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TREATMENT OF POSTOPERATIVE NAUSEA AND VOMITING THAT IS ALREADY ESTABLISHED DURING THE POST-ANESTHESIA CARE UNIT: A VIGNETTE-BASED SURVEY OF ANESTHESIOLOGISTS

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Abstract

Background: Postoperative nausea and vomiting (PONV) is one of the most uncomfortable adverse effects of patients undergoing surgery and is one of the primary factors influencing their satisfaction with the anesthesia services. Although much attention has been paid to the prevention of PONV, there is little information on the treatment of proven PONV within a regular clinical scenario.

Methods: A questionnaire with five hypothetical clinical vignettes was dispatched to 300 anesthesiologists who were randomly chosen to provide an insight into the treatment measures of established PONV based in the post-anesthesia care unit (PACU). Vignettes involved a description of an ambulatory surgical patient who experienced PONV due to the administration of different prophylactic regimens. The respondents were requested to specify their first and second preference of treatment, both pharmacologic and non-pharmacologic. Such demographic and practice characteristics were also gathered.

Findings: The survey was filled out by seventy-six anesthesiologists. The most commonly chosen first line treatment was 5-HT3 receptor antagonist (50%), when none had been used as prophylaxis. Even though majority of the respondents said that they had switched to another pharmacologic class due to prophylaxis failure, a significant number of respondents repeated dosing of 5-HT3 antagonists. Pharmacologic (18 agents) and non-pharmacologic (12 interventions) treatments were reported in wide range, which means that there was a significant variation in practices patterns.

Conclusions: The therapy of established PONV is still less uniform and does not always follow the recommendations of the consensus. The results noted here emphasize the necessity of standardized treatment recommendations, better clinical decision-making, and additional clinical trials dedicated to the most effective way of managing PONV once it occurs.

Keywords: Postoperative nausea and vomiting (PONV), Antiemetic therapy, Post-anesthesia care unit (PACU), Clinical practice patterns, Vignette-based survey.

Introduction

Postoperative nausea and vomiting (PONV) is always one of their top priorities when patients are questioned about the elements of surgery that lead them to experience the most anxiety [1,2]. Clinicians also identify PONV as a major problem to which patients are affected [3]. Due to its effect on patient experience, the improvement of the quality of anesthesia care is based on the reduction of the occurrence and the intensity of PONV. Many potential randomized controlled clinical trials have been done to assess pharmacologic and non-pharmacologic prevention of PONV [48]. Moreover, it is provided with information about the prophylactic measures that are frequent in the practice of anesthesia [9].

Conversely, there is a relative paucity of studies on efficacy of antiemetic treatment in the management of PONV after the occurrence of the symptoms in the post-anesthesia care unit (PACU). In a systematic review of quantitative studies published in 2001 evaluating treatments used to prevent established PONV, meta-analysis of treatments including metoclopramide, droperidol, inhaled isopropyl alcohol, and midazolam has been done in only a single study with very small sample sizes [10]. It was also established in the review that the effect of 5-HT3 receptor antagonists on nausea was less, but they reduced the possibility of vomiting by about 20-30 per cent compared to placebo.

This lack of balance between the vast body of literature on PONV prevention and small amounts of evidence on treatment of formed symptoms can be in part ascribed to the challenges that methodological treatment studies face. Sufficient sample sizes of those who do experience PONV are needed because of large sample sizes of patients. The evidence-based management of PONV after the onset was, until recently, mostly grounded on the expert consensus rather than on a strong clinical experimentation [11].

There is limited data on the actual practice patterns on how to perform treatment of PONV in the PACU. Prospective and retrospective data collection can be performed with the help of review of medical record, but both methods complicate the comparison of clinician practice since they fail to adequately control patient characteristics, illness severity, and practice environment. Other shortcomings of chart review are documentation bias that can be said to be done but not documented and the requirement of professional personnel to retrieve the data correctly.

Short clinical case vignette is a tool that has been tested to determine clinician decision-making in order to elimination of confounding factors and the enhanced isolation of decision-making in clinician treatment practice [12]. These are written scenarios that are simulations of a real clinical scenario and have been extensively utilized by educators, epidemiologists and health services researchers to assess clinical processes in a variety of settings [13 15].

The aim of the research was to assess the answers to a written questionnaire that includes short hypothetical clinical vignettes to answer the following questions regarding the management of PONV in the PACU: (1) what anesthesiologists treat with when there has been no prophylaxis in ambulatory patients; (2) the use of non-pharmacologic interventions in the PONV treatment; (3) whether anesthesiologists treat PONV with a different type of drug.

Methods

Physician sample

The questionnaire was sent by mail to 300 randomly selected anesthetics professionals out of a professional anesthesiology directory that was in printed form. The random number table was employed to select the participants, by taking place positions in the listing of the directory. A sample population of 300 was selected on basis of the previous experience that estimated that a response rate of about 33 percent will be expected which is likely to give an estimate of about 100 completed surveys. The questionnaires were sent to professional addresses of the participants by mail in December 2004, and with each post, a stamped, self-addressed return envelope was included to make them take part.

Survey measurement methods

There were three sections in the survey tool. A cover letter was on the first page, the second page captured some basic demographic details of the respondents whereas the third contained a series of clinical scenarios (vignettes) [see Additional file 1]. As an example, the base case of vignette 1 was as follows: A 76-year-old female with the history of outpatient laparoscopy of the pelvis under general anesthesia. She was not given prophylaxis on postoperative nausea and vomiting (PONV). She complains of PONV in the post-anesthesia care unit (PACU). Which antiemetic order/s would you order?

The respondents were to imagine that all other pertinent details about the medical history and the physical examination of the patient were non-remarkable and sufficient analgesia was administered. The survey did not limit the respondents to single-agent and combination antiemetic therapy.

In order to determine the effect that previous prophylaxis had on decision making regarding treatment, the base scenario was kept constant in vignettes 2-5, and the amount of prophylaxis antiemetics administered was increased in that order. In vignette 2, a 5-HT3 receptor antagonist was used to provide prophylaxis to the patient. Vignette 3 had an antagonist to 5-HT3A-receptors and metoclopramide. Dexamethasone was added to this regimen in Vignette 4. Vignette 5 involved a patient who was treated with 5-HT3 antagonist, metoclopramide, dexamethasone and droperidol prophylaxis and then experienced the same presentation of PONV in PACU.

On the way of further defining the treatment strategies, the respondents were also asked to specify the second-line treatment, in case of failure of the initial treatment. In each of the vignettes, the question was: What do you like to have as a second option of treatment in case of the failure of the first treatment?

To have clarity and content validity, the vignettes were screened by four senior, board-certified anesthesiologists working in an academic department of anesthesiology.

In order to determine internal reliability, a test-retest reliability of the questionnaire was conducted with five other anesthesiologists. These subjects responded to the questionnaire twice, separated by two days, but not randomized and anonymized. On both occasions, all questions were answered. Out of an eligible 90 responses (the responses were not including demographic items), 82 percent responded the same on the second administration.

The Clopper-Pearson method of calculating proportions was used to obtain two-sided 95% confidence intervals (StatXact-6 Cytel Software Corporation) [16].

Results

There were 76 anesthesiologists who responded to the survey. The mean experience of the respondents was 16 years (SD 7; range 538) and the mean age of the respondents was 48 years (SD 9; range 3569). The majority were in an inpatient hospital practice (63%), then free-standing surgery centers (18%), and finally in outpatient hospital setting (17%). Most of the respondents were of the male sex (81%). Practice environments were well distributed in both academic (44%), and the private practice (56%). The respondents had 18 different regions of representation (Table 1) and 54% of their clinical workload was in ambulatory cases on average.

The first-line forms of treatment of postoperative nausea and vomiting depended on the prophylaxis treatment received during anesthesia (Table 2). Ondansetron was the most commonly chosen (50) followed by metacolopramide (12), dolasetron (12), and dexamethasone (9) when there was no prophylaxis applied. Less frequently chosen in this setting were droperidol and promethazine (8% and 4% respectively).

In the cases where a 5-HT3 receptor antagonist was administered to prevent, the trend of treatment was not based on the re-use of the similar directive. Ondansetron was less frequently used (24), and metoclopramide (20%), droperidol (15%), dexamethasone (14%), and promethazine (12%) were used in preference. This tendency was increased by adding more prophylactic agents. Promethazine (19%),

droperidol (17%), and dexamethasone (18), rather than metoclopramide (5), were the regular ones in patients who received combination prophylaxis with an 5-HT3 antagonist and metoclopramide, though. Promethazine became one of the most commonly used interventions (21%) after triple agent prophylaxis (5-HT3 antagonist, metoclopramide, and dexamethasone), and droperidol (18%). Promethazine was the most initial treatment option in the environment of quadruple prophylaxis with droperidol (26%), whereas the use of ondansetron was rather low (20%).

In general, these results indicate that clinicians are reluctant to repeat the used prophylactic agents and instead choose the antiemetics with different pharmacologic categories in the treatment of the established PONV at the post-anesthesia unit.

Table 1. Demographic and Practice Characteristics of the Respondents (N=76)

Characteristic	Value
Mean years in practice (SD, range)	16 (7, 5–38)
Mean age (SD, range)	48 (9, 35–69)
Primary practice location	
Hospital – Inpatient	63%
Hospital – Outpatient	17%
Free-standing surgery center	18%
Surgeon office	2%
Sex	
Male	81%
Practice characteristics	
Academic	44%
Private practice	56%
Percentage of practice that is ambulatory (mean)	54%
Number of regions represented	18

Table 2. First line management of PONV As per Prophylaxis Regimen (N = 76)
Pharmacologic Treatment by Prophylaxis Regimen (%)

Treatment	None	5-HT3	5-HT3 + Meto	5-HT3 + Meto + Dexa	5-HT3 + Meto + Dexa + Drop
Ondansetron	50%	24%	22%	21%	20%
Dolasetron	12%	4%	3%	5%	4%
Droperidol	8%	15%	17%	18%	8%
Dexamethasone	9%	14%	18%	3%	3%
Metoclopramide	12%	20%	5%	6%	5%
Promethazine	4%	12%	19%	21%	26%
Prochlorperazine	1%	2%	2%	2%	4%
Diphenhydramine	0%	0%	1%	4%	4%
Intramuscular ephedrine	1%	3%	4%	4%	5%
Hydroxyzine	1%	2%	2%	4%	4%
Propofol	0%	1%	1%	2%	4%
Scopolamine patch	1%	1%	1%	2%	3%
Granisetron	1%	1%	1%	1%	1%
Other*	0%	1%	2%	1%	3%
Total	**100%**	**100%**	**100%**	**100%**	**100%**

Other contains trimethobenzamide, perphenazine, haloperidol, atropine or midazolam.
Oh, the initials 5-HT3 are 5-HT3 receptor antagonist, Meto refers to metoclopramide, Dexa to dexamethasone, and Drop to droperidol.

Non-Pharmacologic Treatment by Prophylaxis Regimen (%)

Intervention	**None**	**5-HT3**	**5-HT3 + Meto**	**5-HT3 + Meto + Dexa**	**5-HT3 + Meto + Dexa + Drop**
IV fluid bolus	55%	54%	55%	56%	50%
Oxygen via nasal cannula	23%	20%	20%	20%	21%
Inhaled alcohol swab	7%	6%	7%	7%	6%
Patient reassurance	2%	3%	2%	2%	1%
Forced-air warming	4%	4%	3%	3%	6%
Keep NPO	2%	1%	3%	2%	2%
Acupressure / acupuncture / acustimulation	4%	4%	4%	4%	6%
Supine positioning	3%	3%	3%	2%	3%
Other	0%	5%	3%	1%	5%
Total	**100%**	**100%**	**100%**	**100%**	**100%**

Discussion

The results of this vignette study using questionnaires further prove that 5-HT3 receptor antagonists are the most commonly chosen agents in the treatment of established postoperative nausea and vomiting (PONV), especially when no prophylaxis has taken place. This was the case even with already prophylaxis-treated patients who had a 5-HT3 antagonist notwithstanding the number of prophylaxis agents. These data indicate that clinicians still have high use of this drug class in rescue therapy, even though the evidence of factoring in guideline recommendations of changing the pharmacologic class following unsuccessful prophylaxis is mounting.

The respondents stated that they had used a great variety of therapeutic interventions such as sixteen different medications and a total of twelve non-pharmacologic interventions. This variation in treatment choices is not new as it has been previously reported that there is tendency in clinical practices to vary across physicians with similar patients. This heterogeneity can be due to the lack of certainty about comparative effectiveness of the available therapies, the differences in training, institutional policies, availability of drugs, perceived cost, or adverse effects. Prescripting behavior can also be influenced by external factors, e.g., recent encounter with educational materials or representatives of the industry. It has previously been demonstrated that tailored learning and personalized feedback can make a significant change in practice patterns during anesthesia, which leads to the assumption that the same approach could help decrease unnecessary disparities in PONV treatment.

As regards first line treatment options, almost all the respondents preferred pharmacologic to non-pharmacologic treatment. The antiemetics included in the hypothetical prophylaxis regimens (5-HT3 antagonists, droperidol, dexamethasone and metoclopramide) were selected because they reflect commonly used agents, which act on various receptor pathways involved in the pathophysiology of PONV. There were no dosages, the main focus was to determine drug selection and not dose regimens. Promethazine was not used as prophylaxis agent in the vignettes to save on the length of the survey as well as it is rarely used in the prevention of prophylaxis in the day to day ambulatory practice.

Almost two-thirds of the respondents would use an 5-HT3 antagonist as first-line therapy when no prophylaxis had been used. This could be attributed to the feeling that these agents are more useful

in treating vomiting rather than nausea and that these agents have a good side-effect profile. There is a paucity of evidence on a dose responsiveness of 5-HT3 antagonists and small doses have been advocated in treating established symptoms. Regardless of increasing use of multimodal approaches to prophylaxis, comparatively few of the respondents suggested using combination therapy as the first-line therapy, which implies that they still use single-agent rescue approaches.
Majority of the anesthesiologists reported that they would change to another drug category of treatment in the event of PONV regardless of prophylaxis. Nevertheless, a significant minority of them said that they would give another dose of a 5-HT3 antagonist following prophylactic failure. This is in spite of the recommendation made by experts that it is not advisable to repeat dose within the first few days after surgery since there is no incremental benefit in doing so. The unpredictable failure of treatment in some of the patients could be partially accounted by pharmacogenomic factors, including ultrarapid metabolism through CYP2D6 polymorphisms, which serve as the rationale to choose an agent representing a different class.

Interestingly, the respondents were less likely to repeat dosing of metoclopramide, dexamethasone, or droperidol when prophylaxis had been used. This is an indication that there is a possibility of a decrease in the perception of clinicians with regard to the repeat use of 5-HT3 antagonists over other antiemetics, and it might be as a result of familiarity, perceived safety, and ease of administration.
The significance of the missing standardized and pre-printed post-anesthesia care unit (PACU) orders in PONV was reported by a significant percentage of respondents, and it might be a factor leading to practice variability and may be a barrier to adopting evidence-based care. Better clinical decision support systems and guidelines developed locally can assist in standardizing treatment methods. Few percent of the respondents claimed that their practice had developed formal treatment protocols of PONV.

The most frequently mentioned non-pharmacologic measures were intravenous fluids, supplemental oxygen, and inhaled Isopropyl alcohol. Although some of these methods have been researched more in the prevention aspect as opposed to treatment, clinicians might generalize the intuitive benefits to the treatment environment. The evidence-based practice of some of these interventions is rather scarce, which highlights the necessity of further research.
The comparisons of the PONV treatment effectiveness are made complex due to the disparate definition and measurement of outcome. The definitions, measurement and combination of nausea and vomiting into composite endpoints between studies vary. Interpretation is further confounded by differences in the perception of patients and thresholds of nurses to initiate treatment. To enhance the quality of research on PONV management, standardized definitions and extended observation time should be employed to better the quality of the study conducted.

Conclusion

Postoperative nausea and vomiting is one of the most uncomfortable complications to patients and still a significant measure of the quality of anesthesia treatments. Although significant progress has been made in explaining risk factors and the development of effective prophylaxis conceptualizations, very minimal focus has been placed on the management of established PONV in usual clinical settings. The results of this vignette survey are possible to discuss as insightful to the current trends of treatment preferences as well as to indicate significant gaps between evidence, recommendations, and clinical behaviour.

This paper shows that the most widely used agents in the treatment of established PONV are 5-HT3 receptor antagonists, especially those where no prophylaxis is given. Even though the clinicians were overall willing to switch drug classes in case of PONV after prophylaxis, a significant number still preferred to repeat 5-HT3 antagonists even when these agents were already administered. This trend indicates that familiarity, perceived safety, and ease of administration could have a high impact on

treatment choices and override guideline-based recommendations in some instances. Conversely, respondents showed less preference to re-administer other prophylactic agents which included metoclopramide, dexamethasone or droperidol, meaning that they selectively adhered to the principles of pharmacologic class switching.
The extensive number of pharmacologic and non-pharmacologic interventions noted in this study is indicative of the high number of variations in the practices of PONV treatment. This heterogeneity is probably an indicator of uncertainty about the relative effectiveness of the existing therapies, disparities in institutional guidelines, and a lack of high-quality evidence to guide treatment once the symptoms appeared. The high prevalence of non-pharmacologic interventions, commonly with scarce or preventive-oriented evidence, is another example of the extrapolation of preventive measures to treatment contexts where there are no conclusive data.

Absence of unified treatment steps to follow in post-anesthesia care units was reported by most of the respondents as a significant hindrance to effective and evidence-based management of PONV. Implementation and development of structured treatments algorithms with clinical decision support tools and continual education could contribute to decreasing the practice variation and increasing patient outcomes. Moreover, increased sensitivity to pharmacogenomic effects on the effect of antiemetic could also be used in the future to optimize personalized treatment approaches.
These findings can be interpreted with a number of limitations, which can be divided into the relatively small sample size, possible bias in responses, and the limitation of the methodologies based on vignettes per se. The study however presents a controlled evaluation of clinician decision-making and forms a basis of future studies.

To conclude, this paper identifies the continued use of 5-HT3 receptor antagonists in the management of established PONV, a high degree of variation in treatment methods, and lack of adherence to evidence-based guidelines. These conclusions highlight the necessity of effective clinical trials on the topic of PONV treatment, objective delimiting outcomes, and enhanced evidence-based guidance dissemination. These gaps are necessary to solve the management of known PONV and improve the quality of the overall perioperative care.

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