hydrocodone (5 mg) and acetaminophen (500 mg). If the patient complained of nausea or experienced repeated episodes of vomiting or retching, they were treated with 12.5 mg intravenous dolasetron, and if the condition persisted, 6.25-mg intravenous bolus doses of promethazine were administered to a total dose of 25 mg.

Postoperative side effects (e.g., pain, dizziness, nausea, vomiting) and the requirements for “rescue” analgesic and antiemetic drugs were recorded along with the duration of stay in the phase I PACU and phase II step-down unit, as well as the times to be considered “fit for discharge” and actual discharge home. The criteria used to determine fitness for discharge required that the patient to be awake and alert, have stable vital signs on standing, be experiencing no intractable postoperative side effects, and be able to walk without assistance. Patient satisfaction with their postoperative pain management and the quality of their recovery was assessed using a verbal analog scale, with 0 = poor to 100 = excellent at 24 h after surgery. Patients who rated their satisfaction with pain management at 100 were considered to have complete satisfaction with their pain control. The number needed to treat (NNT) for complete satisfaction with pain control was calculated as the reciprocal of the absolute difference in the incidence of complete satisfaction between the two groups.13

Finally, follow-up telephone evaluations at 24 and 48 h after surgery were used to determine the number of doses (pills) of oral analgesic medications consumed after discharge and the occurrence of postdischarge nausea or vomiting and other side effects. The patient also evaluated their maximum (peak) postdischarge pain on the 11-point VRS following discharge.

**Statistical Analysis**

This study was designed to assess the ability of drugs given before induction of anesthesia to prevent postoperative pain. Hence, the standard endpoints of pain intensity difference, pain relief over time, and time to onset of pain relief were not used. The analgesic efficacy of the study drugs was assessed by comparing the maximum (peak) pain score at any time during the study, including the score just prior to receiving rescue analgesia in the postoperative period, and the proportion of patients requiring rescue analgesic medications. Therefore, the primary endpoint of this study was the peak postoperative pain score, and the secondary endpoint was the proportion of patients requiring rescue analgesic medication. An a priori power analysis estimated that 35 patients would be required in each group based on the following assumptions: (1) the log transformation of the mean and SD (6 and 1.8, respectively) of the peak pain score in the placebo group would be similar to that in a previously published study in this patient population where a similar anesthetic regimen was used12; (2) a relative reduction of 33% in the peak verbal pain score rating from 6 to 4 was considered of clinical importance; (3) a type I error of 0.05 not adjusted for multiple comparisons; and (4) power = 90%. This sample size would have an 80% power at the 0.01 level of significance to detect a change in the proportion of patients requiring rescue analgesia in the PACU from 82% in the
placebo group to 40% in the treatment group. This incidence of rescue therapy in placebo and treatment groups is in keeping with previously published studies of postoperative pain.2,11

Data analysis was performed using Statview for Windows Version 5.0.1 (SAS Institute, Cary, NC). Normally distributed continuous data were analyzed using one-way analysis of variance, and if significant differences were noted, a Student-Neuman-Kuels test was used for intergroup comparisons. Continuous data not normally distributed (e.g., pain scores) were analyzed by a Kruskall-Wallis analysis of variance, and if significant differences were noted, a Mann-Whitney U test was used for intergroup differences. The raw postoperative pain scores were analyzed by a repeated-measures analysis of variance. Categorical data, including the cumulative proportion of patients requiring rescue analgesia at various time points, were analyzed using the chi-square test with Yates continuity correction or Fisher exact test where appropriate.

**Results**

There were no significant differences among the four treatment groups with respect to age, weight, gender, type and duration of surgery and anesthesia, and the total doses of remifentanil and desflurane administered during surgery (table 1). There were also no significant differences in the times from the end of surgery to eye opening, responding to verbal commands, or orientation to person, place, and time (table 1). In addition, there were no differences in the time spent in the phase I and II recovery units or in the time to achieve fitness for discharge home.

Baseline pain and nausea VRS scores were similar in all four groups (table 1). The peak pain scores, the number of patients requiring more than one dose of parenteral opioid rescue medication, and the cumulative number of patients requiring rescue analgesic therapy at the end of the first 3 h postoperatively were significantly higher in the placebo group compared with the other three treatment groups. However, the number of patients with severe pain and the cumulative proportion of patients requiring rescue medications at 15 to 150 min after arrival in the PACU was not significantly different between the placebo and acetaminophen groups (fig. 1). Interestingly, from 180 min onward the difference was statistically significant ($P < 0.05$). Patients who received rofecoxib alone or in combination with acetaminophen had lower peak pain scores compared with those who did not receive the COX-2 inhibitor. The use of rofecoxib alone or in combination with acetaminophen was also associated with a decrease in the cumulative proportion of patients requiring rescue medications at 45 to 240 min after arriving in the PACU ($P < 0.05$ vs. placebo; fig. 1). However, there were no significant differences in the incidence of nausea, vomiting, or the requirement for antiemetic rescue medication between the four groups (table 2).

The pain scores did not differ between any of the four groups at the time of discharge because analgesic rescue medications were administered. However, the patients who had received the placebo reported higher peak postdischarge pain scores than those in the three active drug treatment groups (table 3). The number of doses of oral analgesic medication after discharge was also significantly higher in the placebo group compared with the other three treatment groups (table 3). In addition, the postdischarge pain scores and the oral analgesic requirements were higher in the acetaminophen group compared with the two rofecoxib groups. Interestingly, there were no differences between the four groups in the incidence of nausea, vomiting, or the peak nausea scores after discharge (table 3).

Patients who received rofecoxib were more highly satisfied with their postoperative pain control and quality of recovery than either the placebo or acetami-
Table 1. Patient Demographic Characteristics, Type of Surgery, Anesthesia and Surgery Times, Intraoperative Analgesic and Anesthetic Dosage Requirements, and Postoperative Recovery Times in the Four Treatment Groups

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Acetaminophen 2 g</th>
<th>Rofecoxib 50 mg</th>
<th>Combination</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>36</td>
<td>35</td>
<td>37</td>
<td>35</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>43 ± 11</td>
<td>46 ± 13</td>
<td>46 ± 11</td>
<td>45 ± 14</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79 ± 22</td>
<td>84 ± 20</td>
<td>79 ± 31</td>
<td>72 ± 19</td>
</tr>
<tr>
<td>Gender (M/F) (n)</td>
<td>21/15</td>
<td>17/18</td>
<td>14/23</td>
<td>15/20</td>
</tr>
<tr>
<td>Surgical procedures (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal sinus surgery</td>
<td>15</td>
<td>8</td>
<td>12</td>
<td>18</td>
</tr>
<tr>
<td>Otologic surgery</td>
<td>14</td>
<td>20</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>Pharyngeal/neck surgery</td>
<td>7</td>
<td>7</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Preoperative verbal pain score (0–10)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
</tr>
<tr>
<td>Preoperative nausea score (0–10)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
</tr>
<tr>
<td>Surgery time (min)</td>
<td>63 ± 29</td>
<td>71 ± 38</td>
<td>66 ± 36</td>
<td>75 ± 43</td>
</tr>
<tr>
<td>Anesthesia time (min)</td>
<td>87 ± 29</td>
<td>94 ± 41</td>
<td>91 ± 36</td>
<td>100 ± 43</td>
</tr>
<tr>
<td>Intraoperative remifentanil (µg)</td>
<td>1,022 ± 610</td>
<td>979 ± 509</td>
<td>831 ± 435</td>
<td>960 ± 469</td>
</tr>
<tr>
<td>Mean end-tidal desflurane concentration (%)</td>
<td>4.2 ± 1.0</td>
<td>5.4 ± 0.7</td>
<td>3.9 ± 1.1</td>
<td>3.9 ± 1.1</td>
</tr>
<tr>
<td>Time in min from end of surgery to:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye opening</td>
<td>7 ± 6</td>
<td>9 ± 6</td>
<td>7 ± 5</td>
<td>7 ± 4</td>
</tr>
<tr>
<td>Obeying commands</td>
<td>13 ± 8</td>
<td>14 ± 9</td>
<td>11 ± 6</td>
<td>11 ± 6</td>
</tr>
<tr>
<td>Orientation</td>
<td>14 ± 8</td>
<td>16 ± 10</td>
<td>14 ± 8</td>
<td>12 ± 6</td>
</tr>
<tr>
<td>Recovery stay (min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase 1 (PACU)</td>
<td>70 ± 26</td>
<td>71 ± 27</td>
<td>64 ± 18</td>
<td>63 ± 32</td>
</tr>
<tr>
<td>Phase 2 (DSU)</td>
<td>194 ± 263</td>
<td>133 ± 136</td>
<td>96 ± 43</td>
<td>178 ± 246</td>
</tr>
<tr>
<td>Discharge criteria achieved</td>
<td>115 ± 20</td>
<td>129 ± 33</td>
<td>119 ± 46</td>
<td>151 ± 60</td>
</tr>
</tbody>
</table>

Values are means ± SD, medians (with interquartile ranges), numbers (n), or percentages (%).

PACU = postanesthesia care unit; DSU = day surgery unit.

Table 1 shows that postoperative nausea and vomiting, which was low in this study as all patients received low-dose droperidol and dexamethasone for routine antiemetic prophylaxis. Finally, the results of this analysis were also sensitive to the costs and efficacy of drugs used to treat postoperative nausea and vomiting in the PACU.

Discussion

Effective pain control after outpatient surgery remains a clinically significant concern as it has a large impact on the recovery process and patient satisfaction with their postoperative care. NSAIDs and acetaminophen have been increasingly used alone and in combination with opioids for the treatment of pain after ambulatory surgery. In this study involving an adult ambulatory surgery population, the oral administration of rofecoxib (50 mg) prior to surgery was effective in reducing pain after ENT surgery and lead to improved satisfaction with their pain management and quality of recovery compared with acetaminophen (2 g).

In a pediatric study involving acetaminophen (35 mg/kg pr), Rusy et al. reported that it was equivalent to ketorolac (1 mg/kg administered intravenously) for the prevention of postoperative pain. However, there are conflicting data on the analgesic efficacy of acetaminophen in adults. While Cobby et al. reported that rectal acetaminophen (1.3 g) had a morphine-sparing effect after hysterectomy procedures, Hein et al. failed to demonstrate analgesia with rectal doses of 1 g.
after minor gynecologic surgery. However, the more reliable absorption by the oral route makes it the preferred route of administration in adults.

In our study, oral acetaminophen in a dose of 25 mg/kg demonstrated significant analgesic efficacy compared with a placebo treatment for the primary outcome of peak pain scores, but not for all secondary outcome variables. These findings are also consistent with other studies showing 650–1,000 mg oral acetaminophen has an analgesic effect after dental surgery and in women undergoing an episiotomy procedure.\textsuperscript{23,24} The differences between the placebo and acetaminophen groups in the need for rescue analgesia did not reach statistical significance until 3 h after arrival in the PACU. The failure to demonstrate an earlier effect on the secondary outcomes in the proportion of patients requiring rescue analgesic therapy may reflect a “ceiling” effect of acetaminophen with respect to pain control in the early postoperative period. It is also possible that the study lacked the sensitivity to detect small changes in the secondary outcome variables in the predischarge period.

Table 2. Peak Pain and Nausea Scores, as well as Requirements for Opioid Analgesics and Antiemetics prior to Discharge from the Hospital in the Four Treatment Groups

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n = 36)</th>
<th>Acetaminophen 2 g (n = 35)</th>
<th>Rofecoxib 50 mg (n = 37)</th>
<th>Combination (n = 35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak pain score (0–10)</td>
<td>6 (3–9)</td>
<td>5 (1–8)*</td>
<td>3 (0–8)*†</td>
<td>3 (0–9)*†</td>
</tr>
<tr>
<td>Patients with severe pain [n (%)]</td>
<td>21 (58)</td>
<td>15 (43)</td>
<td>6 (16)*†</td>
<td>10 (29)*†</td>
</tr>
<tr>
<td>Patients requiring more than 1 dose of analgesic rescue [n (%)]</td>
<td>23 (64)</td>
<td>18 (51)</td>
<td>7 (19)*†</td>
<td>9 (26)*†</td>
</tr>
<tr>
<td>Peak nausea score (0–10)</td>
<td>1 (0–3)</td>
<td>0 (0–4)</td>
<td>0 (0–0)</td>
<td>0 (0–1.5)</td>
</tr>
<tr>
<td>Patients vomiting (or retching) [n (%)]</td>
<td>4 (11)</td>
<td>3 (9)</td>
<td>3 (8)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Patients receiving antiemetics in PACU [n (%)]</td>
<td>10 (28)</td>
<td>15 (43)</td>
<td>8 (22)</td>
<td>8 (23)</td>
</tr>
</tbody>
</table>

Values are medians (with interquartile ranges), numbers, or percentages.

* $P < 0.05$ versus placebo groups.
† $P < 0.05$ versus acetaminophen group.

PACU = postanesthesia care unit.
analgesic efficacy of COX-2 inhibitors may be partly dependent on the type of surgery, with greater efficacy noted when they are used in orthopedic and dental procedures, and they may be less efficacious for pain related to intraabdominal surgery procedures. For example, rofecoxib has recently been reported to be opioid-sparing in patients undergoing spine fusion surgery.9

Combinations of NSAIDs and acetaminophen would be expected to be more effective than either drug alone as they are likely to possess different sites of analgesic action. For example, the combination of diclofenac and acetaminophen has been shown to be more effective than either drug alone in reducing pain following both gynecologic and oral surgery. Similarly, 2 g oral acetaminophen enhanced the postoperative analgesic effectiveness of 200 mg oral celecoxib when administered prior to ENT surgery. However, in the current study the addition of acetaminophen failed to increase the efficacy of rofecoxib.

Since both acetaminophen and rofecoxib appear to inhibit the same brain cyclooxygenase enzymes, the addition of acetaminophen would not be expected to enhance the analgesic efficacy of rofecoxib if the 50-mg dose was producing maximal inhibition of the brain COX-2 enzyme. It is possible that the combination would have been more effective than either drug alone if a lower dose of rofecoxib (25 mg) had been used in the study. Although all patients were discharged home with similar pain scores, fewer patients in the rofecoxib and acetaminophen groups required rescue analgesic medication in the pre-discharge period. Furthermore, the number of doses of opioid-containing oral analgesic medication after discharge remained significantly lower in both of these groups. This apparent prolonged analgesic effect reflects the long duration of action of rofecoxib and the fact that our patients all received a second dose of the study drugs on the morning after surgery.

This study can be criticized because the ENT patient population studied underwent procedures that are not usually considered to be extremely painful. However, more than 50% of the patients in the placebo group experienced moderate-to-severe pain in the early postoperative period, and surveys of postoperative pain after ambulatory surgery have reported that these types of operations can be associated with severe pain in the postoperative period. Furthermore, previous studies have demonstrated that pain after ENT surgery is an acceptable model for studying nonopioid analgesics. The study can also be criticized for not having power to detect small differences in secondary outcomes, such as the time for first patient request for analgesic medication. Finally, this study can be criticized for not comparing the study drugs to traditional NSAIDs such as ketorolac and diclofenac. However, we feel that nonselective NSAIDs are relatively contraindicated prior to ENT surgery because of an increased risk of operative site bleeding. While laboratory studies suggest that the COX-2 inhibitors do not alter platelet function, additional studies are needed to determine if their use is associated with less blood loss. Therefore, it is inappropriate to assume that the use of rofecoxib will result in fewer hemorrhagic complications than ketorolac or diclofenac.

The current results suggest that rofecoxib was not only highly effective in reducing postoperative pain and the need for opioid-containing analgesic medication, but also lead to a better outcome from the patients' perspective as reflected by improvement in their satisfaction with postoperative pain management and their quality of recovery. Our study suggests that the NNTs for increased patient satisfaction with the rofecoxib regimen compared with the placebo and acetaminophen regimens were 1.6 and 3.0, respectively. Therefore, it would take an additional expenditure of $16.76 (95% CI, $7.89–21.03) and $30.24 (95% CI, $5.25–54.23) for rofecoxib to obtain complete satisfaction with the postoperative pain management in one additional patient who would receive the study treatment.
not have been satisfied if he or she had received placebo or acetaminophen, respectively. By comparison, the estimated cost to increase patient satisfaction in one additional patient when ondansetron is administered prophylactically exceeds $400.30

The cost estimates in our study were sensitive to a number of assumptions, including the incidence of postoperative nausea and vomiting, as well as the costs and efficacy of the antiemetic drugs used for prophylaxis and treatment of these side effects. This study was completed before the Food and Drug Administration issued its recent warnings regarding the use of droperidol and their recommendation that a screening 12-lead electrocardiogram be performed and a 3-h monitoring interval be observed when droperidol is administered for antemetic prophylaxis.†† Although these recommendations have been questioned,31 it is reasonable to assume that a decreased use of droperidol will occur in the future with a consequent increase in antemetic drug costs as physicians replace this inexpensive antiemetic with the more expensive serotonin antagonists.

In conclusion, oral premedication with rofecoxib (50 mg) decreases postoperative pain and the need for analgesic rescue medication, thereby improving patient satisfaction with their pain management and quality of recovery after outpatient ENT surgery. However, the addition of acetaminophen (2 g administered orally) failed to enhance the analgesic efficacy of rofecoxib (50 mg administered orally) in this outpatient surgical population.

References


Anesthesiology, V 97, No 4, Oct 2002