Journal of the Pediatric Orthopaedic Society of North America 11 (2025) 100174

Contents lists available at ScienceDirect

Journal of the Pediatric Orthopaedic Society of North America

journal homepage: www.jposna.com

Original Research

Fosaprepitant Use as an Antiemetic to Prevent Postoperative Nausea and Vomiting in Pediatric Spinal Fusion Patients May Be Associated With More Rapid Transition to Oral Pain Medication and Reduced Length of Stay

Jennifer Busse [1,*]; Aaron Louie [1]; Jennifer Crotty [2]; Albert Lin [1]; Zarema Muratova [3]; Matan Malka [2]; Ritt Givens [2]; Benjamin Roye [2]; Michael Vitale [2]; William Schechter [1,4]

[1] Department of Anesthesiology, Columbia University Irving Medical Center, New York, NY, USA
[2] Department of Orthopedics, Columbia University Irving Medical Center, New York, NY, USA
[3] Department of Pharmacy, Columbia University Irving Medical Center, New York, NY, USA
[4] Department of Pediatrics, Columbia University Irving Medical Center, New York, NY, USA

ARTICLE INFO

Keywords:
Pediatrics
Spinal fusion
Postoperative nausea and vomiting
Length of stay

ABSTRACT

Background: Significant postoperative nausea and vomiting (PONV) in pediatric patients undergoing posterior spinal fusion is common and limits recovery, prolonging hospital stay. Fosaprepitant is a long-acting antiemetic and works by blocking substance P binding to the neurokinin-1 (NK_1) receptor. There is evidence that its perioperative use substantially reduces PONV in adults, but there is a dearth of literature on its use in pediatric PONV. We seek to elucidate whether a postoperative dose of fosaprepitant in pediatric posterior instrumentation and fusion (PSIF) patients decreases PONV, thus improving recovery and decreasing the length of hospital stay.

Methods: This is a retrospective chart review of 173 pediatric patients with idiopathic scoliosis undergoing PSIF. The anesthetic methodology was standardized among both groups. The cohort was divided into two groups according to the use of fosaprepitant intraoperatively (or within four hours postoperatively) or no use. We examined patient characteristics, fosaprepitant dose, incidence of PONV, time to transition from parenteral to oral opioids, and length of hospital stay.

Results: 78 (45%) patients received fosaprepitant and 95 (55%) did not. There were no statistically significant differences between groups based on demographics or intraoperative management. No significant difference was found in the incidence of PONV between the groups, but there was a reduction in the number of rescue antiemetics required and a quicker transition from parenteral to oral opioids in the fosaprepitant group. There was also a significantly decreased length of stay.

Conclusions: While fosaprepitant did not significantly decrease PONV in pediatric PSIF patients, it was associated with decreased use of additional antiemetics. The patients also demonstrated a more rapid transition to oral from parenteral opioids and a shorter length of hospital stay. A larger study may show a statistically significant reduction in PONV in patients who received fosaprepitant. Future studies are needed to elucidate the optimal dose and timing needed to treat PONV in pediatrics.

Key Concepts:
(1) Spinal fusion surgery patients are at risk of having significant postoperative nausea and vomiting.
(2) Fosaprepitant is an effective agent to treat postoperative nausea and vomiting in adults, but has not been extensively studied in pediatrics for this purpose.

Level of Evidence: The level of evidence is a 3 as it is a cohort study looking at the relationship between an exposure and an outcome.

* Corresponding author: Columbia University, 622 West 168th Street, New York, NY 10032, USA.
E-mail address: jab2243@cumc.columbia.edu (J. Busse).

https://doi.org/10.1016/j.jposna.2025.100174
Received 10 December 2024; Received in revised form 7 March 2025; Accepted 7 March 2025
Available online 14 March 2025

Introduction

Antiemetics are prescribed in a wide range of clinical scenarios where nausea and vomiting are prevalent, such as chemotherapy, pregnancy, opioid intake, and post-surgery. The incidence of postoperative nausea and vomiting (PONV) in pediatric patients is reported to be between 33.2% and 82%, twice as frequent as adults [1–3]. Most commonly, antiemetics within the class of serotonin 5-HT3 receptor antagonist (e.g., ondansetron, palonosetron, and granisetron) are used to treat PONV [4–6]. Fosaprepitant, a prodrug of aprepitant, prevents acute and delayed vomiting by inhibiting central emetic pathways triggered from the binding of substance P to the NK_1 receptor. It also augments the antiemetic activities of corticosteroids and 5-HT3 receptor antagonists to further inhibit emesis [7]. It is less frequently used for PONV, especially in pediatrics, and is not yet FDA-approved for this purpose.

Nevertheless, promising evidence exists in adult studies where aprepitant (another NK_1 receptor antagonist), with doses as low as 40 mg (mg) administered within four hours of anesthesia induction, effectively reducing PONV postoperatively [8]. There is further evidence that, in adults, fosaprepitant may be more effective than 5-HT3 receptor antagonists in treating PONV postoperatively [9–11]. Fosaprepitant is approved for use in children aged 6 months or older for treatment of chemotherapy-induced nausea and vomiting. We chose a similar dosing to that recommended for pediatric patients receiving chemotherapy [12–14]. Currently, the data on the efficacy and dosing of fosaprepitant for PONV prevention in pediatric patients is limited [15–17].

Patients undergoing posterior spinal instrumentation and fusion (PSIF) are exposed to a variety of factors that promote nausea and vomiting, such as exposure to anesthesia, opioid intake, intestinal dysmotility, and fluid shifts. As such, they frequently suffer from substantial PONV; however, data on this is limited [17]. This limits their ability to tolerate physical therapy and oral intake of medication and nutrition, delaying hospital discharge. Upon reviewing our highly standardized perioperative management of pediatric patients who had PSIF surgery, we identified risk factors associated with PONV. As part of the development of our enhanced recovery after surgery (ERAS) guidelines, we decided to start including fosaprepitant based on the literature in adults that it was efficacious for PONV, and because it is safe and effective for nausea and vomiting in pediatric oncology patients. Our primary aim was to see if patients who received fosaprepitant intraoperatively, or within the first four hours postoperatively (while in the post-anesthesia care unit), had a reduced incidence of PONV throughout the hospital stay. Our secondary aims included: determining whether there was a decreased requirement for rescue antiemetics in the first 24 postoperative hours, a reduction in time for transition to oral opioids (dictated by the ability to take oral fluids and ability to ambulate), and whether length of hospital stay was shortened consequently.

Methods

This study was a retrospective chart review of 173 consecutive pediatric scoliosis patients who underwent PSIF surgery from 2021 to 2023. Patients were 5–23 years of age and had an American Society of Anesthesiologists (ASA) physical status ranging from I-III. We excluded any patients with neuromuscular or syndromic scoliosis. Fosaprepitant administration prophylactically during the intraoperative or postoperative period became standardized in these patients in 2022. The cohort was divided into two groups: those who were given fosaprepitant intraoperatively or within four hours postoperatively (fosaprepitant+), and those who were not (fosaprepitant-). Patients who received fosaprepitant were dosed as per the recommended pediatric guidelines for nausea prevention in chemotherapy administration at 5 mg/kg (kg) to an upper limit of 150 mg [12–14]. Through the anesthetic record, we examined patient characteristics (i.e., age, sex, and weight), fosaprepitant dose, intraoperative administration of intraoperative crystalloid, blood products (packed red blood cells and albumin), and opioids (based on morphine milligram equivalents). We reviewed the electronic medical record and the standardized notes from our Pediatric Pain Service, which followed all PSIF patients postoperatively, and noted every patient's incidence of PONV, time to transition to oral from parenteral opioids, and length of hospital stay. PONV was determined from the Pain Service's daily progress note starting on day one after PSIF, where the occurrence of nausea and vomiting was marked as either present or absent up until the transition to oral opioids from intravenous opioids.

For all PSIF cases, standardized induction medications included a combination of midazolam and/or fentanyl, propofol and rocuronium with doses based on weight and titrated to hemodynamic effect. Maintenance of anesthesia included infusions administered at the discretion of the anesthesia provider of propofol, phenylephrine, remifentanil, with additional fentanyl, morphine or hydromorphone as needed. Rocuronium was administered in low doses or by infusion when indicated at doses that allowed for interpretation or enhancement of evoked potentials. Low doses of sevoflurane were occasionally administered by inhalation. Phenylephrine by infusion was utilized in some cases to maintain acceptable mean arterial pressures. The infusion rates used during maintenance were usually and approximately as follows: propofol at 100–250 μg/kg/minute (mcg/kg/min), phenylephrine at 10 mcg/min, and remifentanil at 0.05–0.2 mcg/kg/min.

In addition, all patients were also given antibiotic prophylaxis with tobramycin and cefazolin, tranexamic acid 5 mg mg/kg/hour, dexamethasone 6 mg and intravenous acetaminophen 15 mg/kg at the start of surgery. Ondansetron 0.15 mg/kg up to 4 mg/dose was administered to all patients at the end of surgery, and thereafter as needed to treat residual PONV. Neuromuscular blockade was reversed with suggamadex 2 mg/kg. To be included in the fosaprepitant group, the patient had to receive it intraoperatively or in the first four hours postoperatively while in the PACU. A demand only hydromorphone patient-controlled analgesia (PCA) machine was started for each patient postoperatively at standardized doses based on weight, with a demand dose of 0.003 mg/kg available every 10 min and a clinician bolus of 0.005 mg/kg.

The incidence of pediatric PONV reported in the literature was a minimum of 33%. When the non-superiority margin of fosaprepitant was set at 25% with an α value of 0.05 and statistical power of 80%, the required number of patients for each group was 46. Statistical analysis was performed using R version 4.2.2 using the readxl package [18,19]. Data are presented as means±standard deviations and medians with a range. Categorical parameters were compared by Pearson's Chi-squared test, numerical parameters were compared by Mann–Whitney *U* Test, and statistical significance was determined as a *P* value below .05.

Results

The study included 173 pediatric PSIF patients, of which 79 (46%) patients received fosaprepitant and 94 (54%) did not. The most frequently used dose was 120 mg and the mean age of the whole cohort was 14.6 years. There were no statistically significant differences between groups in age, weight, BMI, sex, duration of surgery, intraoperative opioid intake, procedure duration, amount of intraoperative crystalloid or blood products given, or estimated blood loss (Table 1).

There was no statistically significant difference in the incidence of nausea or vomiting between the groups (36% in the fosaprepitant+group and 23% in the fosaprepitant-group), but there was a statistically significant decrease in the number of doses of additional antiemetics required ($P = .016$, median 1 with a range of 0–4 in the fosaprepitant+ group and median 1 with a range of 0–6 in the fosaprepitant-group). There was also a significant reduction in time to transition from parenteral to oral opioids ($P = .012$, 90% transitioned in the first 24 h postoperatively in the fosaprepitant+group and 74% in the fosaprepitant-group). Length of hospital stay among those in the fosaprepitant+group was significantly shorter by 24 h ($P = .0001$, median of 72 h in the fosaprepitant+ group and 96 h in the fosaprepitant-group). In a subgroup analysis, the length of hospital stay and transition to oral from

Table 1
Demographic and clinical data.

	Fosaprepitant (+) (n = 79)	Fosaprepitant (−) (n = 94)	*P* value‡
Age (years)*	14.75 (2.87)	14.42 (3.09)	.62
Weight (kg)*	51.29 (19.21)	52.35 (14.81)	.553
BMI*	22.03 (7.45)	20.70 (4.91)	.185
Sex†			
Nonbinary	2 (3%)	0 (0%)	.131
Female	51 (65%)	56 (59%)	
Male	25 (32%)	39 (41%)	
Duration of surgery (min)*	271.76 (65.61)	276.59 (74.25)	.955
MMEs/kg (ideal body weight) intraoperative opioid*	8.22 (14.17)	6.36 (2.63)	.41
Intraoperative crystalloid (ml)*	2319.96 (797.03)	2235.74 (768.88)	.6409
Blood loss (ml)*	392.95 (172.97)	420.11 (205.60)	.3249
Blood products given (ml)*	190.99 (262.11)	267.15 (367.78)	.223

* Data are presented as the mean (standard deviation).
† Data are presented as total number (percent) in each group.
‡ Data were analyzed using Pearson's Chi-squared test for categorical parameters and Mann–Whitney U Test for numerical parameters.

parenteral opioids in those with any PONV was also shorter among those in the fosaprepitant+ group ($P = .047$and 0.029, respectively) (Table 2).

Discussion

The antiemetic class of choice for PONV in pediatrics, 5HT-3 inhibitors, are limited by their duration of action as well as at times, efficacy. This class of antiemetics does have considerable side effects including headache, fatigue, dizziness, constipation, and QTc prolongation [20–22]. There are a variety of alternative or adjunctive antiemetics with different mechanisms of action including dexamethasone, diphenhydramine, metoclopramide, prochlorperazine, and fosaprepitant, which has been promising in adults as a superior treatment to ondansetron in PONV as described above. Like 5HT-3 inhibitors, side effects related to fosaprepitant include fatigue, drowsiness, dizziness, headache, diarrhea, and abdominal discomfort. Fosaprepitant is, however, unlikely to cause QTc prolongation [23].

Table 2
Postoperative outcomes.

	Fosaprepitant (+) (n = 79)	Fosaprepitant (−) (n = 94)	*P* value‡
Incidence of isolated nausea*	29 (36%)	22 (23%)	.813
Incidence of isolated vomiting*	12 (15%)	10 (11%)	.263
Incidence of any PONV*	34 (43%)	36 (38%)	.53
Transition to oral opioids in first 24 h*	70 (89%)	70 (74%)	.012
Number of doses of additional antiemetics needed per patient in the first 24 h†	1 (1)	1 (2)	.016
Length of stay (hours)†	72 (24)	96 (48)	.0001
Length of stay (hours) in patients with any PONV†	84 (24)	95 (24)	.047
Transition to oral opioids in first 24 h in patients with any PONV*	32 (94%)	27 (75%)	.029

* Data are presented as total number (percent) in each group.
† Data are presented as median (interquartile rage) in each group.
‡ Data were analyzed using Pearson's Chi-squared test for categorical parameters and Mann–Whitney U Test for numerical parameters.

This study suggests a prophylactic single dose of fosaprepitant given intraoperatively, or soon after surgery to pediatric PSIF patients, may have facilitated an earlier transition to oral opioids and therefore may have contributed to a decreased length of stay observed in those who received the medication. We have not studied this specifically, but we believe these patients may have had a more rapid ability to tolerate physical therapy early on postoperative day 1 without nausea and vomiting associated with standing, thus allowing for early transition to oral opioids, reducing the length of stay by an average of 24 h. There is evidence that the NK_1receptor may play a role in the autonomic nervous system responses to both blood pressure as well as colonic dilatation, both of which may play a unique role in mitigating nausea and vomiting in post-surgical PSIF patients [24]. While we did not find fosaprepitant decreased the frequency of nausea or vomiting in pediatric PSIF patients, over the course of their hospitalization, it did slightly decrease the likelihood of requiring additional antiemetics. It is likely that in the fosaprepitant group, episodes of vomiting were brief and resolved quickly. This contrasted with the group where fosaprepitant was not given, where vomiting was more prolonged, repetitive, and more likely to require multiple additional antiemetics. We believe this is why giving fosaprepitant may have allowed for a more rapid transition to oral from enteral opioids, leading to a shorter length of hospital stay.

Before this study, our standard prevention of nausea and vomiting in pediatric PSIF patients was a combination of ondansetron and dexamethasone given intraoperatively as per usual guidelines [4,5]. Given the data, it seems the addition of fosaprepitant to this regimen may be more effective than ondansetron and dexamethasone alone in the prevention PONV in these patients, therefore our institution now includes fosaprepitant administration as part of our postoperative PSIF protocol. Since fosaprepitant has a longer half-life elimination than ondansetron, it seems that fewer additional antiemetics were needed and tolerance for oral medications was hastened.

There are limitations to our small, retrospective analysis. First, the dosing and timing of fosaprepitant administration were not standardized across all patients. We decided that to be included in the fosaprepitant group, the drug had to be given intraoperatively or within four hours postoperatively. Confounding factors like patients' comorbidities, the duration of time the patient spent asleep during the first 24 postoperative hours, and even the timing of when patients were evaluated by the Pediatric Pain Service may influence the incidence of nausea and vomiting across the patient groups. Some of the data was simply too difficult to extract retrospectively from the patient record, while other information was not recorded at all. For example, we expected variability in the amount of postoperative opioids received by each patient, which is usually titrated using PCA, but we could not collect this data in our study due to the large heterogeneity in how PCA usage was documented. Additionally, the transition to oral opioids and length of stay could be contributed to other factors not examined, like the return of bowel function, pain control, and time to ambulation. Minor variations in anesthetic and neuromuscular reversal agents were unlikely to affect outcomes.

Given the dearth of data on fosaprepitant use in pediatric PONV [15–17,25], a larger, ideally prospective study may have also shown a statistically significant reduction in nausea and vomiting in patients who receive fosaprepitant in the immediate postoperative period, as well as a more robust decrease in the need for additional antiemetics. Utilization of a standardized measurement for nausea and vomiting severity for each patient in such a study would also be useful to explain the need for less additional antiemetics better. Future studies are needed to elucidate the ideal dose and timing needed to prevent and treat PONV in pediatric patients after long, taxing surgeries like PSIF.

Conclusions

This study showed that administration of fosaprepitant intraoperatively, or within four hours postoperatively, to pediatric PSIF patients appears to decrease the need for additional antiemetics in the first 24 h postoperatively, which may shorten the time to transition to oral opioids, and potentially therefore reduce the length of stay by nearly a full day. No significant differences were seen in the incidence of nausea and vomiting reported on postoperative day one, however. A larger prospective study looking at factors such as severity of nausea and vomiting, pain control, return of bowel function, and timing to first ambulation would be important in further elucidating the effectiveness of fosaprepitant on decreasing length of stay and incidence of PONV in pediatric spinal fusion patients.

Consent for publication

The author(s) declare that no patient consent was necessary as no images or identifying information are included in the article.

Author contributions

Jennifer Busse: Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Aaron Louie:** Writing – review & editing, Investigation, Data curation, Conceptualization. **Jennifer Crotty:** Writing – review & editing, Methodology, Investigation, Data curation, Conceptualization. **Albert Lin:** Writing – review & editing, Methodology, Conceptualization. **Zarema Muratova:** Writing – review & editing, Visualization, Methodology, Investigation. **Matan Malka:** Writing – review & editing, Data curation. **Ritt Givens:** Data curation. **Benjamin Roye:** Writing – review & editing, Visualization, Methodology, Conceptualization. **Michael Vitale:** Writing – review & editing, Methodology, Conceptualization. **William Schechter:** Writing – original draft, Visualization, Supervision, Methodology, Investigation, Conceptualization.

Funding

None.

Declarations of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical approval

This study was approved by the Institutional Review Board of Columbia University and the requirement for informed consent was waived.

References

[1] Höhne C. Postoperative nausea and vomiting in pediatric anesthesia. Curr Opin Anaesthesiol 2014 Jun;27(3):303–8. https://doi.org/10.1097/ACO.0000000000000073. PMID: 24722005.
[2] Lerman J. Surgical and patient factors involved in postoperative nausea and vomiting. Br J Anaesth 1992;69:24S–32S.
[3] Apfel CC, Kranke P, Piper S, Rüsch D, Kerger H, Steinfath M, et al. Nausea and vomiting in the postoperative phase. Expert- and evidence-based recommendations for prophylaxis and therapy. Anesthetist 2007;56:1170–80.
[4] Gan TJ, Belani KG, Bergese S, Chung F, Diemunsch P, Habib AS, et al. Fourth consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg 2020 Aug;131(2):411–48. https://doi.org/10.1213/ANE.0000000000004833. Erratum in: Anesth Analg. 2020 Nov;131(5):e241. doi: 10.1213/ANE.0000000000005245. PMID: 32467512.
[5] Jin Z, Kovac AL, Meyer TA, Urman RD, Apfel CC, Ayad S, et al. Fourth consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg 2020 Aug;131(2):411–48. https://doi.org/10.1213/ANE.0000000000004833. Erratum in: Anesth Analg. 2020 Nov;131(5):e241. PMID: 32467512.
[6] Kovac AL. Management of postoperative nausea and vomiting in children. Paediatr Drugs 2007;9(1):47–69.
[7] Lasseter KC, Gambale J, Jin B, Bergman A, Constanzer M, Dru J, et al. Tolerability of fosaprepitant and bioequivalency to aprepitant in healthy subjects. J Clin Pharmacol 2007 Jul;47(7):834–40. https://doi.org/10.1177/0091270007301800. Epub 2007 May 24. PMID: 17525168.
[8] Singh PM, Borle A, Rewari V, Makkar JK, Trikha A, Sinha AC, et al. Aprepitant for postoperative nausea and vomiting: a systematic review and meta-analysis. Postgrad Med J 2016 Feb;92(1084):87–98.
[9] Emend (fosaprepitant) for injection [prescribing information]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; May 2022.
[10] Murakami C, Kakuta N, Kume K, Sakai Y, Kasai A, Oyama T, et al. A comparison of fosaprepitant and ondansetron for preventing postoperative nausea and vomiting in moderate to high-risk patients: a retrospective database analysis. BioMed Res Int 2017;2017:5703528. https://doi.org/10.1155/2017/5703528. Epub 2017 Dec 19. PMID: 29410964; PMCID: PMC5749222.
[11] Padilla A, Habib AS. A pharmacological overview of aprepitant for the prevention of postoperative nausea and vomiting. Expet Rev Clin Pharmacol 2023 Jan-Jun;16(6):491–505. https://doi.org/10.1080/17512433.2023.2209722. Epub 2023 May 8. PMID: 37128935.
[12] Huang Q, Wang F, Liang C, Huang Y, Zhao Y, Liu C, et al. Fosaprepitant for postoperative nausea and vomiting in patients undergoing laparoscopic gastrointestinal surgery: a randomised trial. Br J Anaesth 2023 Oct;131(4):673–81. https://doi.org/10.1016/j.bja.2023.06.029. Epub 2023 Jul 7. PMID: 37423834.
[13] Weinstein C, Jordan K, Green SA, Camacho E, Khanani S, Beckford-Brathwaite E, et al. Single-dose fosaprepitant for the prevention of chemotherapy-induced nausea and vomiting associated with moderately emetogenic chemotherapy: results of a randomized, double-blind phase III trial. Ann Oncol 2016 Jan;27(1):172–8. https://doi.org/10.1093/annonc/mdv482. Epub 2015 Oct 8. PMID: 26449391; PMCID: PMC4684151.
[14] Roila F, Molassiotis A, Herrstedt J, Aapro M, Gralla RJ, Bruera E, et al. Participants of the MASCC/ESMO Consensus Conference Copenhagen 2015. 2016 MASCC and ESMO guideline update for the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting and of nausea and vomiting in advanced cancer patients. Ann Oncol 2016;27(suppl 5):v119–33.
[15] Ames WA, Machovec K. An update on the management of PONV in a pediatric patient. Best Pract Res Clin Anaesthesiol 2020 Dec;34(4):749–58. https://doi.org/10.1016/j.bpa.2020.05.007. Epub 2020 Jun 10. PMID: 33288124.
[16] Kanaparthi A, Kukura S, Slenkovich N, AlGhamdi F, Shafy SZ, Hakim M, et al. Perioperative administration of Emend® (aprepitant) at a tertiary care children's hospital: a 12-month survey. Clin Pharmacol 2019 Nov 27;11:155–60. https://doi.org/10.2147/CPAA.S221736. PMID: 31819673; PMCID: PMC6885572.
[17] Syed AN, Baghdadi S, Muhly WT, Baldwin KD. Nausea and vomiting after posterior spinal fusion in adolescent idiopathic scoliosis: a systematic and critical analysis review. JBJS Rev 2024 Jan 9;12(1). https://doi.org/10.2106/JBJS.RVW.23.00176. PMID: 38194592.
[18] R Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2022. 3-900051-07-0, URL, http://www.R-project.org/.
[19] Wickham H, Bryan J. Readxl: read excel files. https://readxl.tidyverse.org; 2023. https://github.com/tidyverse/readxl.
[20] Mehta D, Sanatani S, Whyte SD. The effects of droperidol and ondansetron on dispersion of myocardial repolarization in children. Paediatr Anaesth 2010;20:905–12.
[21] Lau Moon Lin M, Robinson PD, Flank J, Sung L, Dupuis LL. The safety of metoclopramide in children: a systematic review and meta-analysis. Drug Saf 2016 Jul;39(7):675–87. https://doi.org/10.1007/s40264-016-0418-9. PMID: 27003816.
[22] LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): national institute of diabetes and digestive and kidney diseases. Antiemetic Agents; 2012 [Updated 2018 Jan 15].
[23] Marbury TC, Jin B, Panebianco D, Murphy MG, Sun H, Evans JK, et al. Lack of effect of aprepitant or its prodrug fosaprepitant on QTc intervals in healthy subjects. Anesth Analg 2009 Aug;109(2):418–25. https://doi.org/10.1213/ane.0b013e3181ac1066. PMID: 19608812.
[24] Kurogochi K, Uechi M, Orito K. Involvement of neurokinin-1 receptors in the autonomic nervous system in colorectal distension-induced cardiovascular suppression in rats. Front Pharmacol 2022 Oct 19;13:1020685. https://doi.org/10.3389/fphar.2022.1020685. PMID: 36339556; PMCID: PMC9627219.Aug;109(2):418-425. doi: 10.1213/ane.0b013e3181ac1066. PMID: 19608812.
[25] Saito Y, Kumamoto T, Arima T, Shirakawa N, Ishimaru S, Sonoda T, et al. Evaluation of aprepitant and fosaprepitant in pediatric patients. Pediatr Int 2019 Mar;61(3):235–9. https://doi.org/10.1111/ped.13780. Epub 2019 Mar 5. PMID: 30615239.