

Postoperative Nausea and Vomiting: Prophylaxis Versus Treatment

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Controversy continues to surround the optimal approach to managing postoperative nausea and vomiting (PONV). In a recent article, Scuderi et al. (1) reported that routine antiemetic prophylaxis with ondansetron, 4 mg IV, given before the start of surgery did not result in a clinically important improvement in patient outcome compared with symptomatic treatment. In an accompanying editorial, Fisher (2) stated, "there appears to be little evidence to support routine prophylactic administration of antiemetics." Fisher (2,3) has also criticized studies of antiemetic efficacy that were limited to what he termed surrogate end points (e.g., the incidence and frequency of emesis). He recommended that investigators examine the more important effects of antiemetic drugs on the duration of stay in the postanesthesia care unit (PACU), the incidence of unplanned hospital admissions, and patient satisfaction. In this issue of *Anesthesia & Analgesia* Sadhasivam et al. (4) report a study that examined the effect of routine prophylaxis with ondansetron (4 mg IV) given at the end of surgery on patient outcome after a modified radical mastectomy. These investigators found that routine prophylaxis not only improved so-called surrogate end points, but also led to greater patient satisfaction after surgery. These findings are of even greater interest because the study was performed in a country with economic, developmental, and cultural differences that reduce patient expectations and demands on the healthcare system compared with more developed parts of the world.

How can we reconcile the apparent differences in patient satisfaction with prophylaxis of PONV in the studies by Scuderi et al. (1) and Sadhasivam et al. (4)? Scuderi et al. (1) reported a significant difference in

patient satisfaction with control of emesis in the prophylaxis group compared with the treatment group (97% vs 93%) but stated that this difference lacked clinical importance. In addition, Scuderi et al. (1) found a significantly higher level of satisfaction with prophylaxis than with treatment in a subgroup of women with a history of motion sickness or PONV undergoing highly emetogenic procedures. This observation supports an earlier study by Tang et al. (5), which demonstrated improved patient satisfaction with ondansetron prophylaxis of high-risk gynecologic surgery patients. The incidence of PONV in the placebo group studied by Sadhasivam et al. was >80%, a very high incidence by any standard. Although the timely treatment of PONV can also be effective (1), nursing personnel may not always be readily available to respond to the needs of patients experiencing uncomfortable emetic symptoms, and this can markedly affect patient satisfaction.

The timing of prophylactic administration of ondansetron can have a significant effect on its efficacy in preventing severe PONV and, consequently, on patient satisfaction (6,7). In a high-risk gynecologic laparoscopic surgery population, Tang et al. (7) found a higher percentage of satisfied patients (90% vs 67%) when ondansetron was administered near the end of surgery, rather than before surgery. Scuderi et al. (1) administered ondansetron at the induction of anesthesia, whereas Sadhasivam et al. (4) waited until the end of the operation before administering the drug. These studies suggest that, in the very high-risk group, prophylactic management of PONV with ondansetron at the end of surgery may be associated with greater patient satisfaction than a strategy of simply waiting for a patient to develop persistent symptoms before administering an antiemetic drug. The value placed by patients in avoiding PONV has been further demonstrated by questionnaires that quantify patients' willingness to pay "out of their own pocket" for prophylaxis (5,8).

Accepted for publication August 17, 1999.

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Table 1. Success Rates with Ondansetron Prophylaxis in Preventing Emetic Symptoms^a

	Ondansetron					
	4 mg			8 mg		
	<i>n</i>	Success	%	<i>n</i>	Success	%
Early nausea prevention	325	257	79.1	88	54	61.4
Early vomiting prevention	595	514	86.4	465	353	75.9
Early PONV prevention	233	149	64.0	NA	NA	NA
Late nausea prevention						
Including all studies	1908	1119	58.7	521	256	49.1
Excluding two studies	1412	724	51.3	521	256	49.1
Late vomiting prevention	2058	1483	72.1	722	409	56.7
Late PONV prevention	327	198	60.6	40	39	97.5

PONV = postoperative nausea and vomiting.

^a Modified from Tramer et al. (11).

The debate over prophylaxis versus treatment has taken on great significance because of economic concerns related to the cost-effectiveness of routine antiemetic prophylaxis with 5-HT₃ receptor antagonists (9,10). Fisher (2) has argued that meta-analyses by Tramer et al. (11,12) demonstrated that "treatment with a 1 mg dose of ondansetron is more cost-effective than giving 4–8 mg prophylactically to many patients who would not have vomited anyway." We (13) have recently cautioned against accepting clinical practice guidelines based solely on these meta-analytic techniques because of their inherent deficiencies. Tramer et al. (11,12) did not directly compare the prophylactic and therapeutic efficacy of 1-, 4-, and 8-mg doses; they compared the efficacy of each dose against a placebo. These investigators determined the numbers-needed-to-treat to avoid PONV in one patient and the 95% confidence limit of this estimate. When we reanalyzed data used by Tramer et al. (11), the absolute success rates for prophylaxis with ondansetron 4 and 8 mg IV did not significantly differ for the separate incidences of nausea and vomiting (Table 1).

Tramer et al. (14) performed a subsequent cost analysis based on their systematic reviews of the literature and concluded that the most cost-effective scenario was treating patients with a 1-mg dose of ondansetron in the PACU if they developed symptoms. Unfortunately, this analysis was limited to the number of milligrams of ondansetron required to achieve a desired end point and did not take into consideration costs of resources used to manage PONV, unanticipated admission, or nursing labor costs. Watcha and Smith (10) used a decision analysis model that included these costs to show that prophylaxis with ondansetron is associated with decreased costs if the incidence of PONV exceeds 30%. Others have shown that exclusion of nursing costs does not alter the conclusion that prophylaxis with ondansetron is cost-effective in high-risk cases compared with therapy in the PACU (15). In contrast to ondansetron, prophylaxis with droperidol is associated with decreased costs if the incidence of PONV exceeds 10% (10). Blinded studies have

shown that prophylaxis with small-dose droperidol (<1.25 mg) is not associated with increased drowsiness or restlessness, or prolonged stays in the PACU compared with placebo (5,16). Systematic reviews have also concluded that the efficacy of ondansetron and small-dose droperidol in the prophylaxis against PONV is similar in adults, but not in children (17). Others have confirmed the relative cost-effectiveness of prophylaxis with small-dose droperidol compared with ondansetron (5,15). However, the persistently high incidence of PONV in "at risk" populations, despite prophylaxis with any single antiemetic drug, suggests that drug combinations [e.g., droperidol-ondansetron (18), ondansetron-dexamethasone (19,20)] should be considered for those at highest risk of developing this side effect.

In contrast to Scuderi et al. (1) and Tramer et al. (14), we believe that routine antiemetic prophylaxis does indeed improve clinically meaningful outcomes in patients at high risk of PONV. As always, the cost-effectiveness of "routine" prophylaxis will depend on the underlying incidence of PONV in a given patient population, as well as the cost and intrinsic efficacy of the antiemetic drugs itself. Apfel et al. (21) and Sinclair et al. (22) have quantified the risks of PONV for a given patient using statistical analyses that take into account patient age, gender, smoking status, history of prior motion sickness or PONV, and the type of surgical procedure.

Therefore, we recommend routine antiemetic prophylaxis of all high-risk patients using either single or combination drug therapy administered at the optimal time using the smallest effective dose. For low-risk patients (<10% risk of PONV), routine prophylaxis with antiemetics is difficult to justify. For adult patients with a 10%–30% risk, we recommend prophylaxis with 0.625–1.25 mg of droperidol. For pediatric patients, ondansetron 50–100 µg/kg IV may be more useful (17). For patients at higher risk, we recommend combination drug therapy with a steroid and a 5-HT₃ antagonist. For patients at the highest risk, a two- or even three-drug regimen (e.g., droperidol-ondansetron-dexamethasone)

may be justified. If a 5-HT₃ antagonist such as ondansetron or dolasetron is used, it should be given near the end of surgery. Finally, if patients experience breakthrough PONV despite prophylaxis, they should be treated with a drug from a group other than the one used for prophylaxis (e.g., metoclopramide).

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