Original Article

Antiemetic Prophylaxis with Droperidol in Morphine-Based Intravenous Patient Controlled Analgesia

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ABSTRACT

Objective: To assess the antiemetic advantages and sedative impacts of droperidol when used in conjunction with morphine-based intravenous patient-controlled analgesia (IV-PCA).

Study Design: Cohort study

Place and Duration of Study: This study was conducted at the Lady Reading Hospital in Peshawar from December 2022 to November 2023.

Methods: Patients who underwent major surgery and utilized morphine-based IV-PCA experienced a primary outcome characterized by the rate of any postoperative nausea and/or vomiting (PONV) occurring within 72 hours after the surgical procedure.

Results: Nausea and vomiting between 0-12 hours after operation in Droperidol Group was 10.7% and 14.7% in control group. Nausea and vomiting between 12-36 hours after operation in Droperidol Group was 12.0% and 17.3% in control group. Nausea and vomiting between 36-60 hours after operation in Droperidol Group was 13.3% and 16.0% in control group. Nausea and vomiting between 60-72 hours after operation in Droperidol Group was 12.7% and 16.7% in control group.

Conclusion: Droperidol into intravenous patient-controlled analgesia (IV-PCA) regimens has demonstrated a notable reduction in the risk of postoperative nausea and vomiting (PONV).

Key Words: Droperidol, Morphine, Antiemetic prophylaxis, Patient controlled analgesia

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INTRODUCTION

Postoperative nausea and vomiting (PONV) emerges as a prevalent source of patient distress post-surgery, with reported rates ranging from 20% to 40%[1]. The multifactorial nature of PONV is evident, encompassing patient-related factors such as sex, smoking status, and a history of PONV[2], as well as surgery-related factors like the type of surgical procedure, and factors related to anesthesia including the use of volatile and opioids anesthetics. Incidence of PONV can vary around 80% in high risk patients[3].

PONV is often reported by surgical patients as a more challenging issue than postoperative pain, despite its typically self-limited nature[4]; however, vomiting can persist rarely in but it can contribute in serious complications, including pneumothorax, pulmonary aspiration, wound dehiscence and elevated intracranial pressure[5]. Moreover, PONV may extend the duration ICU stay and lead to unexpected hospitalization after ambulatory surgery. The treatment of PONV imposes a significant burden on healthcare economy[6].

IV-PCA proves to be a highly effective approach for alleviating postoperative acute pain; however, the prevalent use of opioids as the primary analgesic in IV-PCA is associated with a common adverse event[7], PONV, with reported rates ranging from 18 to 23%[8]. Notably, approximately twelve percent of surgical patients opt to discontinue IV-PCA prematurely due to the challenging nature of intractable PONV[9]. To address this issue, droperidol, a D2 receptor antagonist, is employed for its central action on the chemoreceptor trigger zone, serving as an antiemetic agent in the context of IV-PCA[10].

The antiemetic effectiveness of droperidol was proven in opioid-based IV-PCA; however, prior investigations exhibited methodological shortcomings, such as small patient samples (n < 1,000), inadequate adjustment for confounding factors, exclusive focus on female patients, and a narrow scope of surgical procedures[11]. Moreover, the majority of earlier studies relied on data dating back more than two decades, failing to capture the advancements in different surgical interventions and anesthetic related care, like multimodal analgesia and

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minimally invasive surgery that have occurred in recent years[12].

METHODS

The study conducted at Lady Reading Hospital in Peshawar from December 2022 to November 2023. Study approved by Ethical committee and consent form patients was obtained. Patients who underwent any surgical intervention under neuraxial or general anesthesia and were given opioid-based IV-PCA for pain management in post-operative time were enrolled. Patients < 20 years, switching droperidol, using non-morphine analgesics for IV-PCA were excluded. Patients were divided into control groups and droperidol group.

IV-PCA is contraindicated for patients unable to maintain consciousness, those with cognitive impairment, and those requiring intensive care and mechanical ventilation after 24 hours. It is initiated in the intensive care unit after anesthesia using an ambulatory infusion pump programmed for morphine sulfate delivery.

The infusion settings for the IV-PCA system encompass a loading dose range of 0 to 5.0 mL, a demand dose varying from 0.5 to 2.0 mL, a basal infusion rate spanning 0 to 1.5 mL per hour, and a lockout time set between 5 and 10 minutes. Additionally, antiemetic prophylaxis is implemented by incorporating droperidol at a concentration ranging from 0.025 to 0.075 mg/mL into the IV-PCA infusate.

The researcher assessed patients' responses every 12 hours, increasing frequency for inadequate analgesia or adverse events. PONV severity was categorized using a 4-point scale: no PONV, mild PONV (nausea without antiemetic), moderate PONV (nausea with antiemetic request), and severe PONV (nausea with vomiting requiring antiemetic treatment).

The main focus of the study was to assess the incidence of PONV within 72 hours as the primary outcome. Certified nurse regularly evaluated the pain intensity, sedation level and occurrence of PONV at 12-hour intervals during the 72-hour postoperative period at the institution.

Anesthesia was induced with 1–2 mg/kg propofol and 1–2 µg/kg fentanyl, using 0.6–1.0 mg/kg rocuronium for intubation. Maintenance involved sevoflurane or desflurane. Reversal agents like 2 mg/kg sugammadex were used for neuromuscular blockade. Spinal anesthesia utilized 6–15 mg bupivacaine without opioids. Combined neuraxial and general anesthesia included epidural ropivacaine (5 mg/mL) with or without fentanyl (2.5–5 µg/mL). Midazolam (2–5 mg) provided anxiolysis. Perioperative fluid management involved crystalloid fluids following practice guidelines.

RESULTS

Overall, 300 patients were included in this study both sex. They were two equal groups in this study as Droperidol, 150 (50.0%) and Control, 150 (50.0%). The distribution of demographics and baseline characteristics in Droperidol and Control group were almost equal, and the differences were statistically significant, (p>0.050). (Table 1).

Table No.1: Demographic and baseline characteristics of both the study groups

Characteristic	Group		p-value
	Droperidol	Control	
Age (years)	53.80±5.94	54.88±5.59	0.904
BMI (kg/m^2)	26.67±2.19	27.57±2.18	0.696
Sex			
Male	82 (54.7)	80 (53.3)	0.817
Female	68 (45.3)	70 (46.7)	
ASA status			
I	32 (21.3)	30 (20.0)	0.515
II	111 (74.0)	120 (80.0)	
III	7 (4.7)	0 (0.0)	
Smoking status	36 (24.0)	25 (16.7)	0.115
Previous PONV	12 (8.0)	21 (14.0)	0.097
Hypertension	45 (30.0)	39 (26.0)	0.654
Diabetes mellitus	46 (30.7)	42 (28.0)	0.612
Major depression	3 (2.0)	8 (5.3)	0.125
Malignancy	24 (16.0)	25 (16.7)	0.876
Hemoglobin (g/dL)	12.28±2.51	12.13±2.25	0.600
eGFR (mL/min/1.73 m^2)	98.22±3.09	98.71±3.46	0.187
Alanine aminotransferase (U/L)	19.21±2.38	19.02±2.24	0.479
Aspartate aminotransferase (U/L)	22.25±1.48	22.34±1.32	0.525
Type of anesthesia			
Neuraxial anesthesia	60 (40.0)	56 (37.3)	0.771
General Anesthesia	89 (59.3)	92 (61.3)	
Combined	1 (0.7)	2 (1.3)	
Mean ± S.D, N (%)			

Nausea and vomiting between 0-12 hours after operation in Droperidol Group was 16 (10.7%) and 22 (14.7%) in control group, (p=0.741). Nausea and vomiting between 12-36 hours after operation in Droperidol Group was 18 (12.0%) and 26 (17.3%) in control group, (p=0.462). Nausea and vomiting between 36-60 hours after operation in Droperidol Group was 20 (13.3%) and 24 (16.0%) in control group, (p=0.862). Whereas, nausea and vomiting between 60-72 hours after operation in Droperidol Group was 19 (12.7%)

and 25 (16.7%) in control group, (p=0.868). Further, the severity of nausea and vomiting in both the groups were almost equal, (p>0.050). (Table 2).

Table No.2: Distribution of nausea and vomiting of both the study groups

	Group		p-value
	Droperidol	Control	
POH 0–12	16 (10.7)	22 (14.7)	0.741
Mild	12 (75.0)	17 (77.3)	0.532
Moderate	3 (18.8)	4 (18.2)	
Severe	1 (6.2)	1 (4.5)	
POH 12-36	18 (12.0)	26 (17.3)	0.462
Mild	11 (61.1)	18 (69.2)	0.741
Moderate	5 (27.8)	4 (15.4)	
Severe	2 (11.1)	4 (15.4)	
POH 36-60	20 (13.3)	24 (16.0)	0.862
Mild	18 (90.0)	18 (75.0)	0.684
Moderate	1 (5.0)	4 (16.7)	
Severe	1 (5.0)	2 (8.3)	
POH 60-72	19 (12.7)	25 (16.7)	0.868
Mild	15 (78.9)	21 (84.0)	0.796
Moderate	2 (10.5)	4 (16.0)	
Severe	2 (10.5)	0 (0.0)	
N (%)			

DISCUSSION

The study revealed a significant reduction in the incidence of postoperative nausea and vomiting (PONV) with the addition of droperidol to morphine-based intravenous patient-controlled analgesia (IV-PCA). Subgroup analyses demonstrated that the droperidol effect was particularly notable in patients under 65 years of age, females, non-smokers, and those without a history of PONV.

In a study conducted by an author, it was observed that patients administered with droperidol exhibited significantly lower levels of nausea at the 12-hour mark, and within the first 24 hours, only 31% of these patients required prochlorperazine, compared to 59.3% of those not receiving droperidol. Additionally, the droperidol group showed a significantly higher number of patients experiencing sedation at the 24-hour mark. Similar findings were reported in another study that addition of droperidol significantly reduced PONV in morphine-based IV-PCA, especially in patients under 65, females, non-smokers, and those without a history of PONV.

Another study reported that the antiemetic impact of droperidol was notably effective within the first 36 hours post-surgery but diminished thereafter. Uda et al[13] conducted a study in which they proposed that the incorporation of droperidol into intravenous patient-controlled analgesia (IV-PCA) regimens resulted in a notable reduction in the incidence of postoperative nausea and vomiting (PONV) within the initial 36 hours following surgery. However, their findings indicated that the antiemetic efficacy of droperidol appeared to diminish beyond this specified time frame, suggesting a time-dependent attenuation of its preventive effects against PONV in the postoperative period.

In their study, Kuo et al[14] found that the inclusion of droperidol resulted in a notable decrease in both the frequency and intensity of postoperative nausea and vomiting (PONV) specifically on postoperative days 2 and 3, with no significant impact observed on day 1. Different droperidol regimens in IV-PCA, concluding that a 0.10 mg/mL dose demonstrated optimal antiemetic efficacy with minimal sedation risk. Combining their results with ours, it suggests that adding droperidol at 0.025–0.10 mg/mL to opioid-based IV-PCA is appropriate, considering the benefit-risk balance.

Tan et al[15] found that the addition of droperidol to intravenous patient-controlled analgesia (IV-PCA) effectively decreased the risk of postoperative nausea and vomiting (PONV) without causing an increase in opioid consumption or altering the level of sedation; nevertheless, they emphasized the necessity for supplementary prophylactic interventions to address the occurrence of late-onset PONV. Gan et al[16] conducted studies indicating a significant reduction in postoperative nausea and vomiting (PONV) over a 24-hour period when administering a perioperative 1.25 mg bolus of droperidol in patients utilizing patient-controlled analgesia (PCA).

CONCLUSION

The incorporation of droperidol into intravenous patient-controlled analgesia (IV-PCA) regimens has demonstrated a notable reduction in the risk of postoperative nausea and vomiting (PONV), while concurrently exhibiting no discernible impact on opioid consumption or the level of sedation. Despite these encouraging outcomes, it is important to acknowledge that the efficacy of droperidol may be limited to the prevention of immediate postoperative PONV, thereby suggesting a potential need for supplementary prophylactic interventions to address the occurrence of late-onset PONV.

Author's Contribution:

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