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To Evaluate Prophylactic Use of Antiemetic (Ondansetron) with Opioid Analgesics (Tramadol) for Acute Pain in Emergency Department

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Abstract

Use of Ondensetron (antiemetic) is quite common practice before giving Tramadol(analgesics). Many of the ED patients present with pain and Tramadol is the drug of choice for us. It is usually given intravenously. This is an Opoid analgesic and acts via binding to the mu opioid receptor, but also inhibits the reuptake of serotonin and norepinephrine due to its action on the noradrenergic and serotonergic systems, such as its "atypical" opioid activity. Vomiting is due to central stimulation of CTZ and by peripheral labrynthine stimulation. A major proportion of patients presenting to our emergency department have various painful conditions. In our department, tramadol has been the intravenous opioid of choice. In our experience, the advantages of IV tramadol are its titratability (dose range 1-2 mg/kg) and predictability. Traditionally, it has been the norm to use prophylactic antiemetics along with opioids to counter their emetic side effects. All opioids have the well recognised side effects of nausea and vomiting, with some being worse than others. These symptoms are mediated both centrally, by stimulation of the chemoreceptive trigger zone and dopamine receptors in the medulla, and peripherally, by labyrinthine stimulation and reduced gastric emptying. Thus antiemetic prophylaxis is particularly common with the use of opioids for acute pain,and also in postoperative acute pain, where the incidence of nausea and vomiting varies between 8% and 92%.It is a normal practice in our ED to give prophylactic ondensetron before giving tramadol for prevention of vomiting.This sole aim of this work was to find out how far the practice of using prophylactic antiemetic before opioid was correct and how effective it was in preventing nausea and vomiting.

Keywords: Antiemetic; Analgesics; Pain Threshold; Chemoreceptor Trigger Zon(CTZ).

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Introduction

A major proportion of patients presenting to our emergency department have various painful conditions. In our department, tramadol has been the intravenous opioid of choice. In our experience, the advantages of IV tramadol are its titratability (dose range 1–2 mg/kg) and predictability. Traditionally, it has been the norm to use prophylactic antiemetics along with opioids to counter their emetic side effects. All opioids have the well recognised side effects of nausea and vomiting, with some being worse than others. These symptoms are mediated both centrally, by stimulation of the chemoreceptive trigger zone and dopamine receptors in the medulla, and peripherally, by labyrinthine stimulation and reduced gastric emptying. Thus antiemetic prophylaxis is particularly common with the use of opioids for acute pain,and also in postoperative acute pain, where the incidence of nausea and vomiting varies between 8% and 92%. It is a normal practice in our ED to give prophylactic ondensetron before giving tramadol for prevention of vomiting.This sole aim of this work was to find out

how far the practice of using prophylactic antiemetic before opioid was correct and how effective it was in preventing nausea and vomiting.

Mechanism of Emetogenic Effects of Opioids

Various stimuli that lead to nausea and vomiting act on the "vomiting center" in the medulla oblongata of the brain. This "center" is not a discrete locus but rather consists of groups of loosely organized neurones (sensory and motor control nuclei located mainly in the medulla but also in the spinal cord), which can be activated in a co-ordinated sequence[7] . Nausea and vomiting can be stimulated or repressed via chemoreceptors present in the vomiting center [8] , receiving inputs from different locations [9]. Nausea and vomiting are usually initiated by peripheral irritant stimuli acting on the gastrointestinal tract, which are transduced into sensory signals transmitted centrally to the vomiting center by vagal and sympathetic afferent nerves. However, the same sensations can be induced by direct stimulation of particular brain regions [10]

The vomiting center receives input from four major areas: the chemoreceptor trigger zone (CTZ) for vomiting, the GI tract, the vestibular apparatus in the temporal lobe, and the cerebral cortex. Opioids exert emetogenic effects through multiple mechanisms, principally involving three of these areas,namely: direct stimulation of the CTZ, inhibition of gut motility, and stimulation of the vestibular apparatus. The role of the cortex in opioid-induced nausea is unclear, but may be related to a patient recalling previous episodes of nausea and / or vomiting after opioid therapy [9] . The effects are mediated via interaction with specific opioid receptors (mu, delta, and kappa subtypes) in the brain and spinalcord and, in some circumstances, at peripheral sites [11,12].

Opioid Stimulation of the CTZ

The neurons that make up the CTZ are found within the area postrema at the floor of the fourthventricle. The permeability of the blood-brain barrier at the CTZ means that these neurons may be directly stimulated by many toxins, metabolites or drugs, including opioids, that are present inthe systemic circulation [9]. The mechanism ofopioid-induced stimulation of the CTZ occurs via the activation of opioid mu and delta receptors and signaling to the vomiting center occurs primarily via dopamine D2 receptors as well as via serotonin (5-HT3) receptors present in the CTZ [9].

Opioid-evoked emesis mediated via the CTZ decreases with repetitive opioid administration,with the development of tolerance to emesis possibly dependent on the type of opioid administered [13,14,15]

The Complexity of Opioid Effects

The emetogenic mechanisms involved for a specific opioid depend on the specificity of an opioid for mu, delta, or kappa receptors. Thus, for example,mu opioid receptor agonists have been associated with nausea and vomiting, but kappa opioid receptor agonists may not be [20] . The clinical situation is often complicated by the variety of different opioid-related emetogenic mechanisms. These can vary from patient to patient, more than one may be active in any one patient at the same time, and the mechanisms may change from acute- to long-term opioid use. For example, emetogenic effects caused by medullary CTZ stimulation often decrease very rapidly [11,15] . In some patients, however, nausea and vomiting side effects are known to persist during long-term treatment [21]. Furthermore, analgesic tolerance (a reduction in the pain relieving effect of opioids) usually manifests overtime as multiple cellular and molecular adaptations take place, including neuroplastic changes[11,15,22,23,24] As a consequence, dose escalation is common in order to maintain the same level of pain relief, but this is likely to enhance the risk of recurring nausea and vomiting as well as other side effects. Dose escalation must therefore be controlled in order to maintain opioid efficacy while limiting the risk of adverse events [25] .

Conversely, higher doses of some opioids (such as morphine) may actually reduce nausea and vomiting by interacting with mu opioid receptors in the vomiting center rather than the CTZ [26,27] .

Thus, the relationship between opioid use and the incidence of nausea and vomiting is complex.Other potential complicating factors include the choice of opioid. Although the incidence of nausea and vomiting appears to vary little with the type of opioid analgesic used, some opioids have been reported to induce less nausea and vomiting than others [28] , even at carefully controlled equianalgesic doses[29]. For example, oral morphine was associated with a significantly greater incidence of nausea than any other opioid or treatment modality studied [29]. A randomized, double-blind, placebo-controlled trial of ondansetron and metoclopramide in 92 patients failed to show a significant reduction in emesis in either treatment group compared with those given placebo.

In addition to tolerability issues surrounding the use of opioids, most antiemetics are associated with their own tolerability problems associated with very low probability of eventual survival.

Aim and Objective

Aim of the Study

Is it indicated to use prophylactic antiemetic before iv opioid analgesia? The rationale behind this study is to find out if prophylactic ondansetron is realy needed before iv tramadol used for pain relief (pain of >6 on pain scale). Based on the result of this study we would be able to know, how correct is the practice of using prophylactic ondansetron, before tramadol, which is widely used in our ED.

Objective of the Study

To evaluate Prophylactic use of ondansetron for prevention of Nausea and Vomiting along with Tramadol for Acute pain (Pain Score >6) in Emergency Department.

Outcome

We would like to see the difference between the two groups in this study, and also we would like to see if the difference is statistically significant so that our ED practice changes accordingly.

Materials and Methods

The study was done at Max Super Speciality Hospital, Saket, New Delhi. It is a 450 bedded tertiary care, multi-specialty hospital. The ED at Max Hospital sees approximately 20,000 patients per year out of which approximately 4000 patients admitted for acute pain related problems. The study was done after clearing the Scientific Committee Review and the Ethics Committee Review over a period of 04 months.

All patients who meet the inclusion criteria and none of the exclusion criteria was enrolled in the study after taking a voluntary consent from the patients or their relative for participating in the study. Using the electronic health record (EHR), a prospective analysis of 280 consecutive patients' was done.

Study Population

All the patient with pain scale of more than 6 on visual analogue scale and in age group of 18yrs to 65 yrs and who will give consent for this study and who will fill the inclusion criteria will be included. All the patients above or below this age group and those who do not fulfill the inclusion criteria will be excluded.

Inclusion Criteria

1. Age more than 18 yrs and below 65 yrs.
2. All patient in above mentioned age group and who have a pain scale of above 6 on visual analogue pain scale, and who have not taken any analgesic or antiemetic outside hospital before 6 hrs were included.
3. All patient who fullfill the above mentioned criteria and can give a written / verbal consent were included.

Exclusion Criteria

1. Patient below 18 yrs and above 65 yrs .
2. Those patients who have already received any analgesic or antiemetic in 6 hrs before coming to hospital and those who have already vomited or are having nausea.
3. Those patient who are unable to give conset .
4. Those patients who are expected to vomit or have nausea due to their underlying clinical condition were excluded, eg acute gastritis, acute pancreatitis, acute cholecystitis, biliary colic etc.
5. Those patients who are diagnosed cases of malignancies and are on active radiotherapy or chemotherapy.

Statistical Analysis

For the sample size calculation in the study proposed, we chose 20% of Nausea and Vomiting along with Tramadol for Acute pain (Pain Score >6) in Emergency Department. Sample size of 100 patients per group was calculated with 90% power at an alpha 0.05 to detect a difference 15% in Nausea and Vomiting in patients with or without ondanstron for acute pain treated with tramadol Formula for calculated sample size is given below

$$n = \frac{[z_{1-\alpha/2}.\sqrt{2P(1-P)} + z_{1-\beta}.\sqrt{\{P_1(1-P_1) + P_2(1-P_2)\}}]^2}{(P_1-P_2)^2}$$

Where

P_1 = Anticipated proportion of Nausea and Vomiting in patients with ondanstron for acute pain treated with tramadol

P_2 = = Anticipated proportion of Nausea and Vomiting in patients without ondanstron for acute pain treated with tramadol

$$P = (P_1+P_2)/2$$

Observation and Results

Results

Data was collected from Max Super Speciality Hospital, Saket, New Delhi over a period of 04 july 2013 to October 2013months. A total of 280 patients were included in the study during this time. The study group comprised of 280 patients. The mean age of the included patients was observed to be 35.38 years with standard deviation of 12.28 years.

The Table 1 and Figure 1 shows age distribution of the patients recruited for this study. Maximum number of patients were in age group 21-41 yrs (40.4%) followed by 31-40 yrs (22.5%), more than 50 yrs(18.6%), 41-50 yrs(12.5%) and 18-20 yrs (6.1%) respectively. The mean age of the included patients was observed to be 35.38 years with standard deviation of 12.28 years.

The Table 2 and Figure 2 shows sex distribution of the patients recruited for this study.majority of the patients were males 64% of the total i.e 179 patients and rest of them were females 36% i.e 101 patients.

Table 1:

Age Groups	Frequency	%
18 - 20 yrs	17	6.1%
21 - 30 yrs	113	40.4%
31 - 40 yrs	63	22.5%
41 - 50 yrs	35	12.5%
>50 yrs	52	18.6%
Total	280	100%
Mean ± SD	35.38 ± 12.28	
Min - Max	18 - 61	

Fig. 1:

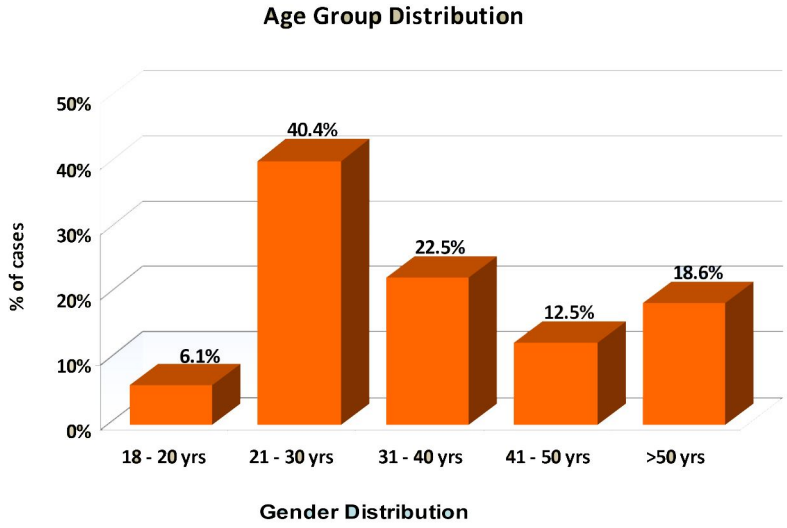


Fig. 2:

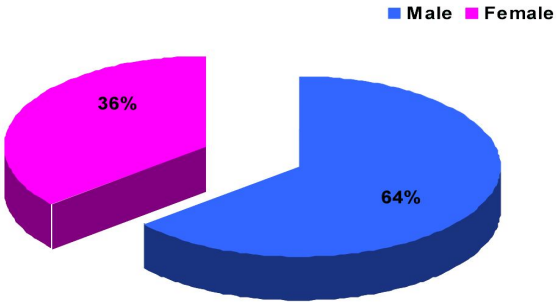


Table 2:

Sex	Frequency	%
F	101	36.1%
M	179	63.9%
Total	280	100%

Table 3:

Final Diagnosis	Frequency	%
Dengue Fever	193	68.9%
Dislocation	16	5.7%
Fracture	35	12.5%
Lacaration	15	5.4%
Soft Tissue Injury	13	4.6%
Others	8	2.9%
Total	280	100%

Fig. 3:

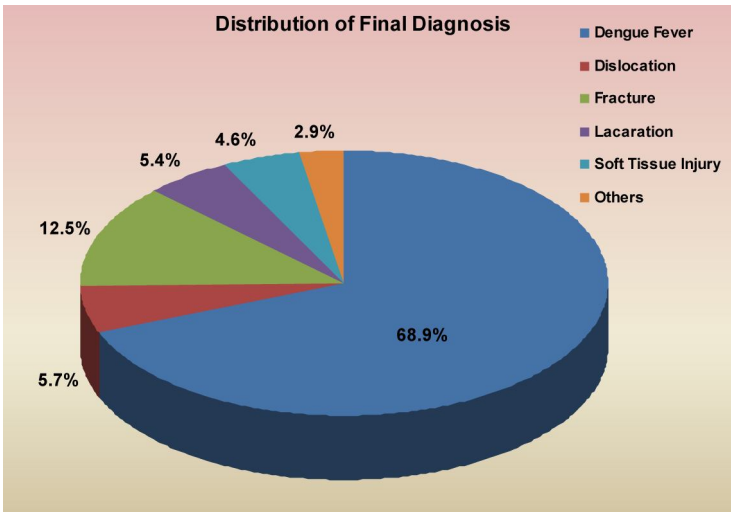
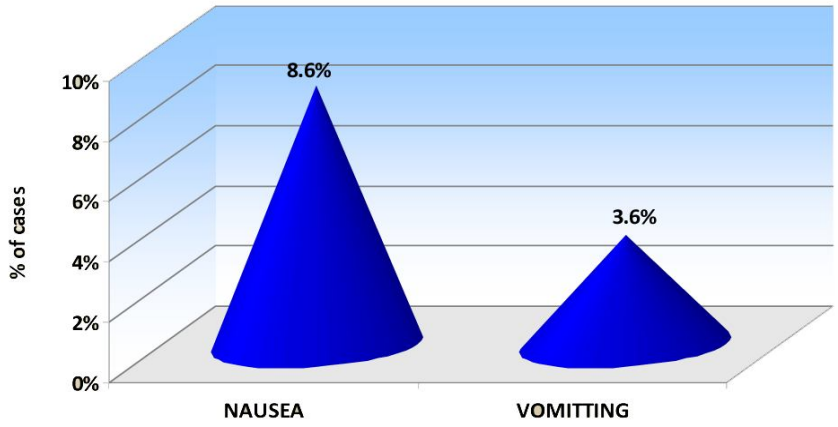


Table 4:

	Frequency	%
Nausea	24	8.6%
Vomitting	10	3.6%

Fig. 4:



The Table 3 and Figure 3 mentions the distribution of final diagnosis of the patients recruited for this study. As we can see majority of the patients were having dengue fever 193 (68.9%), followed by fractures

35(12.5%), dislocations 16 (5.7%), lacerations 15(5.4%), soft tissue injury 13(4.6%), and lastly others 8(2.9%).

The Table 4 and Figure 4 shows overall incidence of nausea and vomiting among the total number of patients recruited for this study, ie 280 pts:24 (8.6%) had nausea and 10(3.6%) vomited.

The Table 5 and Figure 5 shows comparision of age groups between group A and group B, with maximum number of patient in the age group of 21 yrs to 30 yrs in both the groups, 39.1% in group A and 41.5% in group Brespectively, and lowest number of patients in age group 18yrs to 20 yrs with 6.5% in group A and 5.6% in group B respectively. p value calculated was 0.992

The Table 6 and Figure 6 shows comparision of gender in group A and group B, with 65.2% males in group A and 62% in group B and 34.8% females in group A and 37.3% females in group B, respectively. p value calculated was 0.658

The Table 7 and chart 7 shows comparision of nausea at different time intervals (at 1 hr and 2 hrs respectively) between group A and group B, 3.6% in group A had nausea after 1 hour and 6.5% after 2 hrs, while 7.7% had nausea in group B after 1 hour and 10.6% after 2 hrs. p values calculated after 1 hrs time was 0.137 and after 2 hrs was 0.227

Table 5:

Age Groups	Group A		Group B		P Value
	Frequency	%	Frequency	%	
18 - 20 Yrs	9	6.5%	8	5.6%	0.992
21 - 30 Yrs	54	39.1%	59	41.5%	
31 - 40 Yrs	32	23.2%	31	21.8%	
41 - 50 Yrs	17	12.3%	18	12.7%	
>50 Yrs	26	18.8%	26	18.3%	
Total	138	100%	142	100%	

Fig. 5:

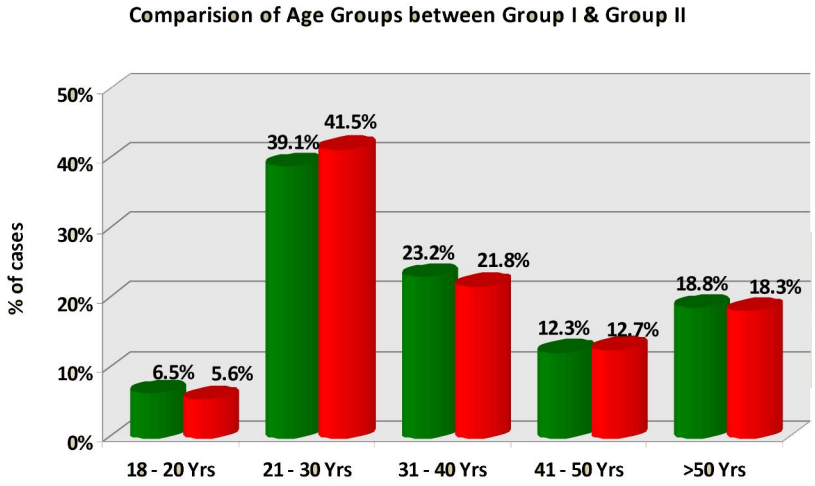


Fig. 6:

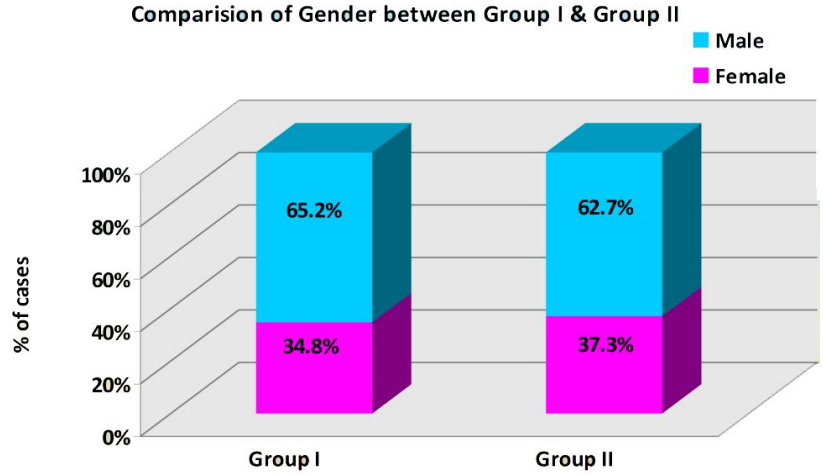


Table 6:

SEX	Group A		Group B		P Value
	Frequency	%	Frequency	%	
F	48	34.8%	53	37.3%	0.658
M	90	65.2%	89	62.7%	
Total	138	100%	142	100%	

Table 7:

Nausea	Group A		Group B		P Value
	Frequency	%	Frequency	%	
At 1 hr	5	3.6%	11	7.7%	0.137
At 2 hrs	9	6.5%	15	10.6%	0.227

Fig. 7:

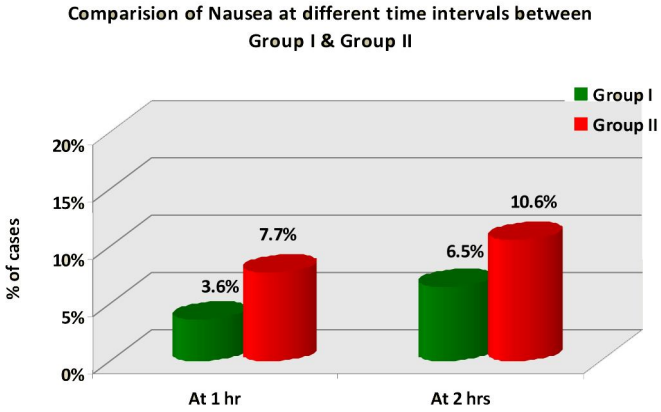


Table 8:

Vomiting	Group A		Group B		P Value
	Frequency	%	Frequency	%	
At 1 hr	2	1.4%	4	2.8%	0.684
At 2 hrs	4	2.9%	6	4.2%	0.750

Fig. 8:

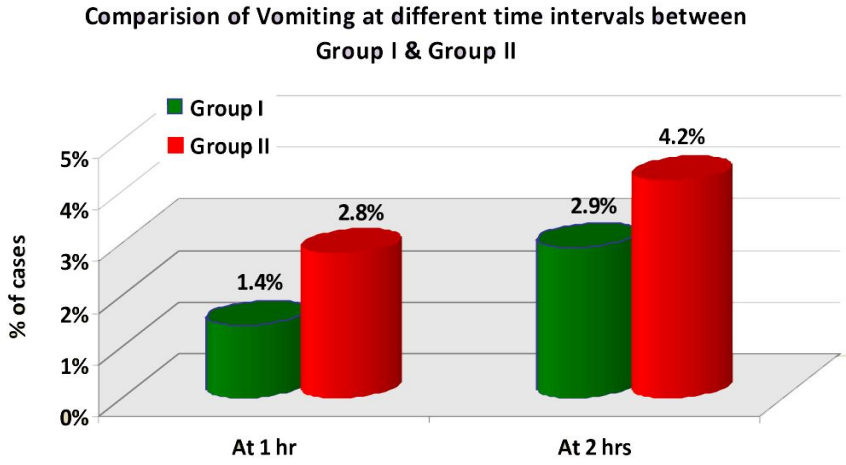
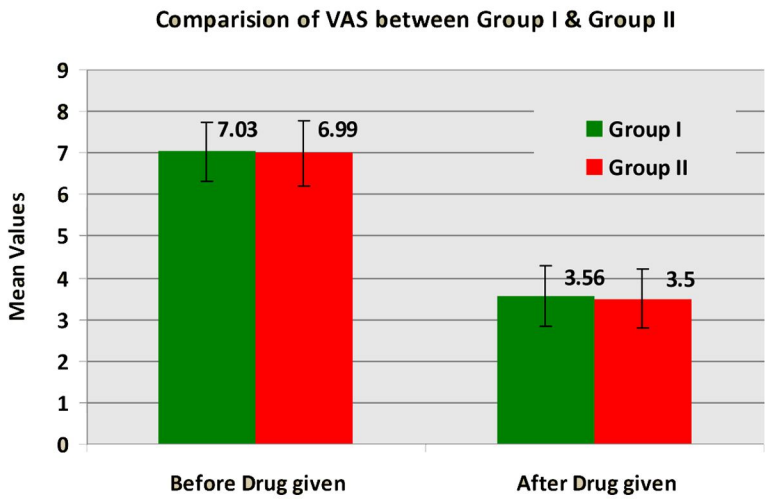


Table 9:

VAS	Group A		Group B		P Value
	Mean ± SD	Min - Max	Mean ± SD	Min - Max	
Before Drug given	7.03 ± 0.78	6 - 8	6.99 ± 0.719	6 - 8	0.629
After Drug given	3.56 ± 0.70	3 - 5	3.50 ± 0.73	3 - 5	0.448

Fig. 9:



The Table 8 and Figure 8 shows comparision of vomiting at different time intervals (1 hr &2 hrs) between two groups. 1.4% of group A patients had vomiting in 1 hour and 2.9% had vomiting in 2 hrs, while 2.8% patients in group B had vomiting in 1 hour and 4.2% patients vomited in 2 hrs. p values calculated after 1 hour was 0.684 and after 2 hours was 0.750

The Table 9 and Figure 9 shows comparision of VAS score between two groups before analgesic was

Table 10:

Final Diagnosis	Group A		Group B		P Value
	Frequency	%	Frequency	%	
Dengue Fever	94	68.1%	99	69.7%	0.772
Dislocation	9	6.5%	7	4.9%	0.566
Fracture	18	13.0%	17	12.0%	0.786
Lacaration	5	3.6%	10	7.0%	0.204
Soft Tissue Injury	6	4.3%	7	4.9%	0.817
Others	6	4.3%	2	1.4%	0.140
Total	138	100%	142	100%	

Fig. 10:

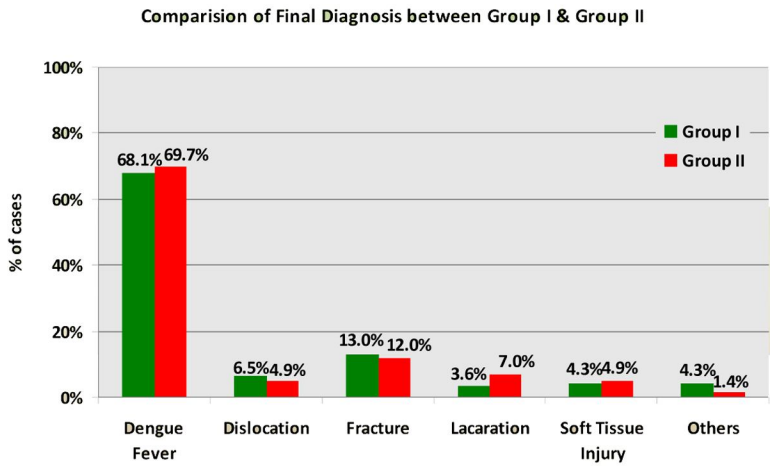
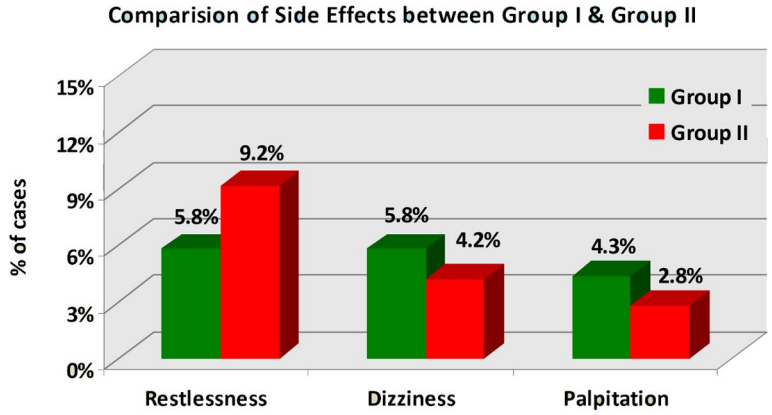


Table 11:

Side Effects	Group A (n=138)		Group B (n=142)		P Value
	Frequency	%	Frequency	%	
Restlessness	8	5.8%	13	9.2%	0.286
Dizziness	8	5.8%	6	4.2%	0.546
Palpitation	6	4.3%	4	2.8%	0.549

Fig. 11:



given and after that.so mean VAS score±SD in group A before drug was given was 7.03±0.78 and after drug was3.56±0.70.similarly in group B before drug administration VAS was 6.99±0.719 SD and after drug administration it was 3.5±0.73.p value calculated before drug given was 0.629 and after drug given was 0.448.

The Table 10 and Figure 10 shows comparision of final diagnosis between the two groups,with bulk of the patients in both the groups being of dengue fever. Group A had 68.1% patients of dengue fever while group B had 69.&% patients of dengue,and p value was 0.772:6.5% in group A had dislocations while 4.9% had dislocations in group B and p value was 0.566:13.0%of patients in group A were having fractures while 12.0% in group B had fractures,and p value was 0.786:3.6% of patients in group A had lacerations while 7.0% of patients in group B had lacerations and p value calculated was 0.204:4.3% of the patients in group A has soft tissue injuries while 4.9% in group B had soft tissue injuries,and p value was 0.817:4.3% of patients in group A had other diagnosis while 1.4% in group B had other diagnosis, and p value calculated was 0.140.

The Table 11 and Figure 11 shows comparision of the adverse effects between the two groups. 5.8% of patients in group A had restlessness while 9.2% of patients in group B had restlessness, and calculated p value was 0.286:5.8% of patients in group A had dizziness while 4.2% of patients had dizziness and p value calculated was 0.546, 4.3% of patients in group A had palpitations while 2.8% of patients in group B had palpitations and calculated p value was 0.549.

Discussion

A major proportion of patients presenting to our emergency department have various painful conditions. In our department, tramadol has been the intravenous opioid of choice. In our experience, the advantages of IV tramadol are its titratability (dose range 1–2 mg / kg) and predictability. Traditionally, it has been the norm to use prophylactic antiemetics along with opioids to counter their emetic side effects. All opioids have the well recognised side effects of nausea and vomiting [28], with some being worse than others [37]. These symptoms are mediated both centrally, by stimulation of the chemoreceptive trigger zone and dopamine receptors in the medulla, and peripherally, by labyrinthine stimulation and reduced gastric emptying [38]. Thus antiemetic prophylaxis is particularly common with the use of opioids for postoperative acute pain, where the incidence of nausea and vomiting varies between 8% and 92% [39]. Our study clearly shows that the overall incidence of nausea and vomiting is low when tramadol is used in acute pain. Comparision of nausea at different time intervals (at 1 hr and 2 hrs respectively) between group A and group B, 3.6% in group A had nausea after 1 hour and 6.5% after 2 hrs, while 7.7% had nausea in group B after 1 hour and 10.6% after 2 hrs. p values calculated after 1 hrs time was 0.137 and after 2 hrs was 0.227, which is not significant. Comparision of vomiting at different time intervals (1 hr &2 hrs) between two groups. 1.4% of group A patients had vomiting in 1 hour and 2.9% had vomiting in2 hrs, while 2.8% patients in group B had vomiting in 1 hour and 4.2% patients vomited in 2 hrs. p values calculated after 1 hour was 0.684 and after 2 hours was 0.750, which again are not significant.

This low incidence was equally evident in both study groups (ondensetron and without ondensetron groups), and there was no statistically significant difference between the two groups. All the patients who reported nausea (n=24) and vomiting (n =10) responded to a single IV dose of metoclopramide10 mg . This applied to the period of observation in the

department, which was at least two hours or longer depending on the clinical condition or outcome. There is no evidence in the literature to show that the nausea or vomiting, which occurs when tramadol is used in acute pain in the emergency setting, is clinically significant. This is the first prospective, observational, study of this kind to be conducted in an Indian emergency department. We have come across two similar studies in the literature with comparable conclusions. Lambie et al [2] recruited a similar number of patients, but restricted the patients to those with musculoskeletal trauma. They concluded that the incidence of nausea and vomiting was 3.7% overall with more vomiting (5.4%) in the metoclopramide group compared with the placebo group (1.9%) (difference not statistically significant). Talbot Stern and Paoloni [3], in a study conducted in Australia, recruited a smaller number of patients with a wide spectrum of painful conditions, and used both morphine and pethidine for acute pain in the emergency department and reported a 6.5% incidence of nausea and vomiting. This study had a slightly higher incidence of vomiting in the placebo group (not statistically significant) and concluded that routine use of prophylactic metoclopramide cannot be justified. Interestingly, a subsequent observational study of all patients receiving opioid analgesia in the same department confirmed the low incidence (2.4%) of nausea and vomiting, a higher incidence (9.3%) of pre analgesia nausea and vomiting, and yet a persistent practice of giving prophylactic antiemetics (33%) [4].

In contrast with the setting of acute pain, the incidence of opioid induced vomiting has been reported at 28% with morphine in non chemotherapy cancer patients, with a slightly lower incidence of nausea [28]. We suspect that the long tradition of prophylactic antiemetic use has derived from the experience of nausea and vomiting in postoperative acute pain, where opioids are commonly used in patient controlled analgesia. Even in this setting, the claims of opioid induced nausea and vomiting have been challenged and the symptoms ascribed to other factors related to the surgical procedure [39]. Moreover, the expected relief of nausea and vomiting with prophylactic use of metoclopramide [40], droperidol, and ondansetron [41] has not been reported. Dundee and Jones [11] using cyclizine therapeutically, not prophylactically, reported significant reduction in vomiting but not nausea in ambulatory patients with chronic pain. In another large multicentre study, Sussman et al [36] recommended against any prophylactic use of antiemetics for opioid induced nausea and vomiting in both acute and chronic pain in various settings. The same study also found ondansetron to be a superior therapeutic antiemetic.

In the present study, apart from the exclusion criteria detailed above, we aimed to recruit any patient who needed tramadol irrespective of the painful condition. Typically, generalized pain in dengue fever as a cause of pain predominated in keeping with the fact that the data collection for this study was done during the months of dengue fever in delhi,but we did not intend to limit recruitment to this group of patients. The randomisation process involved division of the patients in two groups which was done by the statistician as per the computerized randomization code.patients were divided in to two groups as per this code. we instructed the nurse observing the patient for nausea and vomiting to document the patient's yes / no response from after 1 hour of starting tramadol infusion because this is the peak time of analgesia achieved by tramadol. The nature of the question asked by the nurse ensured that any nausea or vomiting reported by the patient since receiving morphine was recorded, and no such event was missed.

Our study has some limitations.. The recruited patient population has resulted in a selection bias towards dengue fever paients, although this was unintended. Both limitations are partly related to patient consent but mostly to the inability of busy doctors to devote time to patient recruitment. Thus the results of this study may not be immediately applicable to the general patient population who present in acute pain. Also we only used tramadol as the opioid in our study, the low incidence of nausea and vomiting may not apply to other opioids used in acute pain as these drugs have varying emetic potential.

However, we believe that, in the light of our findings, we could no longer justify using ondensetron prophylactically, and our department is planning to discontinue this practice. The authors of this study had anecdotal experience of this low incidence prior to the study and felt that routine use of prophylactic ondensetron was unnecessary.

In conclusion, it would appear wise to reserve the use of antiemetics for patients who actually vomit, and then to select an antiemetic like cyclizine or ondansetron, which have a safer side effect profile. Our practice has already changed accordingly.

Conclusion

Nausea and vomiting are well recognised side effects of tramadol use. Traditionally it has been

recognised practice to use prophylactic anti-emetics with tramadol to ameliorate these potential side effects. A chart review published in 2009 from an Australian ED found 22.6% of patients had been given anti-emetics prophylactically, and Paoloni et al (2002) noted the figure to be higher at 33% despite departmental education advising against their routine use [4]. The mechanisms by which tramadol is believed to cause nausea and vomiting include central stimulation of the chemoreceptor trigger zone and dopamine receptors in the medulla, and peripheral stimulation of labyrinthine receptors and reduced gastric emptying [38]. It must be remembered that confounding factors such as pain, via vagal stimulation, and the pathology of an underlying diagnosis will often be responsible for nausea and vomiting. Paoloni et al (2002)[4] noted the baseline prevalence of nausea in adult ED patients in acute pain was 20%, and after opiate administration the point prevalence dropped to 10.2% at one hour [4]. This reduction was statistically significant.

Greenwald et al (2005) similarly noted a reduction in nausea (from 24mm to 10mm on a visual analogue scale) with the administration of morphine. Significantly more patients report nausea than experience vomiting, as nausea precedes vomiting in most cases, and being a subjective symptom will often be reported even if mild. Mild cases of nausea may not be significant enough to require treatment from the patient's perspective. Most data regarding opiate-induced nausea and vomiting comes from anaesthetic literature, post-operative rates averaging 20-30% and varying from 8-92%. Interestingly a few studies collected pre-operative data on the use of intramuscular morphine and noted a low incidence of nausea (4-11%) and vomiting (1-6%) at 90 minutes. Many reasons to account for the apparently low incidence of nausea and vomiting in the ED setting have been postulated. The higher rates seen amongst post-operative compared to ED patients will partly be attributable to anaesthetic agents and a surgical procedure. Tramadol is often given in isolation in the ED, reducing the risk of adverse interactions with other medications [3]. The route of administration may be important. Small studies have demonstrated less nausea and vomiting with parenteral administration when compared to the oral route.

Papers reporting the highest incidence of nausea and vomiting were those following patients for a considerable period of time, anything from 4 to 24 hours. This could simply reflect the increased likelihood of nausea and vomiting from confounding factors with time, but could represent a delayed emetic-effect of opoids. One could postulate that pharmacokinetic factors may be responsible for this delayed effect, if metabolites of opioids had greater emetic properties than opioid itself. Patients may become more mobile as their pain lessens over time, and this could further aggravate labyrinthine stimulation. If there is indeed a delayed emetic-effect, it would add weight to the argument against the co-administration of anti-emetics with tramadol, as the action of a prophylactic drug may have begun to wear off before the emetic sequelae of tramadol had appeared, if they were going to appear at all. Anti-emetics are not without side-effects. The incidence of side-effects from ondensetron, the anti-emetic used in this study is that. 5.8% of patients in group A had restlessness while 9.2% in group B had restlessness, while 5.8% of patients in group A had dizziness and 4.2% in group B, 4.3% of patients in group A had palpitations while 2.8% group B. Whilst it would appear that routine prophylactic anti-emetics should not be given with tramadol there are circumstances where consideration should be given to their use, such as in patients with a significant head injury where increases in intracranial pressure would be potentially harmful, patients immobilized with presumed unstable spinal injuries, obtunded patients where the airway is not secure and vomiting could lead to aspiration, and patients with known prior sensitivity to tramadol..

In conclusion, this study has found not only a very low rate of nausea and vomiting with intravenous tramadol in adult ED patients in acute pain, but also no statistical change to this rate when anti-emetics (in all cases ondensetron) were co-administered. With such an apparent low rate of nausea and vomiting it seems to be unjustified to use routine ondensetron prophylactically, considering its side effect profile and indeed cost. Further research is needed on other commonly used anti-emetics such as cyclizine.we therefore recommend that practice of using prophylactic antiemetics before the opioid analgesics should be changed in our deparment.

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