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RESEARCH ARTICLE

A CASE OF TRAMADOL INDUCED ANAPHYLACTIC SHOCK

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ABSTRACT

Tramadol is a centrally acting analgesic and has serotonergic and noradrenergic action. The metabolite of Tramadol is O-desmethyltramadol and acts on the μ-opioid receptor. It is 10 times less potent then morphine. Tramadol is used to treat both acute and chronic pain of moderate intensity. Tramadol is considered to be a relatively safe analgesic. Commonadverse effects of tramadol are nausea, dizziness, and vomiting, particularly at the start of the therapy. At therapeutic doses, tramadol does not cause respiratory depression, however, in patients with diminished respiratory function and who are taking additional Benzodiazipine drugs it may cause respiratory depression and hence not advisable. Orally administered tramadol can produce opioid-like effects (both mentally and physically but these effects are mild and not produced following parenteral administration. Fatal intoxications are rare and appear to be associated with large overdoses of tramadol and co-ingestion of other drugs (including alcohol). Tramadol is used worldwide and is listed as a step-2 analgesic in the WHO guidelines for cancer pain relief. Tramadol is also listed on several national essential medicines lists. Tramadol was first synthesized in 1962 by Grünenthal GmbH in Germany by coupling of the corresponding cyclohexanon with 3-methoxyphenylmagnesium bromide in a Grignard reaction.(1:2) Tramadol shows structural resemblance with codeine and both have a 3-methoxy group on the phenyl ring. Tramadol hydrochloride is readily soluble in water and methanol. Mechanism of Action The (+)-enantiomer of tramadol contributes to analgesia by inhibiting the reuptake of serotonin, the (-)-enantiomer by inhibiting the reuptake of noradrenaline, and the O-desmethyl metabolite by binding with relative high affinity to the μ-opioid receptor (4). Tramadol binds with low affinity to the human μ-opioid receptor. This affinity is approximately 4000-fold less than that of morphine (3:4) There are less chances of anaphylaxis to Tramadol. The Allergy Unit, Department of Paediatrics, University of Florence, Anna Meyer Children's University Hospital, Florence, Italy reported a case of Anaphylaxis to Tramadol in a child in 2015.No more cases of Anaphylaxis reaction to Tramadol are found in the literature We are reporting here a case of anaphylactic shock after intravenous injection of tramadol hydrochloride in emergency department.

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INTRODUCTION

Tramadol is a centrally acting analgesic and has serotonergic and noradrenergic action. The metabolite of Tramadol is O-desmethyltramadol and acts on the μ-opioid receptor. It is 10 times less potent then morphine. Tramadol is used to treat both acute and chronic pain of moderate intensity. Tramadol is considered to be a relatively safe analgesic. Common adverse effects of tramadol are nausea, dizziness, and vomiting, particularly at the start of the therapy. At therapeutic doses, tramadol does not cause respiratory depression, however, in patients with diminished respiratory function and who are taking additional Benzodiazipine drugs it may cause respiratory depression and hence not advisable. Orally administered tramadol can produce opioid-like effects (both mentally and physically) but these effects are mild and not produced following parenteral administration. Fatal intoxications are rare and appear to be associated with large overdoses of tramadol and co-ingestion of other drugs (including alcohol). Tramadol is used worldwide and is listed as a step-2 analgesic in the WHO guidelines for cancer pain relief. Tramadol is also listed on several national essential medicines lists. Tramadol was first synthesized in 1962 by Grünenthal GmbH in Germany by coupling of the corresponding cyclohexanon with 3-methoxyphenylmagnesium bromide in a Grignard reaction

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(Chemie Grünenthal GmbH, 1965; Chemie Grünenthal GmbH, 1967). Tramadol shows structural resemblance with codeine and both have a 3-methoxy group on the phenyl ring. Tramadol hydrochloride is readily soluble in water and methanol.

Mechanism of Action: The (+)-enantiomer of tramadol contributes to analgesia by inhibiting the reuptake of serotonin, the (-)-enantiomer by inhibiting the reuptake of noradrenaline, and the O-desmethyl metabolite by binding with relative high affinity to the μ-opioid receptor (Handley, 2014). Tramadol binds with low affinity to the human μ-opioid receptor. This affinity is approximately 4000-fold less than that of morphine (Gillen et al., 2000; Handley, 2014). There are less chances of anaphylaxis to Tramadol. The Allergy Unit, Department of Paediatrics, University of Florence, Anna Meyer Children's University Hospital, Florence, Italy reported a case of Anaphylaxis to Tramadol in a child in 2015.No more cases of Anaphylaxis reaction to Tramadol are found in the literature

We are reporting here a case of anaphylactic shock after intravenous injection of tramadol hydrochloride in emergency department.

CASE REPORT

A 54yrs male patient present with complain of severe abdominal pain since last 3 hour prior arrival to emergency and was continuous in nature, there was associated history of vomiting 1 episode at home. The pain was 6/10 in severity and was localized to upper abdomen with no radiation and no aggravating and relieving factor. There was no history of loose motion, constipation, fever, melaena, hematemesis, burning micturation and trauma. The patient gave the history of similar episode in past which resolved by itself. The patient also gave history of eating spicy food outside on the night before. The patient did not give any history of any chest pain, shortness of breath and dizziness.

PRIMARY SURVEY

Airway: Patent, Talking.

Breathing: RR-16 spo2-100%on roomair.

Circulation: BP 140/80mmhg pulse – 110beat/min.

Dissability: Gcs-15/15 with no focal neurological deficiet seen.

Exposure: no abdominal mass or ecchymosis seen.

Sample History

S- Pain over epigastric area with no intake of alcohol and illicit drug abuse
A – History of allergy to nonsteriodal antiinflamattory drugs
M- Tab pantoprazole and syp sucralfate
P – No past medical or surgical history
L- 3 Hrs before arrival
E- There was no significant event prior to arrival

Secondary Survey

Heent: No pallor icterus cyanosis seen.jvp not raised, neck gland not palpable, no neck mass, tongue dry.

CHEST: On inspection- there was no deformity or scar mark seen and no swelling or lump on the chest seen, and equal chest rise is present.
On palpation--equal chest rise, no tenderness seen On percussion—chest is bilateral resonant on percussion on auscultation – bilateral equal vesicular breath sound and no rhonchi, wheezes and crepitus seen.

CVS: First and second heart sound audible, no murmur or friction rub sound heard

CNS: Patient is conscious, alert and oriented to time. Place and person. higher mental function within normal limit. motor and sensory function bilateral limb normal, no flapping tremor seen

ABDOMEN

Inspection: No scar seen, no ecchymosis, no swelling, umbilicus normal and in position, no engorged vein seen.

Palpation: Tenderness on deep palpation over the epigastric region and right hypochondria. There is no rebound tenderness and no guarding or rigidity seen. No palpable mass felt and normal bowel sound.

Percussion: Dull on percussion, no fluid thrill or shifting dulness observed.

Auscultation: Bowel sound heard, no bruit heard, no inguinal hernia seen, normal external genitalia, no testicular tenderness observed, per rectal examination was within normal limit.

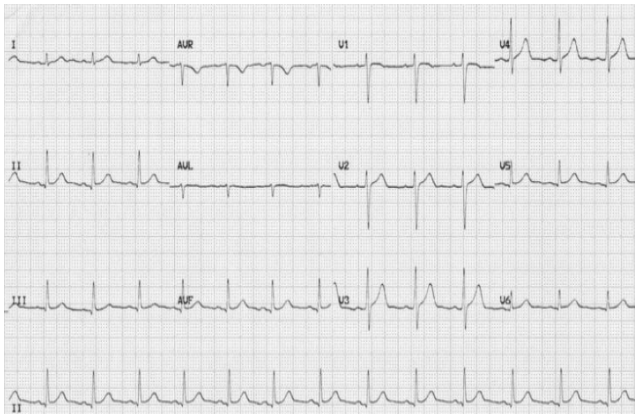
Extremities: Within normal limit

Treatment in Ed

Patient was Canulated with 18G canula over the left anti-cubital vein.

- Iv fluid with normal saline 0.9% 500ml iv stat
- Injection pantoprazole 40mg iv stat
- Injection ondensetron 4mg iv stat
- Injection paracetamol 1000 mg iv stat

ECG DONE IN ED AND SHOWED NSR



The patient was re-evaluated after 15 min, but the the pain severity was still the same. As the patient was having a history of allergy to NSAID, so Injection Tramadol 100mg slow intravascular was given to the patient. Immediately after the

injection Tramadol Hydrochloride was given slowly intravascular, the patient started having palpitation and started complaining of itching over the injection site.
Over the next few minutes there was development of rash and wheals over the left arm and it started to itch. The patient started feeling restless and even started sweating.

Re-evaluation done in ED

Airway- maintained and talking. Breathing- Bilateral mild to moderate wheezes heard and Spo2 in room air dropped to 88%, RR 30/m

Circulation: The pulse was feeble on palpation with the heart rate 134beats/minute, Blood pressure was found to be 88/60 and extremity was cold.
Disability: none, GCS 15/15

Extremity: Urticarial wheal and Rashes seen

DIAGNOSIS – ANAPHYLACTIC SHOCK

Management in ED

- Patient connected to Monitor
- O2 started by NRB@6 L/min
- Second IV canulation done in right anti-cubital vein with 18g canula
- IV fluid started with Normal Saline 1000ml iv bolus through both iv canula.
- INJECTION ADRENALINE 0.5ML given intramuscular over Right Anterior Thigh
- INJECTION PHENIRAMINE (AVIL) 22.75MG(2ml) given intravascular stat

The patient was re-evaluated again in ED after 5 minutes

Airway: Patent and talking
Breathing: RR 15/m, Spo2-100%, bilateral normal vesicular breath sound.
Circulation: BP 130/70, Pulse- 88/m, CRT-wnl

The patient was feeling better and was less anxious and the pain abdomen was still there but the severity was about 2/10. The patient was advised to get an Ultrasound whole abdomen to rule out the cause of pain abdomen. A general surgery consult was taken in view of pain abdomen. The patient felt much better and wanted to follow up in the OPD. The patient was advised from the ED for admission for observation as he had anaphylaxis to Tramadol Hydrochloride and the chance of rebound phenomenon. But the patient was reluctant for admission. The patient was kept in the emergency Observation area for next 4 hrs and the vitals were checked and close monitoring was done. The patient was completely pain free and no other associated complaint and took oral fluids. He was then discharged from the ED with advice to come to ED in presence of any red flag signs and the allergy record of the patient was thoroughly documented regarding Allergy to Tramdol and incident reported.

This was a very rare case of Anaphylactic Shock to Injection Tramadol Hydrochloride. The incidence of anaphylaxis has been reported very rarely in literature. The Allergy Unit, Department of Paediatrics, University of Florence, Anna Meyer Children's University Hospital, Florence, Italy reported a case of Anaphylaxis to Tramadol in a child in 2015[7]. There has not been any newly reported data of anaphylaxis to Tramadol in India. The use of Tramadol has been increasing in the ED over the past few years and also it has been prescribed for some acute pain and sometimes for chronic pain. There has been reports of OTC use of tramadol and there has been few cases of fatal poisoning due to tramadol alone have been reported in the literature.[8:9:10]

DISCUSSION

As an analgesic, tramadol is approximately equipotent as Codeine after parental administration. Tramadol has a higher oral bioavailability than morphine and potency of tramadol is about 20% of oral morphine (Handley, 2014). Few cases of fatal poisoning due to tramadol alone have been reported in the literature (Barbera et al., 2013; de Backer et al., 2010; de Decker, 2008). More frequent are intoxications occur with co-ingestion of other drugs or alcohol (Alvarado, 2005; Ardakani et al., 2008). Symptoms following a tramadol intoxication are similar to those of other opioids analgesics. These include central nervous system (CNS) depression, including coma, nausea and vomiting, tachycardia, cardiovascular collapse, seizures, and respiratory depression up to respiratory arrest.[5] Moreover, in combination with serotonergic agents tramadol may induce the serotonin syndrome (Electronic Medicines Compendium, 2014; Houlihan, 2004)[.] Few cases of tramadol-related severe respiratory depression have been described in the literature[.] (Marquardt, 2005); Risk of respiratory depression is low compared to other Opiods. This case is being submitted now as the reported rate of Anaphylaxis by Injection Tramadol Intravenous is 0.01% so far.

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