

Clinical Evaluation of Prochlorperazine Risk / Benefit in Emergency Department Patients Receiving I.V Tramadol

Bahir Abdul- Razzaq Mshiemish* BSc (Pharm.) , Msc , PhD (Pharmacology)

Summary:

Background: antiemetics are commonly prescribed as prophylactic for nausea and vomiting when opiates analgesics are prescribed in the emergency department.

Objective: to assess the incidence of nausea and vomiting after tramadol analgesia, and the effect of prochlorperazine on this incidence.

Patients and methods: I.V tramadol was administered with prochlorperazine (group I) or pyridoxine (group II) to 44 patients with acute sever pain.

Results: the incidence of nausea and vomiting was not significant between patient groups; while the occurrence of extrapyramidal side effects was only seen in the prochlorperazine group. The low incidence of nausea and vomiting after opiate analgesic and higher incidence of side effects with prochlorperazine are consistent with controlled data in literature.

Conclusion: prophylactic prochlorperazine should not be used routinely in emergency department for patients receiving narcotic analgesia.

Keywords: tramadol, pyridoxine, prochlorperazine, nausea & vomiting, extrapyramidal side effects.

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Introduction:

Prochlorperazine has been shown to be effective prophylaxis for the prevention of vomiting postoperatively (1, 2). The use of prophylactic prochlorperazine with tramadol (opioid analgesic) in the emergency department (ED) appears to have been extrapolated. It has been documented from the previous experience that the incidence of vomiting with opioid analgesics in acute pain within ED is quite low. For this reason we studied the incidence of nausea and vomiting after parenteral tramadol, and the potential value of an antiemetic (prochlorperazine, vitamin B6) given prophylactically.

Patients and Methods:

This randomized, double- blind controlled trial was conducted in the ED of AL-Yarmok Teaching Hospital. Patients aged 20 years or older with an acute pain syndrome requiring parenteral tramadol for pain control were considered for the study. Clinical exclusion were: previous administration of opioid analgesic, patients who had nausea or vomiting before administration of tramadol or study medication, GI conditions which mechanically predispose to vomiting (e.g. bowel obstruction), family or personal history of parkinsonism or dystonia, and current use of psychotropic agents. This exclusion was to prevent selective bias in our study design. For ethical considerations, patients who developed nausea and vomiting despite prophylactic antiemetics were to be given a known dose of antiemetic to counteract the symptoms. Tramadol was administered by I.V route as a bolus dose (100 mg/2ml) .An equal number of ampoules of prochlorperazine (10 mg/ml; group. I) and pyridoxine

(100mg/2ml; group II) had been supplied by the pharmacy department. The patient received the contents of the selected ampoule as I.V bolus immediately after tramadol. Data collected include the number code of the study drug which was recorded on the patient's study sheet, and the patient's name and the medical record number to allow collection of demographic data. Information about the amount of narcotic given, incidence of nausea and vomiting at 60 minutes, and any movement disorders were recorded. Vomiting was recorded as "all" or "none" after administration of the study drug. Clinical data were verified on review of the patient's record.

Statistical analysis: Chi square test was done by applying Excel Program for statistical analysis. P-value <0.05 considered significant.

Results:

A total of 50 patients were enrolled in this study, just 44 patients were within study protocol requirements and complete this trial. The baseline characteristics for both patient groups did not differ significantly ($p < 0.05$)(table-1). As expected for an ED acute pain population, musculo- skeletal injuries predominated (like fracture, dislocation and crush injury). However, the indications for analgesia covered a wide spectrum like abdominal (renal colic, appendicitis, and chest pain) or miscellaneous causes of pain (stab wounds, bullet injuries, and burns). Regarding the efficacy of antiemetics used, table (2) clarified that the difference for the incidence of nausea and vomiting between the groups were not significant ($p > 0.05$). No patient in either group required second antiemetic dose and there were no complications related to nausea or vomiting. Concerning the safety of antiemetics, table (2) illustrated that the incidence of extrapyramidal and other neurological side effects in those taking

* Department of Pharmacotherapy / College of Pharmacy / AL- Mustansiriya University.

prochlorperazine (gr. I) was significantly higher ($p < 0.05$) than those taking pyridoxine (gr. II) (15% versus 0.0%). These side effects include dystonic reaction, vertigo, dizziness lasting 45 minutes, restlessness and drowsiness.

Table (1): Characteristics of patients according to treatment assigned.

Characteristic	Group I: Tramadol + prochlorperazine	Group II: Tramadol + pyridoxine	P-value
No. of patients	23	21	>0.05
No. of females	13	11	>0.05
Mean age (yrs)	40	37	>0.05

Table (2): incidence of nausea and vomiting (efficacy) and extra- pyramidal side effects (safety) for patient groups.

Patient group	% nausea and vomiting	P-value	% side EP effects	P-value
Group I (N=23) Tramadol + Prochlor .	Nausea= 4.3% Vomiting=4.5%	>0.05	15.0%	<0.05
Group II (N=21) Tramadol + Pyridoxine	Nausea = 4.7% Vomiting=4.7%		0.0%	

N= number of patients; EP = extrapyramidal.

Discussion:

The practice of administering an antiemetic at the same time as opioid analgesics has been based on the expected GI side effects of these narcotics. Central effects are mediated by stimulation of emetic chemoreceptors, including dopamine receptors in the medulla (3). Peripheral effects include increase labyrinthine sensitivity, with vomiting more frequent in ambulant recipients of opiates. Delayed gastric emptying rate has been described particularly in labor with a supposed increased risk of aspiration (4). This study support other previous observations that I.V narcotics used in ED setting for pain relief is associated with a low incidence of nausea and vomiting. Several factors could explain this low incidence: our patients were generally immobile and this minimized vestibular stimulation, and the amount of tramadol required to achieve adequate analgesia, is less when given by I.V route than with I.M injection (5,6). Without adequately controlled studies, it is difficult to draw conclusions regarding emesis from opiates, particularly when used in conjunction with other medications or in painful conditions where vagal stimulation occurs and may in itself produce emesis. Nausea and vomiting patients undergoing minor gynecologic surgery have been reported in a series of papers titled "studies of drugs given before anesthesia" but results show wide variation in frequency of nausea (2% to 41%) and vomiting (0% to 17%) (7,8). The largest study reported that emesis with morphine reached significance and emesis with pethidine was not (7). In an observational study of symptoms associated

with AMI, the incidence of vomiting was lower in the patients who received morphine than in the group not receiving this analgesic (32% versus 44%) (9). Another acute pain population commonly treated with opiates is women in labor. There are no data to support claims that women are more prone to emetic effects of opiates than male (7). Our data also do not support this result. The average age of patients in this study is lower than most of the referenced articles (table-1). However, there is no evidence of a correlation between opiate-induced emesis and age in the literatures (3). Prochlorperazine is a dopamine- receptor antagonist which acts on the CNS to raise the threshold for vomiting at the CTZ. It also acts peripherally on gastric receptors (2). There was no significant difference in the incidence of nausea or vomiting between patients who received prochlorperazine and those received pyridoxine (table-2). Pyridoxine has been widely used for the treatment of nausea and vomiting, especially when occurring during pregnancy, with unknown mechanism (may be just placebo) and doubtful effect (10). The use of prochlorperazine is not without risk. In large surveys, the overall incidence of side effects was $\approx 11\%$. It's neurotoxicity is secondary to the action on dopaminergic neurons in the striatum, affecting modulation of muscle tone, and in mesocortex, influencing mood (11). The most common extrapyramidal effects involve akathisia (restlessness) and drowsiness (up to 10%) and dystonic reaction. Patients considered more susceptible to these reactions are those with AIDs, renal impairment, cancer, age younger than 30 years, patients taking other dopamine antagonist, and possibly women (12). Overall, in this study, the incidence of side effects was significantly higher in prochlorperazine group compared with pyridoxine ($p < 0.05$) which did not show any side effects (table-2). Drug- induced movement disorder are often not recognized by physicians (13). Extrapyramidal side effects may even mimic anxiety, depression, and catatonia (12). It is likely that the true incidence of these side effects from prochlorperazine is higher than our results would suggest, as formal assessment for akathisia was not performed as part of the study protocol.

Conclusion:

Because the incidence of nausea and vomiting in association with tramadol use for acute pain in the ED setting is low, it's our recommendation that prophylactic prochlorperazine should not be used routinely in the ED patients. The frequency and severity of side effects with prochlorperazine, particularly in female patients and / or patients younger than 30 years of age, cannot be ignored. The likelihood of side effects is therefore higher than the expected benefit of the drug. It should only be prescribed for the small number of patients who may experience severe nausea and / or vomiting after opiate analgesia.

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