



ORIGINAL INVESTIGATION

Impact of extending prevention of postoperative nausea and vomiting for cancer surgical patients in the PACU: a before and after retrospective study

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Abstract

Backgrounds: Procedures for Postoperative Nausea and Vomiting (PONV) prevention are mostly based on identification of the risk factors before administering antiemetic drugs. The purpose of this study was to evaluate the impact of the extended use of antiemetic on the PONV in the Postanesthetic Care Unit (PACU).

Methods: Two separate 4-year periods (2007–2010, P1, and (2015–2018, P2) were evaluated. During P1, the protocol consisted of dexamethasone and droperidol for patients with a locally adapted high PONV score, followed by ondansetron for rescue in the PACU. For Period 2, dexamethasone (8 mg) and ondansetron (4 mg) were administered in patients under general or regional anesthesia, or sedation longer than 30 minutes, while droperidol (1.25 mg) in rescue was injected in cases of PONV in the PACU. An Anesthesia Information Management System was used to evaluate the intensity score of PONV (1 to 5), putative compliance, sedation, and perioperative opioid consumption upon arrival in the PACU.

Results: A total of 27,602 patients were assessed in P1 and 36,100 in P2. The administration of dexamethasone and ondansetron increased several fold ($p < 0.0001$). The high PONV scores were more improved in P2 than in P1, with scores (3+4+5) for P1 vs. P2, $p < 0.0001$. Overall, 99.7% of the patients in P2 were asymptomatic at discharge. Morphine consumption decreased from 6.9 ± 1.5 mg in P1 to 3.5 ± 1.5 mg in P2 ($p < 0.0001$).

Discussion: The extension of pharmacological prevention of PONV was associated with a decrease in the intensity of severe PONV. However, uncertainty regarding confounding factors should not be ignored.

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Introduction

Postoperative Nausea and Vomiting (PONV) is one of the oldest and most frequently cited complications of surgical anesthesia. This complication continues to occur despite risk-adapted local or general protocols and multiple new medications developed for its treatment.¹⁻⁵ An extensive body of research and publications exists on this topic, but the prevention of PONV remains a substantial matter of debate. We consider treatment of PONV to be a very essential part of our quality assurance program⁶; therefore, we continuously monitor it through our Anesthesia Information Management System (AIMS) and adjust our protocols to improve its outcome and incidence.⁶

A previous retrospective single center database analysis conducted as part of our quality assurance program assessed the incidence and trend of intensity of PONV in our PACU over a 5-year period.⁷ However, to improve outcomes, we changed our local protocol (2013) by shifting from a previous risk-tailored preventive prophylaxis (dexamethasone droperidol, ondansetron) to a generally simpler and broader prophylaxis to further reduce the incidence of PONV. In addition, in response to new general guidelines for the prevention of PONV⁸ we replaced intraoperative droperidol intravenous (IV) with ondansetron IV and used droperidol IV for rescue injection in the PACU.⁸⁻¹¹

We hypothesized that a better outcome would be achieved with the new protocol; therefore, we reevaluated outcomes by an AIMS interrogation. Our primary objective was to reassess the intensity score of PONV from 2015–2018 (P2) and to compare it to the trend of our historical data from 2007 to 2010 (P1), when PONV had been assessed based on a local risk-adapted PONV score protocol and had consisted of the same doses of dexamethasone, followed by intraoperative droperidol and then ondansetron in the PACU as a rescue.⁷ Our secondary outcomes included the putative compliance, defined as the application of the algorithm by expecting a steep increase in anti-PONV medication, the number of antiemetic including rescue medications, and the declared specific or other possible related side effects.

Methods

This study was a retrospective database analysis. Our institutional review board authorized the publication of data extracted from our AIMS system. All patients gave their written consent for the care teams to use anonymized data from their medical records for investigation during the first medical consultation (Avis nº 92012/33465). The study was in compliance with the Declaration of Helsinki and general data protection regulations.

As part of our quality assurance program, all patients were assessed with several multiple mandatory endpoints, which were submitted by the anesthesia providers to the AIMS database using our anesthesia software (Centricity, GE, USA). These points included the intensity of the PONV score, as assessed by the nurse in charge in the PACU, with the following 5-grade scale (1 = no sign, 2 = minor nausea, 3 = mild nausea and vomiting, 4 = severe nausea and vomiting, 5 = incoercible vomiting). If the PONV intensity was above scale 1 upon arrival in the PACU, droperidol (1.25 mg) was

given. Other mandatory manual entry endpoints included pain scores, sedation scores, analgesic requirements, and temperature upon arrival in the PACU.

Sedation scores were recorded on a scale of 0 to 4, being 0: not sedated, 1: lightly sedated, 2: mild sedation, 3: heavily sedated but awakable, 4: not awakable by physical stimulus.

The Centricity anesthesia databases (for P2) and Datex Ohmeda (for P1) servers were interrogated by a Sequential Query Language method (SQL) using Crystal reporting software V8 (USA) and Archive Browser®, respectively. The anesthesia database administrators (JLB-GW) underwent several cycles of formal training to master appropriate data extraction from the database.

Our cancer hospital performs major cervicofacial and general surgery, interventional radiology, brachytherapy, some pediatric surgery, and other diagnostic procedures. All anesthesia providers in our institution used the same classes of different anesthetic medications and identical monitoring for most procedures, although they have liberty to deviate from the established guidelines depending on the patient. Nevertheless, a continuous quality assurance program was ongoing in several areas during P1 through P2.

In this new locally approved protocol, the inclusion criteria were all patients who had undergone general anesthesia or conscious sedation with or without regional or anesthesia longer than 30 minutes, including day care surgery. Patients also had to have received dexamethasone (8 mg IV) after induction of anesthesia or sedation, followed by ondansetron (4 mg IV) before the end of surgery. Exclusion criteria were local anesthesia and missing data. For procedures less than 30 minutes in duration and for local anesthesia patients who transited through the PACU, if PONV was present, medications were given in the PACU.

In P1, a locally adapted protocol was used. This protocol was an algorithm-based on our previous database of PONV scores. We used a multivariate analysis of the early 2000s. Age, gender, history of PONV, and thyroid surgery were rated as major risks of PONV in our specific cancer teaching hospital. Depending on the score obtained, medication was administered incrementally, starting with no medication, droperidol at the end of surgery, or dexamethasone and droperidol during surgery, and finally, if symptoms were present in the PACU, ondansetron was given.

Patients were discharged after being assessed with a modified Aldrete score, including the before-discharge PONV intensity score. Possible adverse events, such as arrhythmia, hypotension, and allergy related to antiemetic medications were also checked.

We also extracted the incidence of PONV for different types of procedures and surgeries, as well as the effects of gender, age, and opioid requirements in P2; however, these extractions were not available in P1, except for opioid requirements, due to failure and shutdown of the old server.

Our new simplified protocol formally started in mid-2013; however, our database underwent a server migration in early 2014, therefore we judiciously skipped the 2013 and 2014 data because of probable loss of some data due to the migration. This also allowed some time for the anesthesia providers to adapt and assimilate the new protocol. Therefore, data were extracted from 2015 to 2018 (time of the study).

We verified each final result by a manual check of data extracted by the same query over a very short period (3 days) before extracting the targeted data for the broader period of time. Data were cleaned of redundancies and the missing data were calculated using Excel 2010 sheets.

Statistics

Prism V7 (Graphpad Software, San Diego, USA) and Microsoft Excel 2010 were used for statistical analysis. For comparison between periods, the patients were grouped as follows: no PONV (score 1), light PONV (score 2), heavy PONV (score 3, 4, and 5).

The Wilcoxon-Mann-Whitney and X² for trend tests were used to compare data between and within periods, respectively. The type I error was set at $\alpha = 0.05$ (two-sided),

Results

From 1 January 2015 to 31 December 2018 (P2), 36,100 patients were screened. PONV scores were extracted from the Centricity anesthesia database using Crystal Report V8 software. We also had PONV scores for 27,602 patients for P1 (1 January 2007 to 31 December 2010); these scores had been extracted from our previous anesthesia database (Datex anesthesia[®]) by Archive Browser[®]. The mean completeness of the data was 94% in P2; this percentage was superior to the completeness in P1 (83%) ($p < 0.0001$).

The number of patients and the medication protocol used during both periods are presented in Figure 1. The administration of dexamethasone and ondansetron increased several fold ($p < 0.0001$). Overall, 18,080 patients in P2 had both dexamethasone and ondansetron (80% of those patients were considered to be eligible for the extended protocol). The demographic characteristics and durations of surgery are reported in Table 1 (for P2 only).

Upon admission to the PACU, the incidence of PONV (score 2 to 5) was 3% in P1 and 0.9% in P2 ($p < 0.0001$) (Table 2). No difference was found when comparing scores 1 and 2, P1 vs. P2 $p = 0.47$. Rescue medication was administered for 787 patients (2%) in P1 and 1418 patients in P2 (4%) ($p = 0.01$). No direct or putative adverse events related to antiemetic could be extracted in this cohort of patients.

No statistically significant difference was noticed in sedation scores between P1 and P2. The incidence of patients who had sedation scores above 1 was of 6.9% in P2 vs. 6% in P1 ($p = 0.2$).

No significant difference was noticed in the intensity of PONV scores when assessing the different types of surgery or procedures in P2 (Table 3). At PACU discharge, the incidence of no PONV (score 1) was $99 \pm 0.5\%$.

The mean intraoperative morphine consumption was significantly less during P2 (3 ± 1.3 mg) than during P1 (6.9 ± 1.6 mg) ($p < 0.0001$). The mean PACU morphine consumption was significantly lower in P2 (2.6 ± 0.91 mg) than in P1 (11.6 ± 2.3 mg) ($p < 0.0001$). PONV scores higher than 2 were more frequent in the patients who received morphine than in the patients who had no morphine ($p = 0.0028$).

The intensity of the PONV score in P2 was significantly higher in women under 50 years old (8%) than in their male counterparts (2.2%) ($p < 0.0001$).

Discussion

The findings of this study show that expanding the indications of prevention of PONV from a "locally-adapted PONV risk" to a "fit-for-most" protocol improved the intensity of heavy PONV scores upon arrival in the PACU when compared with our historic data of previous years. However, while the amounts of administered antiemetic medications increased several folds, the intraoperative opioid consumption was decreased by 50%. The protocol reduced by half the absolute number of patients having severe nausea and vomiting, despite the increase (30%) in the total number of patients. Nevertheless, the need for rescue medications increased by 100%, which was mostly due to low-intensity PONV (score 2) since scores of 3 to 5 were significantly less common in this period. In addition, medications were not administered intraoperatively for sedation and procedures of less than 30 minutes or for local anesthesia, as directed by the new protocol. Other factors, such as increased attention by the nursing staff and improved medical education through a sustained quality assurance program, could also have played a part.

Overall, 80% of the patients apparently underwent a double treatment (dexamethasone followed by ondansetron); however, we can only indirectly confirm this 80% compliance because of the retrospective nature of the study. We also cannot interrogate our old database (P1); therefore, no comparative previous data about minimum putative compliance could be extracted.

In our new extended protocol, we administered dexamethasone and ondansetron in all anesthesia cases longer than 30 minutes, and we used droperidol as a rescue treatment in the PACU since potentially more cardiovascular effects, such as QT prolongation, occur with droperidol than with ondansetron.¹² We therefore used droperidol for cases requiring additional PONV in the PACU as a rescue administration. Despite this "fit-for-most" strategy, a very small proportion of patients still had moderate to severe PONV scores. Nevertheless, the patients with very high PONV scores (incoercible vomiting) showed significantly decreased scores (tenfold). A recently published "before and after" study assessed the effect of the simplified algorithm in a restricted number of patients over two weeks.¹³ Our study had a retrospective design and concerned all our patients in a much longer period in a real-life situation.

We believe that the use of a simplified algorithm, without calculating the local score,¹⁴ had a better outcome for most patients regarding a high PONV score than was obtained with our historical group of patients whose preventive treatment administration was based on a locally adapted risk score. We acknowledge that this improvement might not totally be related to the change in the protocol and that other factors, such as the decrease in morphine consumption, might have played a part. However, we did not assess a cost-benefit or conduct a cost-effect analysis, and this could be considered a shortcoming. In addition, we were unable to detect any significant adverse effects related to the threefold increase in PONV medications. We also cannot exclude the potential effects of missing data in relation to the medications used for PONV, especially when a putative event might have been reported elsewhere or in another folder by mistake.

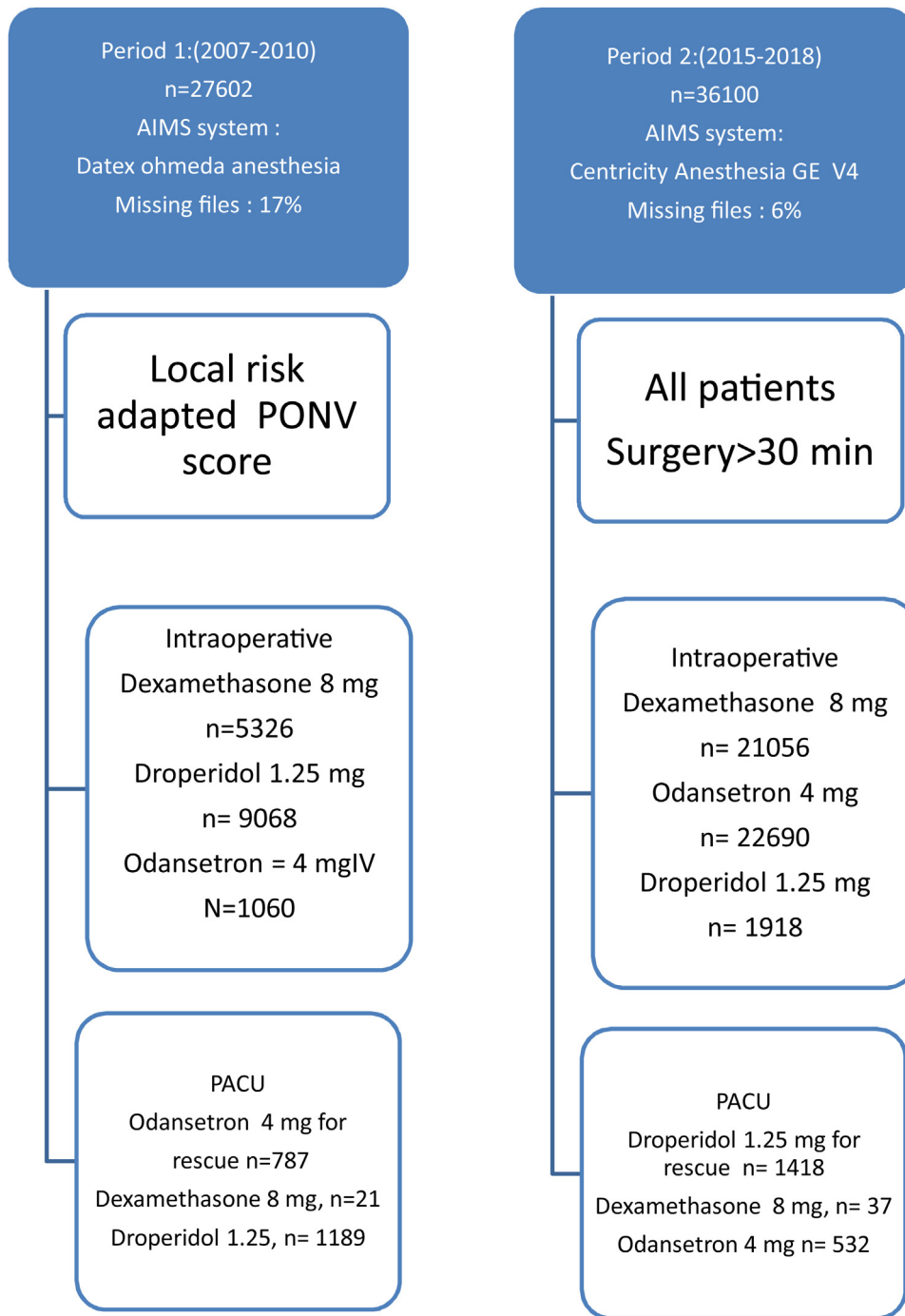


Figure 1 Number of patients and medication used in both periods.

Table 1 Gender ratio, weight, age, height, and duration of surgery (2015–2018).

Year	Number of anesthesia	Gender ratio F/M	Weight Kg (SD)	Age year (SD)	Height cm (SD)	Duration of surgery (SD)
2015	8590	69%	69.2 (15.8)	56 (14)	165 (9)	129 (108)
2016	8900	67%	69.9 (16.4)	57 (15)	166 (9)	146 (129)
2017	9306	67%	69.6 (16.3)	56 (15)	166 (10)	179 (153)
2018	9304	66%	69.6 (16.8)	57 (15)	166 (10)	180 (161)

Table 2 Comparison of Light and heavy intensity PONV score between P1 and P2 for intensity PONV score (3–4–5) P2 vs. P1. $p < 0.0001$, PONV score (1–2) P2 vs. P1.

Period	Score	1	2		3	4	5	% Missing data
P1	2007	4196	198	P1	68	29	2	32.4%
	2008	4908	228		92	26	14	20.7%
	2009	5708	158		87	36	3	10.7%
	2010	6360	141		63	28	5	13.9%
	2015	8527	314		56	23	1	5.5%
P2	2016	8295	353	P2*	59	19	1	5.7%
	2017	8485	280		43	14	0	5.2%
	2018	8551	253		41	17	2	4.9%

Table 3 Type of surgery or interventional procedures and the intensity of PONV in P2 (2015–2018) only.

Score	Surgery					Interventional				Not reported
	Gynecological/ General surgery	Thyroid	Breast	ENT	Plastic and dermatology	Radiology	Endoscopy	Pediatrics	Brachytherapy	
1	3770	1000	6120	4050	2120	3120	2388	3188	1426	3045
2	248	37	423	115	93	159	98	13	24	134
3	43	4	45	16	9	28	22	1	5	26
4	18	3	17	4	4	15	9	3	0	8
5	01	0	0	00	1	1	0	0	0	1

ENT, Ear, Nose and Throat.

In addition, the average decrease of 3 mg of intraoperative morphine might have had its own effect on decreasing the intensity of PONV.

Another weakness of this study is the inability to report PONV scores at 24 hours, since our postoperative (Dx Care®) software is not connected to our intraoperative database (Centricity) and cannot be extracted in the same manner. However, we believe these 24-h PONV scores would not change significantly because treatments are given according to demand and are not given preemptively. The major risks for PONV include general anesthesia, morphine consumption, inhalational anesthesia, and type of surgery.^{15–19} We have been decreasing opioid consumption over several years,²⁰ and this trend is ongoing.

Our preliminary goal after each new protocol is to decrease the incidence of PONV. However, since our institution conducts a significant number of surgeries, including gynecologic, breast, thyroid, and general surgeries, and yields, in theory, an incidence of PONV around 60%, we believe that switching to the simplified general algorithm did not overwhelmingly increase the cost, given the benefit of the decrease in the incidence of severe PONV. Nevertheless, because of the positive results, some savings have probably been secured because of the fewer number of patients having severe PONV, which is known to have expensive side effects, especially in ambulatory patients.

One point to note is that this assessment of nearly 63,000 patients over two periods would not have been possible without using our AIMS systems. However, once again, our AIMS system served as part of a quality assurance tool that allowed us to indirectly assess our new protocol.^{6,7}

This study has other limitations, including its monocentric and retrospective nature. In addition, some data, such as all the demographic characteristics and types of surgery, were not available for P1 because the server was shut down in 2011. In addition, the 24-h postoperative scores are not stored on the same server and are not registered with the same software; therefore, they are not accessible by SQL extraction from the anesthetic software and require manual assessment. A last limitation was that the locally-risk-adapted PONV score could not be transcribed from our preoperative anesthetic evaluation to our current intraoperative anesthetic record software (Centricity anesthesia GE, USA). Consequently, we only have putative assumptions for P1, as the patients undergoing intraoperative treatments were high-risk patients according to our own local protocol. By contrast, in P2, this assumption would not be applicable as the indication for treatment included all patients except those having a surgery of less than 30 minutes.

Rescue injection in the PACU showed the efficiency of the protocol, since 99.5% of the patients were discharged with an intensity score of 1 for PONV. These positive findings are probably the maximum achievable when selecting those patients in whom an additional dose of droperidol was given without risking the synergic effect of QT prolongation due to the additional effect of ondansetron and droperidol.¹¹

Conclusions

The change in our practice from adapted risk factors to a simplified “fit-for-most” algorithm was followed by a reduced intensity of severe PONV in the PACU in our population of cancer patients. We do not have enough data to

conclude that this new strategy was fully responsible for the reduction in heavy PONV, as uncertainty about other confounding factors, such as compliance, morphine consumption, and missing data, should also be considered. In addition, before generalizing this protocol, other factors should also be considered, including cost and side effects.²¹ Overall, however, this study showed once again that AIMS systems can serve in quality assurance programs over decades, even if a major switch in equipment or clinical protocol is performed at some point.

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Conflicts of interest

The authors declare no conflicts of interest.

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