Original Article

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Prevention of Postoperative Nausea and Vomiting after Abdominal Surgery : Aprepitant/Dexamethasone Versus Mirtazapine/Dexamethasone

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ABSTRACT

Background: *Patients having elective abdominal surgery under general anesthesia often have Postoperative Nausea and Vomiting (PONV). In this study the main goal is to evaluate the outcome of Aprepitant/Dexamethasone (A/D) combination vs Mirtazapine/Dexamethasone (M/D) combination vs Dexamethasone (D) alone for prevention of PONV in individuals after abdominal surgery.*

Materials and methods: *This cross sectional study was carried out at tertiary medical hospital from January 2021 to January 2022. Where a total of 150 patients scheduled for abdominal surgery were randomly allocated to receive 8 mg dexamethasone Intravenous Infusion (IVI) only in the D group or in addition to 80 mg aprepitant capsule in the A/D group or in addition to 30 mg mirtazapine tablet in the M/D group. In each 50 patients divided to each group. Assessment of PONV was carried out at 0–2 h (Early) and 2–24 h (Late). The primary outcome was the complete response 0-24 h after surgery. Collective PONV, postoperative pain, side effects and patient satisfaction score were considered as secondary outcomes.*

Results: *Majority of the study populations belonging to 41-50 years age group (65%) and 60% of them were male. In concordance to that, the intraoperative variables of duration of surgery and mean given intravascular fluid volume were comparable between groups. In the early postoperative period (0–2 h), there was a statistically significant difference between the A/D group and the D group in the number of vomiting episodes with comparable efficacy between the A/D and M/D groups. There were no statistically significant differences between the studied groups regarding nausea episodes, collective PONV, rescue antiemetic usage, and the number of patients exhibiting a complete response. Pain score at (0–2 h) was significantly higher in the D group in comparison to the A/D and M/D groups with comparable efficacy between the A/D and M/D groups ($p < 0.001$). The rescue analgesic doses were significantly higher in the D group compared to the A/D and M/D groups with statistically significant differences between the A/D and M/D groups ($p < 0.001$). in addition, more patients in the A/D and M/D groups were satisfied with the PONV prevention protocol compared to the D group.*

Conclusion: *The combination of aprepitant and dexamethasone, as well as mirtazapine and dexamethasone, has been proven to be more effective than dexamethasone alone in reducing postoperative nausea and vomiting in critically ill patients following abdominal surgery.*

Key words: Abdominal surgery; Aprepitant/ dexamethasone; mirtazapine/ dexamethasone.

Introduction

Patients may experience great suffering from Postoperative Nausea and Vomiting (PONV) one of the most uncomfortable and prevalent adverse effects of anesthetics.[1] Furthermore, PONV might cause postoperative admission delays and increased healthcare expenses.[2]

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It has been observed that without a prophylactic antiemetic, the incidence of PONV in patients undergoing different kinds of surgery ranges from 20% to 70%.[3,4,5]

Several variables, including age, sex, surgery type and anesthetic-related ones, may contribute to PONV, which may cause significant pain among patients.[6,7,8] Preoperative volume loading and variables such as obesity, a history of motion sickness, and/or a history of past postoperative emesis may potentially play a role in PONV.[9,10,11]

Concerns persist about what should be done to protect against PONV.[12] Although it has been shown to be cost-effective in high-risk individuals, global prophylaxis for PONV is not routinely advised.[13,14] Patients receiving procedures on the lower abdomen region are particularly at risk for PONV.

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Dexamethasone is a glucocorticoid with a half-life of 36-48 hours , and it is used in a dose of 8-10 mg to prevent PONV in patients undergoing abdominal surgery due to its inexpensive cost and reduced adverse effects. It may function via antagonizing prostaglandins, preventing serotonin release in the stomach, and potentiating other antiemetics by sensitizing the pharmacological receptor.[11]

In this study the main goal is to evaluate the outcome of Aprepitant/Dexamethasone (A/D) combination vs Mirtazapine/Dexamethasone (M/D) combination vs dexamethasone (D) alone for prevention of PONV in morbidly patients undergoing abdominal surgery.

Materials and methods

This cross sectional study was carried out at tertiary medical hospital from January 2021 to January 2022. Where a total of 150 patients scheduled for abdominal surgery were randomly allocated to receive 8 mg dexamethasone Intravenous Infusion (IVI) only in the D group or in addition to 80 mg aprepitant capsule in the A/D group or in addition to 30 mg mirtazapine tablet in the M/D group. 50 patients were selected for each group. Assessment of PONV was carried out at 0–2 h (early) and 2–24 h (late). The primary outcome was the complete response 0-24 h after surgery. Collective PONV, postoperative pain, side effects and patient satisfaction score were considered as secondary outcomes.

Results

Table I shows age distribution of the study group where majority were belonging to 41-50 years age group (65%). Followed by 25% belonged to >60 years group and 10% belong to 31-40 years age group.

Table I Age distribution of the patients

Age group	%
31-40 years	10%
41-50	65%
>60 years	25%

Figure-1 shows gender distribution of the study group where 60% were male and 40% were female.

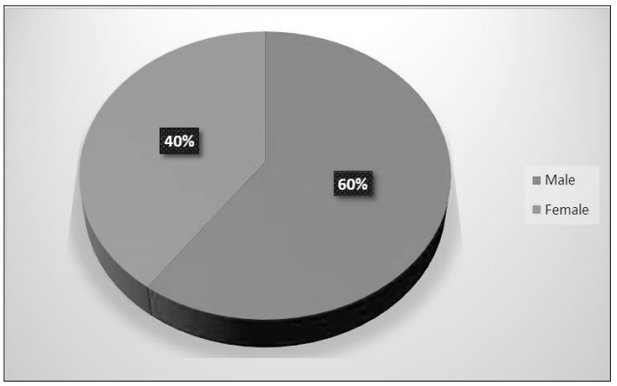

Figure 1 Gender Distribution of the study group

Table II shows baseline status of the study group where in concordance to that, the intraoperative variables of duration of surgery and mean given intravascular fluid volume were comparable between groups.

Table II Baseline status of the study group

	A/D group, %	M/D group, %	D group, %	p value
Comorbidities DM HTN	 24% 16%	 20% 17%	 16% 10%	0.234
Smoking	50%	46%	44%	0.431
Motion sickness history	14%	13%	12%	0.541
History of PONV	11%	8%	20%	0.988
Operation duration, min	104.1	101.10	102.5	0.188
Intraoperative fluids, ml	1081.0	1098.2	1070.7	0.561

In Table III shows post operative nausea and vomiting status where in the early postoperative period (0–2 h), there was a statistically significant difference between the A/D group and the D group in the number of vomiting episodes with comparable efficacy between the A/D and M/D groups. There were no statistically significant differences between the studied groups regarding nausea episodes, collective PONV, rescue antiemetic usage, and the number of patients exhibiting a complete response.

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Table III Post operative nausea and vomiting status

Cases (0–2 h)	A/D group, %	M/D group, %	D group, %	p value
Nausea episodes	15%	11%	18%	0.999
Grade of Nausea				
I	0	10%	0%	0.231
II	31%	30%	44%	
III	69%	60%	56%	
Vomiting episodes	0	12%	22%	0.5411
PONV	13%	22%	38%	1.112
Use of rescue antiemetic,	11%	10%	32%	2.321
Complete response	90%	88%	71%	<0.001
Cases (2–24 h)	A/D group, %	M/D group, %	D group, %	p value
Nausea episodes	24%	12%	57%	<0.001
Grade of nausea				
I	15%	60%	40%	<0.001
II	50%	40%	60%	
III	35%			
Vomiting episodes	4	11	36	<0.001
PONV	27	25	91	<0.001
Use of rescue antiemetic	12	13	71	<0.001
Complete response	90	87	31	<0.001
Cases (0–24 h)	A/D group, %	M/D group, %	D group, %	p value
Vomiting episodes	5	22	46	<0.001
Grade of Nausea				
I	11%	49%	39%	<0.001
II	39%	51%	61%	
III	50%			
PONV	35	36	94	<0.001
Use of rescue antiemetic	21	22	80	<0.001
Complete response	80	77	21	<0.001

Table IV shows postoperative findings among the groups where pain score at (0–2 h) was significantly higher in the D group in comparison to the A/D and M/D groups with comparable efficacy between the A/D and M/D groups ($p < 0.001$). The rescue analgesic doses were significantly higher in the D group compared to the A/D and M/D groups with statistically significant differences between the A/D and M/D groups ($p < 0.001$).

Table IV Postoperative findings among the groups

Sedation	A/D group, %	M/D group, %	D group, %	p value
Ramsay sedation scale (preoperative)	1.6	2.4	1.3	^<0.001
Ramsay sedation scale (postoperative)	1.6	3.0	1.3	^<0.001
Postoperative pain and analgesia	A/D group, %	M/D group, %	D group, %	P value
Pain score 0–2 hour	2.0	2.2	2.7	^<0.001
Pain score 2–24 hour	2.4	3.8	4.4	^<0.001
Time to first rescue analgesia (ketorolac) (min)	89.4	77.9	53.5	^<0.001
Total dose of rescue analgesia (ketorolac), (mg) 0–24 hour	40.6	59.4	70.3	^<0.001

Figure-2 shows side effects where in all group Diarrhea and dizziness most commonly seen however apart from that, incidences of the studied side effects weren't statistically significant among three groups.

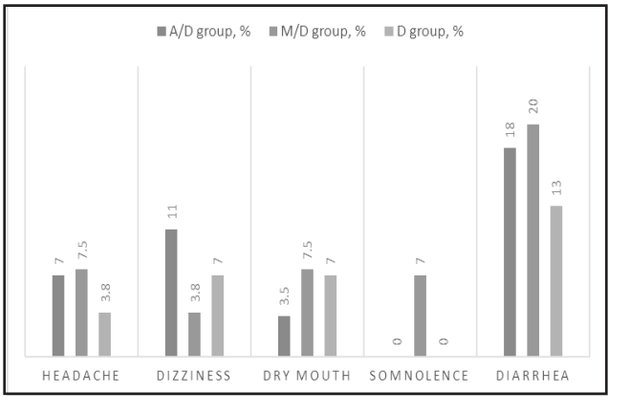

Figure 2 Side effects STATUS

Table V shows satisfaction score of the study group where more patients in the A/D and M/D groups were satisfied with the PONV prevention protocol compared to the D group.

Table V Satisfaction score of the study group

Satisfaction score	A/D group, %	M/D group, %	D group, %	p value
	5.5	1.3	2.9	^<0.001

Discussion

PONV after bariatric surgery can lead to dehydration, electrolyte imbalances, and possibly increase hospital length of stay. A standard regimen has not yet been identified.[7]

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A multimodal antiemetic approach including 2 or more interventions is recommended.[8]

Doses of the aprepitant and dexamethasone combination were based on a previous study which revealed an efficient antiemetic effect in patients at high-risk of PONV from epidural fentanyl analgesia.[9] While doses of mirtazapine and dexamethasone combinations were based on research conducted by others, who documented that premedication with this combination significantly reduced PONV in patients undergoing gynecological procedures.[10]

In addition, the timing and method of administration of preemptive dexamethasone were based on research conducted by one study.[11]

Dexamethasone is recommended as a single perioperative injection of 8–14 mg to decrease PONV in the first 24 h after abdominal surgery.[12] It also has analgesic effects, improves respiratory parameters, decreases fatigue, low-cost drug, and promotes better recovery. [13] However, PONV prevention with 8 mg dexamethasone intravenously increased postoperative blood glucose values in nondiabetic and diabetic patients, irrespective of baseline blood glucose levels.[14]

In concordance with our study, other study concluded that a single preoperative dose of 80 mg aprepitant capsule significantly lowered PONV and pain medications 2–24 h after surgery in patients undergoing abdominal procedures.[11]

Other study documented the efficacy of adding oral 80 mg aprepitant to 4 mg ondansetron intravenously in the reduction of vomiting episodes at 72 h after laparoscopic bariatric surgery.[10]

Consistent with the study, other study reported that the combination of oral 80 mg aprepitant and 8 mg dexamethasone intravenously had a lower incidence of vomiting episodes from continuous epidural fentanyl analgesia at 24 h after elective knee osteoarthritis surgery.[12]

Other study concluded that a single dose of 40 mg aprepitant was equally effective to 8 mg ondansetron in 3 doses, 8 h apart, in preventing PONV, reducing the severity of nausea and the number of rescue antiemetics during the 24 h postoperative period in 125 women underwent breast and thyroid surgeries.[13]

In addition, other demonstrated that aprepitant was superior to ondansetron in patients assigned to obtain a one preemptive dose of oral 40 mg aprepitant or oral 125 mg aprepitant, vs. 4 mg ondansetron intravenously.[14]

Over and above, other study found that a prepitant was noninferior to ondansetron in the prevention of vomiting over 0–24 h and there was no difference in peak nausea scores due to the fact that nausea is subjective and the implementation of different institutional protocols for administration of rescue therapy for nausea and vomiting episodes.[12]

In addition, one study reported that the combination of oral 40 mg aprepitant and 10 mg dexamethasone intravenously was more efficient than the combination of ondansetron and dexamethasone for the prevention of postoperative vomiting in adult patients scheduled for craniotomy under general anesthesia.[9]

Partially consistent with this study, Moon et al. documented a decreased nausea severity and increased rescue analgesics in the aprepitant group compared to the palonosetron group, 2 h after administration, in patients scheduled for laparoscopic gynecological surgeries under general anesthesia.[8]

Furthermore, in contrast to this study, one study reported that the combination of 8 mg dexamethasone intravenously and oral 40 mg aprepitant did not improve the complete response for PONV in comparison to the combination of 8 mg dexamethasone intravenously and 4 mg ondansetron intravenously in patients undergoing laparoscopic surgery.[6]

Results of this study were consistent with the other study who found that a single preoperative oral 30 mg mirtazapine decreased the incidence, delayed the onset and reduced the severity of nausea and vomiting after orthopedic surgery caused by intrathecal morphine in patients scheduled to undergo spinal anesthesia.[5]

Also, one report documented that oral 30 mg mirtazapine premedication significantly reduced preoperative anxiety and the incidence of postoperative early nausea and late vomiting in comparison with 16 mg ondansetron intravenously in 80 female patients underwent breast surgery.[4]

Limitation

The intervention was not placebo, so controlled and blinded to neither clinicians nor patients. Additionally group sizes were small.

Conclusion

Aprepitant/dexamethasone and mirtazapine/dexamethasone combinations were shown to be more effective than dexamethasone alone in relieving postoperative nausea and vomiting in morbidly obese individuals underwent abdominal surgery.

Recommendation

Further studies are necessary to confirm potential benefits between the two eg. A/D & M/D.

Disclosure

The author declared no competing interests.

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