

Safety and Efficacy of Tramadol in Relieving Post Operative Pain¹Dr. N. Junior Sundresh, ²G.Tholkappiyan, ³R. Aswathi¹Professor, Department of surgery, RMMCH, Chidambaram-608002, Tamilnadu, India.^{2,3}Pharm.D. Clerkship, Department of pharmacy, Annamalai University, Chidambaram, Tamilnadu, India.**Corresponding Author:** G. Tholkappiyan, Pharm. D. (Clerkship), Department of Pharmacy, Annamalai University, Chidambaram, Tamil nadu-608002.**Type of Publication:** Original Research Article**Conflicts of Interest:** Nil**Abstract**

Pain is an unpleasant sense represents any inflammation or trauma in the tissue level with irrespective of cause. Among the patients of post-operative ward about 70-80% was experiencing pain in the range of moderate to severe. Pain assessment and reassessment were required to provide effective post-operative pain treatment. The main purpose is to evaluate the evidences and observe the safety and efficacy profile of tramadol for post-operative pain management where in patients undergone various surgical procedures. Tramadol is a centrally acting weak synthetic opioid of amino cyclohexanol group. It inhibits reuptake of norepinephrine and enhances release of serotonin. Suspected adverse events were nausea, emesis, constipation, dry mouth, dizziness, anxiety, hallucination. Prolonged use of opioid analgesia at pregnancy causes neonatal withdrawal syndrome and fetal death. At the course of labor respiratory depression on neonates was found as a major warning. Tramadol is basic analgesia to moderate to severe pain, injectable tramadol is effective for acute pain relief. Also have antitumor effect by inhibiting the proliferation and decrease the risk of recurrence. In rectal suppository tramadol proved as a better alternative for its increased duration of action with less adverse events, when compared with similar intravenous mixture.

Keywords: Tramadol, analgesia, postoperative pain, opioid analgesic, acute pain relief.**Introduction**

Pain is a signal with unpleasant sense represents the symptom of an inflammation or any injury at tissue level with irrespective of cause, its relief is one of the important duties of a clinician. As by standard terms “Pain is an unpleasant sensory and emotional experience of varying intensity, caused by actual or potential damage”. Patient who undergoes surgical procedure experiences pain after surgery called post-operative pain. About 75 to 80 percent of patient reported they were experienced pain in the range of moderate to severe. Pain assessment and reassessment were required to provide the pain management in post-operative condition. The assessment of pain is essential to provide adequate drug therapy. In case of any difficulty in managing pain where, specialty consultations were needed.

Assessment of pain

Pain assessment involves not only just quantifying the intensity of pain but also possess more than quantifying. Some patients not willing to report their pain because of cognitive deficits, sedation and developmental stage. Clinicians need to assess their pain using behavioral tools also with other pain assessment tools. More number of

assessment tools for pain intensity and some are validated for accuracy in detection and presence, quantifying the pain intensity. Although there is inadequate evidence on effect of different pain assessment tools on post-operative pain outcomes to guideline recommendation to use of specific tool. Tools were developed for use in emergency and intensive care unit settings include behavioral pain scale and critical care observational tools. Some examples of validated pain intensity assessment scales are TWENTYONE point NRSs (NRS 0-21), Seven-point Graphic rating scale, Visual analogue scale, Pain thermometer, Face Rating Scales. Pain assessments will be documented routinely in standardised forms by the clinician who involved in the patient care, it helps to promote the effective pain management treatment.

Examples of Pain Rating Scales

Fig: (a) Numeric pain rating, WB Faces pain rating scale.

(b) Visual analogue scale, Verbal rating scale

Fig: (a)

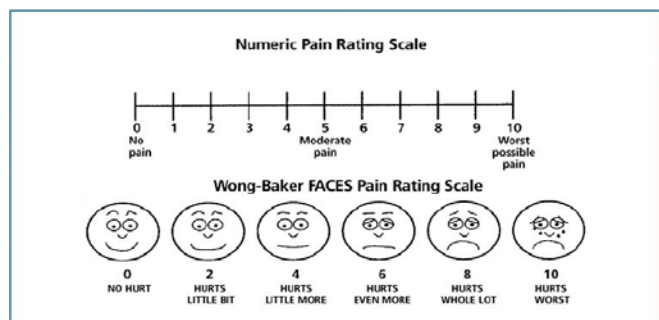
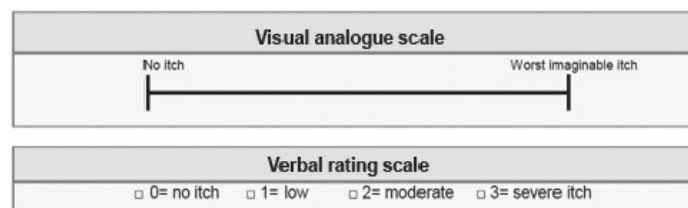


Fig: (b)



Tramadol in relieving pain

Opioids are the mainstay in management of pain but according to the rational therapy, depending on the state of pain one or more classes of drugs are prescribed. The term opiates refer to the compounds structurally related to

products found in opium namely "Papaver somniferum". Tramadol is a centrally acting synthetic opioid analgesic of Amino cyclohexanol group. As a weak opioid agonist property and effect on non-adrenergic and serotonergic neuro-transmission. Inhibit reuptake of norepinephrine, serotonin and enhances serotonin release. It alters perception and response to pain by binding with μ -receptor (Mu) causing inhibition of ascending pain pathway in the central nervous system.

Dosing and administration

Tramadol have 68% bioavailability after a single dose in oral route and IM of 100%. The primary O-demethylated metabolite of tramadol is two to four times as potent as parent drug for the analgesic effect. The racemic mixture of tramadol produces more effective action than enantiomer alone. Enantiomer binds with the receptor and inhibit the uptake of serotonin. Also inhibit nor-epinephrine uptake and stimulates α_2 (alpha-2) adrenergic receptors. It undergoes extensive hepatic metabolism by various pathways including CYP2D6 and CYP3A4. Tramadol should not be used in patient with MAO inhibitors and other drugs for seizure disorder.

On oral administration of adults, providing immediate and extended releasing tablets are available at the dose of 50-100 mg, 200mg, 300mg. However the daily defined dose should not be exceeded 400mg/day. For the administration of child, at the dose of 50-100mg for q-6hr provided initially and it should be followed further not exceeding 400mg/day. Having geriatric patient of less than 75yrs of old may subjected to provide 300mg/day as a defined dose also not exceeding the dose. For above 75 years increase the dosing interval. In IM/IV 50-100mg for 4-6 hourly over 2-3 minutes.

Warning and contraindication

Tramadol mainly used for moderate to severe pain post operating settings some usual warning are opioid

addiction, abuse and misuse of drug, clinician and nurses should monitor the administration of drug. Accidental injection over one dose fatal to children. Ultra, rapid metabolism causes life threatening respiratory depression in children of CYP2D6 polymorphism.

By having the evidence of various clinical-studies it is contraindicated with other equipotent dose of opioids, psychotropic drugs, alcohol, uncontrolled epilepsy, bronchial asthma, hypercapnia, and patient having serious renal and hepatic impairment. Suspected adverse drug reactions were constipation, nausea, dizziness, headaches, emesis, anxiety, hallucinations, seizure, asthenia, cognitive dysfunction. Interaction with drugs affecting cytochrome P450 isoenzymes. Concomitant use of benzodiazepines and other CNS depressants. In pregnancy no fetal risk is involved in short term use. Prolonged use of opioid analgesia at pregnancy cause neonatal withdrawal syndrome, fetal death. During labor period respiratory depression on neonates was found.

Titration of tramadol in post-operative pain

Managing post operative-pain conditions, higher function of demonstration should be provided at perception of pain. Importance were given to respond superior pain relief. It has been traditionally managed analgesics prescribed for more surgical pain patients. Regular use of mild analgesics can be highly effective. Parenteral administrations are only necessary for short time post operative condition, after it can be transferred to oral route. If respiratory depression is the only concern, tramadol can be useful to patients.

Thus, have been found that initially 100mg was given then followed by 50mg for every 10-20 mins if necessary. Up to total of 250mg for the first hour. Thereafter, 50-100mg of 4-6 hourly up to total daily dose of 600mg/day should not be exceeded. For patients above 75yrs increase the dosing interval. Hepatic and Renal impaired patients

having Cr-Cl of 10-30 (ml/min) increase the dosing interval to 12hour.No fetal risk is involved in pregnancy for short-term use but prolonged use of opioid analgesia causes neonatal withdrawal syndrome and so respiratory depression may produce at labor.

Objective

The purpose of the study is to evaluate the evidences and study about safety profile with effectiveness of tramadol in patients undergone pain management treatment of post-operative ward.

Methodology

The study involves retrospective observational analysis of patient undergone treatment of tramadol in conditions like appendectomy, craniotomy, breast cancer surgery, lumbar discectomy, nephrectomy, limb surgery and gynaecological surgery of selective surgeries on post operative pain management. Patients who experiences moderate to severe pain were subjected to this study with sample of one thousand three hundred and thirty-eight (n =1338) using appropriate statistical methodology.

Results and Discussion

After interpretation of the collected data and observations with patients undergone treatment of tramadol (n=1338) on post operatively, the efficacy of injectable tramadol on post-operative cases shown significantly better relieving pain in one hour and also shows higher efficacy with less adverse events on combination with NSAIDs respectively. The comparative efficacy of tramadol intravenous injection of 50mg is equivalent to Morphine of 5mg and Clonidine of 15mcg. Tramadol was recommended as basic analgesia for moderate to severe pain due to its less occurrence of adverse events and lower incidence of cardiac depression in acute pain relief when compared with Morphine. Tramadol also has anti-tumor effect by inhibiting the proliferation and induction of apoptosis and has decreased risk of recurrence and mortality in post-

operative care. On comparison of rectal suppository of tramadol with similar intravenous mixture, rectal route is the better alternative for the prolonged duration of action and has lesser adverse effects like nausea and emesis. By EBM verdict, long acting opioids are avoided for chronic use after discharge.

Conclusion

Tramadol used as a basic choice of drug because of its effective analgesic activity due to the lesser onset of action and produces higher efficacy in combination with acetaminophen. Has shown less incidence of cardiac depression compared with other analgesia. It has been observed that it possessed its own anti-tumor effect by inhibition of proliferation in breast cancer patients. Rectal route of tramadol has increased duration of action when compared with similar intravenous injection and has lesser adverse events. Chronic use and high dose administration of tramadol causes respiratory depression in adults and children respectively.

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