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Original Research Article

Comparison between Clonidine & Tramadol Hydrochloride in Prevention of Intra-Operative Shivering After Sub-Arachnoid Block - An Observational, Analytical & Cross-Sectional Study

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Conflict of interest: Nil

Abstract

Introduction: Shivering is a common side effect of spinal anesthesia. It is a physiological response of body by which heat production occurs to increase the core body temperature. It is defined as involuntary, repetitive action of skeletal muscle. Incidence of shivering has been found up to 40-50% in different studies.

Aims: To study the efficacy, hemodynamic changes and adverse effects of prophylactic administration of Clonidine and Tramadol Hydrochloride for prevention of shivering during surgeries of Lower abdomen and Lower Limbs under Spinal Anesthesia.

Materials and Methods: The present study was an Analytical and Cross- Sectional Observational Study. This Study was conducted from July 2021 to June 2022 at Department of Anesthesia of North 24 Parganas District Hospital. Total 120 patients were included in this study.

Result: Distribution of mean Sedation score at 0 min with Group was statistically significant ($p<0.0001$). Distribution of mean Sedation Score at 5 MIN with Group was statistically significant ($p<0.0001$).

Conclusion: Therefore, to conclude our study, we found that there was no difference of Shivering between the groups, however the patients in Clonidine group was more sedated which may cause a temporary fall in Spo2 so strict monitoring is needed while using it and had less nausea and vomiting than the patients in Tramadol group. This observation enables us to administer these drugs more judiciously, if used at all. (Example: where we know a high-risk group of PONV we can avoid administering Tramadol and rather opt for Clonidine, and where less sedation is required, we can administer Tramadol).

Keywords: Clonidine, tramadol and spinal anesthesia.

Introduction

Shivering is a common side effect of spinal anesthesia. It is a physiological response of body by which heat production occurs to increase the core body temperature. It is defined as involuntary, repetitive action of skeletal muscle. Incidence of shivering has been found up to 40-50% in different studies. It increases the oxygen consumption and carbon di-oxide production by almost three times that may result in myocardial infarction.

Excessive shivering creates an imbalance between body's oxygen demand and supply ratio. The resultant oxygen demand and relative deficit of oxygen supply can lead to various metabolic derangements such as hypoxemia, lactic acidosis, and hypercarbia thereby hampering a smooth recovery from anesthesia. The incidence of shivering has been found to be quite high, approximately 40-50%, in different studies.[1] It can double or even triple the oxygen consumption and carbon dioxide production.[2] Shivering also increases intraocular and intracranial pressure, and may contribute to increased wound pain, delayed wound healing, and delayed discharge from post-anesthetic care.[3][4] Apart from being an uncomfortable experience, its deleterious effects deserve primary prevention and rapid control on occurrence.

Shivering is a physiological response to core hypothermia to raise the metabolic heat production. The main causes of intra/post-operative shivering are temperature loss, increased sympathetic tone, pain, and systemic release of pyrogens. Spinal anesthesia significantly impairs the thermoregulation system by inhibiting tonic

vasoconstriction, which plays a significant role in temperature regulation. It also causes a redistribution of core heat from the trunk (below the block level) to the peripheral tissues. These factors predispose patients to hypothermia and shivering.[5] The treatment of shivering includes both pharmacological and non-pharmacological methods. The non-pharmacological management is by external heating like the use of forced air warming, warming blankets, warmed fluids etc., According to the results of a meta-analysis, the most frequently reported pharmacological interventions include clonidine, pethidine, tramadol, nefopam and ketamine.[6] Unfortunately, no gold standard treatment is known for shivering as the administration of all the available drugs is associated with various adverse effects.

Measures like external heating by forced air warming, warming blankets, are expensive and not practical in all settings. Drugs like clonidine, pethidine, tramadol, dexmedetomidine and ketamine is being used for prevention as well as control of shivering. The desired properties for a drug to prevent shivering include easy availability and minimal side effects. These days tramadol, which is a centrally acting analgesic with its weak opioid features, has become a favoured and commonly used drug. But tramadol has many side effects like nausea, vomiting, dizziness etc. which leads to further discomfort to the patient. Tramadol also inhibits the reuptake of norepinephrine and 5-hydroxytryptamine. This pharmacological mechanism of tramadol is postulated to be useful for control of thermoregulation. Prophylactic use of tramadol is effective in prevention of shivering in post spinal anesthesia. Clonidine, an alpha 2 adrenoreceptor agonist is effective in reducing the incidence of shivering and decrease oxygen consumption during recovery from anesthesia. The anti-shivering effect of clonidine is because of the actions at three levels; hypothalamus, locus coeruleus and spinal cord. The postulated mechanisms include alteration of thermoregulatory threshold for vasoconstriction, activation of alpha -2 receptors at the spinal cord level and release of norepinephrine and other mediators.

Materials and Methods

Study Area: North 24 Parganas District Hospital

Study population: Patients undergoing Surgeries of Lower abdomen and Lower Limbs at North 24 Parganas District Hospital, Barasat.

Study design: Analytical and Cross- Sectional

Period of study: 1 Year

Sample size: 120

Inclusion Criteria –

- Subjects undergoing surgeries for lower limbs and lower abdomen.
- Age between 18-55 years.
- Height between 150-170 cm
- Body weights between 50-80 kg.
- ASA grade 1 & 2

Exclusion Criteria –

- Pregnancy
- Hypertension (SBP> 160 mmHg, DBP> 110 mmHg), Severe Anemia, Severe cardiac disease, Uncontrolled Diabetes Mellitus, Hyperpyrexia, Emergency surgery, blood diathesis.
- Subjects with known history of allergy to the drugs used in this study.
- Subjects having unwillingness OR contraindications for SAB (patients on anti-platelet drugs).
- Urological endoscopic procedures.
- Procedures which may require Blood or blood product transfusion.

Statistical Analysis:

For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Two-sample t-tests, which compare the means of independent or unpaired samples, were used to assess differences between groups. Paired t-tests, which account for the correlation between paired observations, offer greater power than unpaired tests.

Chi-square tests (χ^2 tests) were employed to evaluate hypotheses where the sampling distribution of the test statistic follows a chi-squared distribution under the null hypothesis; Pearson's chi-squared test is often referred to simply as the chi-squared test. For comparisons of unpaired proportions, either the chi-square test or Fisher's exact test was used, depending on the context. To perform t-tests, the relevant formulae for test statistics, which either exactly follow or closely approximate a t-distribution under the null hypothesis, were applied, with specific degrees of freedom indicated for each test. P-values were determined from Student's t-distribution tables. A p-value ≤ 0.05 was considered statistically significant, leading to the rejection of the null hypothesis in favour of the alternative hypothesis.

Result

Table 1: Distribution of Mean at different time interval in Shivering Score with Group

		Number	Mean	SD	Minimum	Maximum	Median	P-Value
Shivering score at 0 min (T0)	Clonidine	60	0.0500	0.2198	0.0000	1.0000	0.0000	0.3024
	Tramadol	60	0.1000	0.3025	0.0000	1.0000	0.0000	
Shivering Score At 5 MIN(T1)	Clonidine	60	0.1167	0.3237	0.0000	1.0000	0.0000	0.1440
	Tramadol	60	0.2167	0.4155	0.0000	1.0000	0.0000	
Shivering Score At 10 MIN(T2)	Clonidine	60	0.1167	0.3237	0.0000	1.0000	0.0000	1.0000
	Tramadol	60	0.1167	0.3237	0.0000	1.0000	0.0000	
Shivering Score At 15 MIN(T3)	Clonidine	60	0.1833	0.1833	0.0000	3.0000	0.0000	0.5745
	Tramadol	60	0.1333	0.1333	0.0000	1.0000	0.0000	
Shivering Score At 20 MIN(T4)	Clonidine	60	0.0667	0.3117	0.0000	2.0000	0.0000	0.0450
	Tramadol	60	0.2000	0.4034	0.0000	1.0000	0.0000	
Shivering Score At 25 MIN(T5)	Clonidine	60	0.1167	0.3237	0.0000	1.0000	0.0000	1.0000
	Tramadol	60	0.1167	0.3237	0.0000	1.0000	0.0000	
Shivering Score At 30 MIN(T6)	Clonidine	60	0.0167	0.1291	0.0000	1.0000	0.0000	0.3132
	Tramadol	60	0.0500	0.2198	0.0000	1.0000	0.0000	
Shivering Score At 35 MIN(T7)	Clonidine	60	0.0167	0.1291	0.0000	1.0000	0.0000	0.0282
	Tramadol	60	0.1167	0.3237	0.0000	1.0000	0.0000	
Shivering Score At 40 MIN(T8)	Clonidine	60	0.0167	0.1291	0.0000	1.0000	0.0000	0.0521
	Tramadol	60	0.1000	0.3025	0.0000	1.0000	0.0000	

Table 2: Distribution of Mean at different time interval in Sedation Score with Group

		Number	Mean	SD	Minimum	Maximum	Median	P-Value
Sedation score at 0 min(T0)	Clonidine	60	1.7667	0.4265	1.0000	2.0000	2.0000	<0.0001
	Tramadol	60	1.3167	0.4691	1.0000	2.0000	1.0000	
Sedation Score At 5 MIN(T1)	Clonidine	60	1.8333	0.5574	1.0000	3.0000	2.0000	<0.0001
	Tramadol	60	1.2500	0.4367	1.0000	2.0000	1.0000	
Sedation Score At 10 MIN(T2)	Clonidine	60	1.9667	0.4860	1.0000	3.0000	2.0000	<0.0001
	Tramadol	60	1.2000	0.4034	1.0000	2.0000	1.0000	
Sedation Score At 15 MIN(T3)	Clonidine	60	2.0500	0.2867	1.0000	3.0000	2.0000	<0.0001
	Tramadol	60	1.2667	0.4459	1.0000	2.0000	1.0000	
Sedation Score At 20 MIN(T4)	Clonidine	60	2.1500	0.3601	2.0000	3.0000	2.0000	<0.0001
	Tramadol	60	1.5500	0.5017	1.0000	2.0000	2.0000	
Sedation Score At 25 MIN(T5)	Clonidine	60	2.1500	0.3601	2.0000	3.0000	2.0000	<0.0001
	Tramadol	60	1.4833	0.5039	1.0000	2.0000	1.0000	
Sedation Score At 30 MIN(T6)	Clonidine	60	2.1167	0.3237	2.0000	3.0000	2.0000	<0.0001
	Tramadol	60	1.4833	0.5039	1.0000	2.0000	1.0000	
Sedation Score At 35 MIN(T7)	Clonidine	60	2.1167	0.3237	2.0000	3.0000	2.0000	<0.0001
	Tramadol	60	1.5333	0.5031	1.0000	2.0000	2.0000	
Sedation Score At 40 MIN(T8)	Clonidine	60	2.1333	0.3428	2.0000	3.0000	2.0000	<0.0001
	Tramadol	60	1.5333	0.5031	1.0000	2.0000	2.0000	

Table 3: Distribution of Mean at different time interval in Nausea Vomiting Score with Group

		Number	Mean	SD	Minimum	Maximum	Median	P-Value
Nausea Vomiting Score At 0 min(T0)	Clonidine	60	1	0	1	1	1	0.0003
	Tramadol	60	1.2167	0.4544	1	3	1	
Nausea Vomiting score at 5 MIN(T1)	Clonidine	60	1	0	1	1	1	0.0002
	Tramadol	60	1.2	0.4034	1	2	1	
Nausea Vomiting Score At 10 MIN(T2)	Clonidine	60	1	0	1	1	1	0.0005
	Tramadol	60	1.2667	0.5783	1	3	1	
Nausea Vomiting Score At 15 MIN(T3)	Clonidine	60	1.0167	0.1291	1	2	1	0.0145
	Tramadol	60	1.1833	0.5039	1	3	1	
Nausea Vomiting Score At 20 MIN(T4)	Clonidine	60	1	0	1	1	1	0.0101
	Tramadol	60	1.15	0.4444	1	3	1	
Nausea Vomiting Score At 25 MIN(T5)	Clonidine	60	1	0	1	1	1	0.0002
	Tramadol	60	1.2333	0.4646	1	3	1	
Nausea Vomiting Score At 30 MIN(T6)	Clonidine	60	1.0167	0.1291	1	2	1	<0.0001
	Tramadol	60	1.3	0.4621	1	2	1	

Nausea Vomiting Score At 35 MIN(T7)	Clonidine	60	1	0	1	1	1	0.009
	Tramadol	60	1.1333	0.3891	1	3	1	
Nausea Vomiting Score At 40 MIN(T8)	Clonidine	60	1.0167	0.1291	1	2	1	<0.0001
	Tramadol	60	1.3333	0.4754	1	2	1	

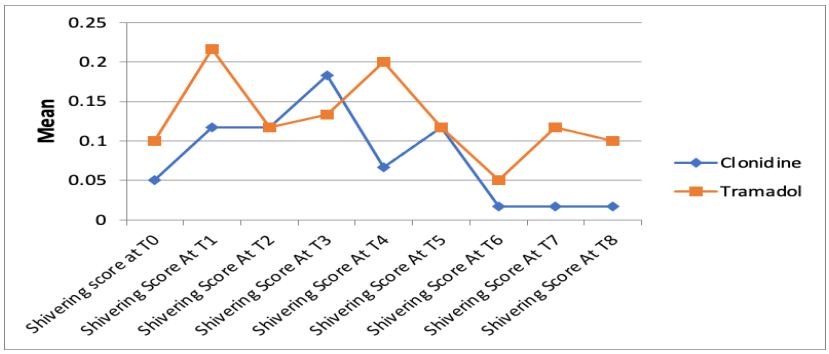

Figure 1: Mean at different time interval in Shivering Score with Group

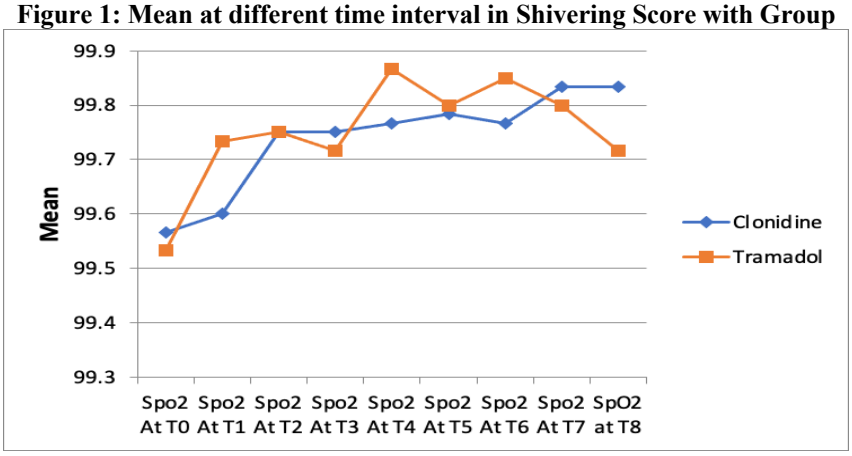

Figure 2: Mean at different time interval in Spo2 with Group

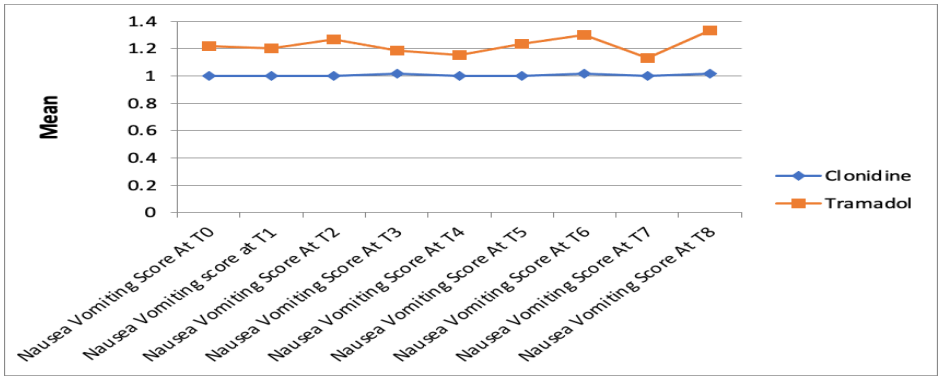

Figure 3: Mean at different time interval in Nausea Vomiting Score with Group

Distribution of mean Shivering score at 0 min with Group was not statistically significant (p=0.3024). Distribution of mean Shivering Score at 5 MIN with Group was not statistically significant (p=0.1440). Distribution of mean Shivering Score at 10 MIN with Group was not statistically significant (p=1.0000). Distribution of mean Shivering Score at 15 MIN with Group was not statistically significant (p=0.5745). Distribution of mean Shivering Score at 20 MIN with Group was statistically significant (p=0.0450). Distribution of mean Shivering Score at 25 MIN with Group was not statistically significant (p=1.0000). Distribution of mean Shivering Score at 30 MIN with Group was not statistically significant (p=0.3132). Distribution of mean Shivering Score at 35 MIN with Group was statistically significant (p=0.0282). Distribution of mean Shivering Score at 40 MIN with Group was not statistically significant (p=0.0521). Distribution of mean Sedation score at 0 min with Group was statistically significant (p<0.0001). Distribution of mean Sedation Score at 5 MIN with Group was statistically significant (p<0.0001). Distribution of mean Sedation Score at 10 MIN with Group was statistically significant

(p<0.0001). Distribution of mean Sedation Score at 15 MIN with Group was statistically significant (p<0.0001). Distribution of mean Sedation Score at 20 MIN with Group was statistically significant (p<0.0001). Distribution of mean Sedation Score at 25 MIN with Group was statistically significant (p<0.0001). Distribution of mean Sedation Score at 30 MIN with Group was statistically significant (p<0.0001). Distribution of mean Sedation Score at 35 MIN with Group was statistically significant (p<0.0001). Distribution of mean Sedation Score at 40 MIN with Group was statistically significant (p<0.0001).

Distribution of mean Nausea Vomiting Score at 0 min with Group was statistically significant (p=0.0003). Distribution of mean Nausea Vomiting score at 5 MIN with Group was statistically significant (p=0.0002). Distribution of mean Nausea Vomiting Score at 10 MIN with Group was statistically significant (p=0.0005). Distribution of mean Nausea Vomiting Score At 15 MIN with Group was statistically significant (p=0.0145). Distribution of mean Nausea Vomiting Score At 20 MIN with Group was statistically significant (p=0.0101). Distribution of mean Nausea Vomiting Score at 25 MIN with Group was statistically significant (p=0.0002). Distribution of mean Nausea Vomiting Score at 30 MIN with Group was statistically significant (p<0.0001). Distribution of mean Nausea Vomiting Score At 35 MIN with Group was statistically significant (p=0.0090). Distribution of mean Nausea Vomiting Score At 40 MIN with Group was statistically significant (p<0.0001).

Discussion

The present study was an Analytical and Cross-Sectional Observational Study. This Study was conducted from July 2021 to June 2022 at Department of Anesthesia of North 24 Parganas District Hospital. Total 120 patients were included in this study.

- Group-Clonidine: 60 patients
- Group-Tramadol: 60 patients

In our study, out of 120 patients most of the patients were 41-50 years old [44 (37.6%)]. 24 (40.0%) patients were 31-40 years of age in Clonidine Group and 18 (30.0%) patients were 31-40 years of age in Tramadol Group, but this was statistically significant (p=0.0194). In our study, Age was higher in Tramadol [44.6333±8.3035] compared to Clonidine [40.1833±8.4522] but this was not statistically significant (p=0.0643).

Guha S et al [7] (2017) found that this study aimed to evaluate the relative efficacy of prophylactic intravenous (IV) clonidine and tramadol for control of intraoperative shivering following spinal anesthesia. The axillary temperatures fell significantly in Group C from the baseline and remained at a significantly lower level up to 60 min after rescue drug was administered in patients who shivered.

We found that, Rescue Drug Given at 30 MIN with Group was not statistically significant (p=0.3152). We found that, Height CMS was less in Clonidine [159.5333±4.7424] compared to Tramadol [160.9667±6.1340] but this was not statistically significant (p=0.1548).

Our study showed that, Weight Kg was more in Tramadol [59.8333±6.7477] compared to Clonidine [59.6000±5.1592] but this was not statistically significant (p=0.8319).

We observed that, SBP At 0 min (p=0.9241), SBP At 5 MIN (p=0.9278), SBP at 10 MIN (p=0.8559), SBP at 15 MIN (p=0.6106), SBP at 20 MIN (p=0.6157), SBP at 25 MIN (p=0.8285), SBP at 30 MIN (p=0.8334), SBP At 35 MIN (p=0.8913) and SBP At 40 MIN (p=0.7753) with Group was not statistically significant. It was found that, DBP At 0 min (p=0.8042), DBP At 5 MIN (p=0.4967), DBP At 10 MIN (p=0.5513), DBP At 15 MIN (p=0.6007), DBP At 20 MIN (p=0.7519), DBP At 25 MIN (p=0.5045), DBP At 30 MIN (p=0.6337), DBP At 35 MIN (p=0.8330) and DBP At 40 MIN (p=0.7532) with Group was not statistically significant. We examined that, MAP At 0 min (p=0.7221), MAP At 5 MIN (p=0.5782), MAP At 10 MIN (p=0.6438), MAP At 15 MIN (p=0.8403), MAP At 20 MIN (p=0.8878), MAP At 25 MIN (p=0.6496), MAP At 30 MIN (p=0.7779), MAP At 35 MIN (p=0.9409) and MAP At 40 MIN with Group was not statistically significant (p=0.6508).

We observed that, HR At 0 min (p=0.5595), HR at 5 MIN (p=0.5833), HR at 10 MIN (p=0.7355), HR at 20 MIN with (p=0.9099), HR at 25 MIN (p=0.7208), HR at 30 MIN (p=0.6658), HR at 35 MIN (p=0.9575), HR at 40 MIN (p=0.8216) with Group was not statistically significant. We observed that, Spo2 at 0 min (p=0.7744), Spo2 at 5 MIN (p=0.2130), Spo2 at 10 MIN (p=1.0000), Spo2 at 15 MIN (p=0.7153), Spo2 at 20 MIN (p=0.1595), Spo2 at 25 MIN (p=0.8240), Spo2 at 30 MIN (p=0.2744), Spo2 at 35 MIN (p=0.6727) and SpO2 at 40 MIN (p=0.1281) with Group was not statistically significant.

Rai A et al [8] (2017) showed that use of dexmedetomidine as an additive to spinal anesthesia is gaining popularity; Sixty American Society of Anesthesiologist (ASA) Grade I and II orthopaedical patients undergoing lower limb surgeries between the ages of 20-60 years and height >150 cm was randomly divided into two groups of 30 patients each: Group D3 to receive 3

µg of Inj. It was found that, shivering score at 0 min (p=0.3024), Shivering Score at 5 MIN (p=0.1440), Shivering Score at 10 MIN (p=1.0000), Shivering Score at 15 MIN (p=0.5745), Shivering Score at 20 MIN (p=0.0450), Shivering Score at 25 MIN (p=1.0000), Shivering Score at 30 MIN (p=0.3132), Shivering Score at 35 MIN (p=0.0282) and Shivering Score at 40 MIN with Group was not statistically significant (p=0.0521).

We examined that, Sedation score at 0 min (p<0.0001), Sedation Score at 5 MIN, Sedation Score at 10 MIN (p<0.0001), Sedation Score at 15 MIN, Sedation Score at 20 MIN (p<0.0001), Sedation Score At 25 MIN (p<0.0001), Sedation Score At 30 MIN (p<0.0001) AND Sedation Score at 35 MIN(p<0.0001), and Sedation Score at 40 MIN (p<0.0001) with Group was statistically significant.

It was found that, Nausea Vomiting Score at 0 min (p=0.0003), Nausea Vomiting score at 5 MIN (p=0.0002), Nausea Vomiting Score at 10 MIN (p=0.0005)), Nausea Vomiting Score At 15 MIN (p=0.0145), Nausea Vomiting Score At 20 MIN (p=0.0101), Nausea Vomiting Score At 25 MIN (p=0.0002), Nausea Vomiting Score At 30 MIN (p<0.0001), Nausea Vomiting Score At 35 MIN (p=0.0090) and Nausea Vomiting Score At 40 MIN (p<0.0001) with Group was statistically significant.

Conclusion

Therefore, to conclude our study, we found that there was no difference of Shivering between the groups, however the patients in Clonidine group was more sedated which may cause a temporary fall in Spo2 so strict monitoring is needed while using it and had less nausea and vomiting than the patients in Tramadol group. This observation enables us to administer these drugs more judiciously, if used at all. (Example: where we know a high-risk group of PONV we can avoid administering Tramadol and rather opt for Clonidine, and where less sedation is required, we can administer Tramadol).

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