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Research Article

A comparative study of oral tapentadol with thoracic epidural analgesia versus intravenous tramadol and paracetamol combination for postoperative analgesia in off pump CABG

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ABSTRACT

Background: Accurate management of post operative pain is quite impossible with single drug therapy approach. For this, our aim was to combine use of tapentadol tablet orally along with thoracic epidural in comparison with intravenous combined use of tramadol, paracetamol and diclofenac for postoperative analgesia in case CABG patients.
Methods: 60 patients of CABG (Coronary Artery Bypass Surgery) randomly and equally divided into two groups. Group TTE (Tab. Tapentadol -Thoracic Epidural, n=30) were given oral Tablet Tapentadol through NG (Nasogastric) tube at the time of shifting the patient from Operation Theatre to postoperative ward along with Tramadol through Thoracic epidural catheter. In Group TPD (Tramadol -Paracetamol -Diclofenac, n=30) were given Inj. Tramadol, Inj. Paracetamol IV at time of shifting of patient. If pain score is too high (>4) then additional analgesia were given with Diclofenac only if preoperative renal and hepatic profile were normal. Patients were monitored for duration of rescue analgesia, total no. of doses of analgesics in first 72 hours, total consumption of analgesics and response to physiotherapy.
Results: Duration of need of rescue analgesia was significantly longer in TTE group ($p<0.05$) while total no. of rescue doses were significantly more in group TPD ($p<0.001$). We also observed that patients of TTE group were recovered earlier, response to chest physiotherapy was significantly better and thus reduces their total length of ICU stay ($p<0.05$).
Conclusions: Our study concludes that Tapentadol with Thoracic epidural is very much effective as a multimodal analgesia approach in controlling acute postoperative pain after CABG. Tapentadol is quite a newer drug so its usefulness for other patients and different surgeries is still to be debated.

Keywords: CABG, Tapentadol, Thoracic epidural, Tramadol, Multimodal analgesia

INTRODUCTION

The experience of pain is complex, multifaceted, and "an unpleasant sensory and emotional experience," as defined in part by the International Association for the Study of Pain. It is a personal, subjective experience that involves sensory, emotional and behavioral factors associated with actual or potential tissue injury.[1,2]

If an appropriate analgesic treatment is not given for postoperative pain post CABG, various respiratory adverse effects (atelectasis, retention of secretions and pneumonia, Inhibition of cough and sputum excretion), cardiovascular side effects (hypertension and arrhythmias, ST-T changes for ischemia and infarction) and CNS side effects (aggressive behavior, agitation and postoperative psychotic trauma) may occur.[3]

The analgesic benefits of controlling postoperative pain are generally maximized when a multimodal strategy to facilitate the patient's convalescence is implemented (Kehlet, 1997). Pain involves multiple mechanisms that ideally require treatment using a multimodal (or 'balanced') analgesic technique (White & Kehlet, 2010) Principles of a multimodal strategy include control of postoperative pain to allow early mobilization, reduce requirement of analgesics, early enteral nutrition, and attenuation of the perioperative stress response through the use of regional anesthetic techniques and a combination of analgesic agents (i.e., multimodal analgesia).

Tapentadol is a novel centrally acting synthetic analgesic with opioid μ-receptor agonist and norepinephrine reuptake inhibitor in a single molecule.[4,5,6] It is structurally and by mechanism similar to Tramadol .It displays a dual mode of action, has mild opioid activity and possesses monoamine reuptake inhibitor activity also.[7]

Thoracic epidural analgesia (TEA) has been advantageous in providing superior analgesia and better respiratory function in comparison to opioid based intravenous techniques in different types of cardiac surgery.[8]

So our aim was to compare oral Tapentadol with thoracic epidural analgesia versus intravenous Tramadol and Paracetamol combination for post operative analgesia in Triple Vessel Disease (TVD) - Off Pump Coronary Artery Bypass Graft Surgery (CABG).

METHODS

After approval from the Institutional Ethical Committee and informed written consent, this prospective randomized double blind study was carried out in our cardiac centre. 60 patients of either sex scheduled for CABG were included in our study.

Patients having contraindication to opioid dependence, blood coagulopathy, history of drug allergy and abuse, spinal deformity, history of asthma, stroke, renal or liver disorder, patients developing intraoperative complications such as hypotension leading to cardiogenic shock and patient is already taking MAO inhibitors or SSRIs and any major systemic illness were excluded from the study.

60 Patients were randomly allocated into two Groups.

In Group TTE (Tapentadol + Thoracic epidural – n=30), Thoracic epidural was put in T2-T3, T3-T4 or T5-T6. Intra-operative Inj. Bupivacaine 0.25%, 10 ml was given just after induction. Just before shifting, Inj. Tramadol 25 mg diluted in 10cc Normal saline was given through epidural along with Tablet Tapentadol 50 mg orally via NG tube. Saphenous venous harvesting causes lots of pain in lower limbs post-operatively. Thoracic epidural is not effective to relieve this pain so to prevent that we had given Tablet Tapentadol 50 mg 6 hourly for 3 days.

In Group TPD (Tramadol, Paracetamol and Diclofenac IV – n=30), Just before shifting from OT Inj. Tramadol 1.5mg/kg, Inj. Paracetamol 15mg/kg were given. If pain score is too high (>4) once patient gets awake then additional analgesia were given with Inj. Diclofenac 1mg/kg only if pre-operative renal and hepatic profile were normal.

Anesthesia was induced with Fentanyl, 10 micrograms/kg, Midazolam 0.1 mg/kg and Vecuronium 0.2 mg/kg, and was maintained along with Isoflurane commenced at 1% (range 0 to 2%). Hemodynamic measurements such as pulse rate, blood pressure, SpO_2, ECG, PAP, ETCO2 were at various sequences of events throughout the surgery.

In the post-operative period, patients were monitored for the duration of 1st dose of rescue analgesia, total no. of doses, total consumption of analgesics in first 72 hours. We had also looked for the patients well being as well their response to chest physiotherapy, mobilization and total length of cardiac recovery stay. They will be also observed for complications such as nausea, vomiting, dizziness, headache, somnolence etc.

Statistical Analysis

All data were analyzed statically using T- test and a value of $P<0.05$ was considered significant. The data's were presented as Mean ± SD and percentage.

RESULTS

A total of 60 patients were recruited for the study. There were no significant differences between the two groups in demographic data and duration of surgery (Table 1). Hemodynamic parameters were comparable in both the groups ($p >0.05$).

Table 1: Demographic profile.

Parameters	Group TTE N=30	Group TPD N=30	P Value	
Mean Age (years)	58.6 ± 11.9	56.06 ± 10.9	p>0.05	NS
Mean Height (cms)	158.53 ± 2.13	159.72 ± 1.62	p>0.05	NS
Mean Weight (kg)	68.53 ± 4.76	65.56 ± 3.76	p>0.05	NS
Sex (m/f)	16/14	17/13		
Duration of surgery (min)	198.6 ± 27.2	192.4 ± 23.4	p>0.05	NS

NS – Non Significant, S- Significant

Table 2: Analgesic profile.

Analgesic Profile	Group TTE	Group TPD	P value
Time to rescue analgesia (min)	492.7 ± 23.6	368.3 ± 19.6	P < 0.05
Mean no. of doses per day	3.0 ±0.7	4.8 ± 0.6	P < 0.05
Average Total consumption of analgesics (mg)	Tramadol ≈ 75 Tapentadol ≈ 150	Tramadol ≈300 Paracetamol ≈ 2500 Diclofenac ≈ 75	

P < 0.05 – Significant, P > 0.05 – Non Significant

Table 2 demonstrates analgesic profile of both the group post-operative. Since the last dose given nearly before extubation, time to rescue analgesia was observed which is significantly higher in Group TTE ($p<0.05$). So the mean no. of total analgesic doses in first 24 hours was significantly less in Group TTE ($p<0.05$). We have also calculated average total consumption of analgesics in both the groups which was also significantly lower in Group TTE ($p<0.05$).

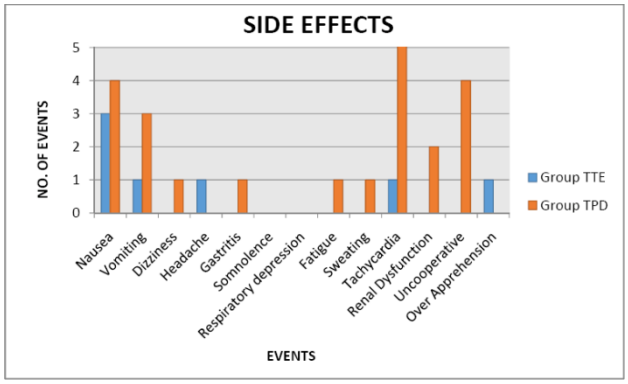

Figure 1: Side effect profile.

Figure 1 demonstrates number of different types of side effects or complications in both the groups of patient. It shows that incidence of nausea is quite high in both the groups. Even incidence of vomiting was also very high in TPD group which is significant ($P<0.05$). We have even observed significant tachycardia followed by intravenous administration of Tramadol in 17/30 cases which is quite significant. We needed to administer Diclofenac in 5 patients out of which 2 patients had increased Serum Creatinine level which is significant as well. We had seen quite a number of patients were uncooperative with intravenous Tramadol. One patient had become very apprehensive after oral Tapentadol which is significant as well. Rest of the events incidence rate was comparable in both the groups.

Table 3: Patient parameters.

Patient Parameters	Group TTE	Group TPD	P value
Chest Drainage Removal (time since extubation)	26.7 ± 2.4	31.6 ± 3.7	P <0.05
Time of Mobilization (in hours since extubation)	42.9 ± 9.42	58.1 ± 8.76	P <0.05
Total length of Cardiac recovery stay (in hours since shifted)	82.9 ± 9.6	96.4 ± 10.9	P <0.05

P < 0.05 – Significant, P > 0.05 – Non Significant

Table 3 demonstrates other important patient parameters which is very much of clinical significance in our study. In group TTE, patients' response to inspiratory chest physiotherapy was very significant. Even chest drainage removal was earlier as compare to TPD group mainly due to better analgesia. Time of mobilization and total length of cardiac recovery stay was also comparable in both the groups.

DISCUSSION

Although guidelines have been developed to improve acute pain management,[9,10] pain relief remains suboptimal for many patients.[11-16] Surveys conducted among patients who had undergone ambulatory surgery indicated that 30%[15] to 40%[12] of patients experience moderate to severe pain following discharge.

A 2004 survey of patients undergoing major abdominal surgery found that many patients were willing to sacrifice pain relief for a reduction in the severity of side effects.[17]

The concept of multimodal analgesia was introduced more than a decade ago as a technique to improve analgesia and reduce the incidence of opioid-related adverse events (Buvanendran & Kroin 2009). A multimodal analgesic regimen should be adjusted to meet the needs of the individual patient by taking into consideration their pre-existing medical conditions, types of surgery, and previous experiences related to both acute and chronic pain management. Several multimodal approaches have been advocated based on different combinations of anti-inflammatory drugs, and regional anesthesia (epidural, peripheral nerve blocks, paravertebral blocks, and local injection/infusion of local anesthetics) (Buvanendran, 2010; Mathiesen, 2009).

Royse CF et al[18] demonstrated that general anesthesia combined with thoracic epidural anesthesia, allowing immediate extubation and longer duration of post-operative analgesia in patients undergoing cardiac surgeries. In our study, postoperative pain relief was superior and cardiac recovery stay was shorter in the TTE group compared to other group as well. This has been shown already in previous clinical studies.[19] A cumulative meta-analysis confirmed that postoperative epidural pain control can significantly decrease the incidence of pulmonary morbidity.[20] Thus, in our study patients of Group TTE had responded very well to chest physiotherapy.

In case of TVD, SVG harvesting was done from the lower limb. Thoracic epidural analgesia is very much effective around the surgical site but it had no effect on lower limb so to provide adequate pain relief over lower limb we have included Tablet Tapentadol in our study.[19]

Tapentadol is a novel centrally acting synthetic analgesic with μ-opioid receptor agonist and norepinephrine reuptake inhibition in a single molecule.[5,6] It is 14 times more efficacious than Tramadol and two times less to

morphine.[21,22] Tapentadol immediate release tablets have been approved by the FDA in 2008 for the relief of moderate to severe acute pain in adults and in 2011, for chronic pain in an extended release form.[23]

In all 4 phase 3 studies of Tapentadol for acute pain, improvements in pain intensity were observed with Tapentadol treatment (50 mg every 4 to 6 hours). The analgesic effects of Tapentadol are independent of metabolic activation, and Tapentadol has no active metabolites.[24,25]

Tapentadol and Oxycodone both have similar effect in terms on analgesia but Tapentadol has better gastric tolerability.[26] In all Phase 3 trials the most commonly reported treatment emergent adverse events were typical of drugs with µ-opioid agonist activity, and those were nausea, vomiting, dizziness, headache and somnolence.[27-30] These are considered the most undesirable side effects associated with opioids leads to its discontinuation.[31]

In our study, group TTE patients had longer duration for rescue analgesia that is mainly because of the combination effects of thoracic epidural and Tapentadol. Because of prompt and sustained analgesia with Thoracic epidural and Tapentadol, patients of group TTE had greater response to chest physiotherapy, less pain score while coughing. So chest drainage was removed earlier and early mobilization started which is quite significant as compare to IV analgesic (TPD) group patients. Because of this, patients had significantly less duration of cardiac recovery stay as well.

We have also observed tachycardia in more than 50% of TPD group patients. It is commonly associated with intravenous Tramadol.[32] Diclofenac is commonly associated with renal dysfunction and it should be avoided with pre-existing deranges renal function.[33] Due to inadequate analgesia we needed to administer Diclofenac in 5 patients out of which 2 (40%) had developed renal dysfunction with raised Serum Creatinine. This finding has remained consistent with previous studies as well.

CONCLUSION

Our study concludes that Tapentadol with Thoracic epidural is very much effective as a Multimodal analgesia approach in controlling acute postoperative pain after CABG. It reduces requirements of opioids and thus provides good compliance to the patients in terms of early mobilization and reduces length of hospital stay. As Tapentadol is quite a newer and novel drug, other benefits and drawbacks still need to be looked for in future as well.

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