Original Article

Analgesic Efficacy of Oral Tramadol in Post Operative Caesarian Section Patients

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Abstract

Objective: To compare the analgesic efficacy of oral tramadol in post-operative lower segment caesarian section patients with intravenous nalbuphine analgesics.

Methodology: The randomized controlled trial was conducted in the department of Obstetrics and Gynecology at Kahuta Research Laboratories (KRL) hospital, Islamabad over a period of four months from Nov 2017 to Feb 2018. Patients were randomly assigned in two groups on the day of operation. One group was given oral tramadol after initial loading intravenous dose and the other one conventional intravenous nalbuphine analgesia along with NSAIDS and paracetamol. Pain scores were compared using a visual analogue scale at 4, 8 and 12 hours postoperatively, using 4 score as a cut-off value. Patients with mean score higher than 4 were noted in both groups and they were then given rescue analgesia Mean pain scores of both groups were calculated using SPSS 23 and independent student t test applied for comparison of means.

Results: A total of 320 patients were randomly divided into two equal groups. The analgesic efficacy of oral tramadol was comparable to intravenous nalbuphine as assessed by the visual analogue score at 4hours (p=0.278) and 12 hours (p=0.470) post operatively. The pain score at 8 hours was less than 4 score in both groups but significantly lower in the intravenous group (p=0.016). A total of 17 patients in oral group were reverted to intravenous analgesia group and given paracetamol infusion only (p=0.008). While 5 patients in the intravenous nalbuphine group were given rescue analgesia as oral tramadol capsules. The majority of patients among both groups have no side effects(p=0.852).

Conclusion: Oral tramadol is a safe post operative analgesic that is as effective in reducing pain as intravenous nalbuphine analgesia and can be used as an alternative.

Keywords:Analgesia, Nalbuphine, Tramadol, Caesarean section.

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Introduction

Caesarian section rates have seen an alarming rise over the last twenty years with varying rates in different regions of world.[1] Post operative pain is one of the greatest deteriorating and unwanted outcome of any surgical procedure including caesarian sections.[2]*The* International Association for the Study of *Pain (IASP)* defined pain as an unpleasant sensory and emotional experience that occurs due to tissue damage.[3] According to a survey, there is 50 to 70% chance that a patient will experience mild to moderate pain postoperatively.[4]Caesarian pain occurs in the form

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of incisional pain as a result of tissue inflammation and the spasmodic pain in uterus due to oxytocin infusion to combat postpartum hemorrhage.[5]

Pain is hence, considered as the fifth vital sign that leads to both physical and psychological distress in patients, therefore, leading to reduced mobility, patient satisfaction, breastfeeding and affective maternal- neonatal bonding.[2,6] Magnitude of this problem makes postoperative analgesia very important for the surgeon and his team. The chosen analgesic should be effective, easy to administer and safe. The analgesic can reduce adverse effects like thromboembolism, prolonged hospitalization and delay in the initiation of breastfeeding. [8,9] Different analgesics and routes have been tried by clinicians to mitigate postoperative pain but there is no clear evidence as to which way is superior to other.[10]

The modern approach to pain control in post operative patients is a multi-modal analgesia approach in which drugs of different classes are given for better pain relief and reduced side effects.[11]The traditional on demand analgesia is replaced by fixed dose interval. The most commonly used drugs are a combination of opoids and NSAIDS. Opoids are considered to be one of the most effective drugs for pain relief. Post operative patients are given different opoids but most commonly used are tramadol or nalbuphine. Tramadol is a centrally acting, synthetic analgesic which is an opioid receptor agonist and serotonin nor-epinephrine reuptake inhibitor. It is approved for oral, intravenous and intramuscular administration and efficiently decreases moderately to severely moderate pain.[12] Nalbuphine is a mixed agonist-antagonist opoid analgesic that is a weak antagonist of meu-receptors and partial agonist at kappa receptors. It is given intravenously and has a faster onset of action.[13]

In this study, oral tramadol was compared with conventional intravenous analgesia being used in this setup in post-operative patients i-e combination of intravenous nalbuphine, ketorolac and paracetamol. The objective of this study was to prescribe oral analgesics on operation day if the efficacy of both intravenous and oral drugs was comparable.

Methodology

This is a prospective single blinded randomized controlled study conducted over a period of 4 months from Nov 2017 to Feb 2018 at the Department of Obstetrics and Gynecology at Kahuta Research Laboratories (KRL) hospital, Islamabad. The study was conducted after taking approval from the ethical committee of the hospital.

A total of 320 patients were consecutively recruited from the post operative gynae/obstetrics intensive care unit. The sample size was calculated on the basis of a pilot study conducted on 30 patients as there was no reference study available. Verbal informed consent was taken from all the patients before the surgery.

The post operative patients underwent emergency and elective LSCS under spinal anaesthesia with an age range of 20 to 40 years and weight varied in a range of 50 to 100 kg were included in the study. Those patients operated under general anaesthesia or epidural analgesia, operated for any other gynecological procedure, prolonged duration of surgery due to any complication, having drug dependence, medical comorbids like liver and renal failure, history of seizures and psychiatric disorder were excluded from our study.

The pain score was assessed before giving analgesia in all the post operative LSCS patients received from operation theater. They were then randomly allocated into one of the intervention group, either A or B. Group A comprises of oral tramadol group and Group B of intravenous nalbuphine group. The specific dosage regimens of these groups were decided beforehand. In both, the groups initial loading dose of respective opoid was given intravenously after receiving the patient in post operative care unit and the patient could not be given the oral drug at that time due to the effect of spinal anaesthesia.

In the case of Group A: (*Oraltramadol Group)*

- Intravenous tramadol 50 mg and dimenhydrinate 20 mg stat dose given intravenously after receiving patient.
- Two doses of oral capsule tramadol 50 mg given 4 hourly at 4 and 8 hour post operatively
- Single oral dose of capsule tramadol 100 mg SR given at 12 hour post operatively.

In case of Group B*: (Intravenous Nalbuphine Group)*

- Intravenous nalbuphine 4mg +dimenhydrinate 20 mg given stat and then as needed.
- Injection paracetamol 1 gm and injection ketorolac 30 mg given 8 hourly intravenously.

The primary outcome studied was the assessment of pain by visual analogue scoring (VAS) system. The patients in both the groups were followed at 4, 8 and 12 hours for pain assessment, before giving the analgesia. VAS system is a type of scale numbered from 1 to 10 with 1 considered as no pain and 10, the worst pain. The patients were explained to point out or rate the severity of pain by looking at the color printed forms of the VAS scale. VAS scoring less than 4 was considered efficacious, and hence this was the cut-off value. The patients with no formal education were guided to score the pain by the pictorial facial expression visual analogue scale.

The secondary outcomes studied were patient satisfaction with the pain relief, side effects like nausea/vomiting, dizziness and sedation in both groups and reversion of analgesic in the respective group to that of the other. All of these parameters were noted on the structured proforma.

All the data was analyzed on SPSS 23. Independent sample t test was applied to compare both oral and intravenous groups for continuous variables like age, weight, and mean pain scores (mean±SD). Chi-square test was applied to compare and analyze the side effects, reversion to analgesia and maternal satisfaction. P-value ≤0.05 was considered statistically significant.

Results

A total of 320 patients were included and randomly allocated into one of the two Groups A or B. Demographic variables were comparable in both groups and included age and weight of patients as shown in table I.

Table I: Demographic Profile

	Group A (oral tramadol) n=160 mean+S.D	**GROUP B (Intravenous Albuphine) n=160 mean+S.D**	**p-value**
Age (Years)	29.01±4.45	29.54±3.87	0.255
Weight (kg)	72.79±9.03	73.51±9.47	0.490

In the post operative period, mean VAS scores were above 4 in both groups before the first intravenous dose but not significant statistically (p=0.930). The patients were assorted into one of the analgesic regimen and then followed in the post operative period. The mean±SD VAS scores were below 4 in both groups at the 4 and 12 hours post operatively which was statistically non significant. While after 8 hours the pain score was less than 4 in both groups but significantly reduced in IV group as compared to oral group(p=0.016). Patient remained catheterized as per hospital protocols for 8 hours post operatively. The pain scores at 4 and 8 hours were measured at rest. While, patients were encouraged to mobilize after 10 to 12 hours post operatively. Although, the mean pain score at 12 hours was recorded when they were at rest. The mean pain scores of both groups are shown in table II.

Table II: Primary Outcomes

Mean Pain Scores	**Group a (Oral Tramadol)** n=160 mean±S.D	**Group B (Intravenous Nalbuphine)** n=160 mean±S.D	**p-value**
Mean VAS at the time of first IV dose	5.57±1.66	5.59±2.12	0.930
Mean VAS at 4 hours	3.49±1.19	3.63±1.07	0.278
Mean VAS at 8 hours	3.40±1.09	3.09±1.21	0.016**
Mean VAS at 12 hours	3.08±1.37	2.97±1.26	0.470

Secondary outcomes like maternal satisfaction and side effects profile consisting of nausea/vomiting, sedation and dizziness shows comparable results in both groups. The reversion of analgesia was noted in about 17(10.6%) patients in group A and 5(3.1%) in group B and this was statistically significant (p=0.008). Group A patients reverted to intravenous analgesia were given placebo first in order to allow the sufficient time for oral dose to be effective. If the pain score was still higher than 4, after 30 minutes then intravenous paracetamol infusion given for pain relief as rescue analgesia. The majority of patients were better after 1 dose of paracetamol infusion while 3 patients required more than 1 dose. About 5 patients in group B complaint of pain not relieving with conventional intravenous nalbuphine and they were given oral capsule tramadol 100 mg SR. All 5 patients responded well to oral capsule. The secondary outcomes are shown in Table III.

Table III: Secondary Outcomes

	Group A (Oral Tramadol) n=160	Group B (Intravenous Nalbuphine)	p-value
SIDE EFFECTS			
None	138 (86.3%)	135 (84.4%)	0.852
Nausea/vomitting	11 (6.9%)	12 (7.5%)	
Sedation	6 (3.8%)	9 (5.6%)	
Dizziness	5 (3.1%)	4 (2.5%)	
Reversion to analgesia			
Yes	17 (10.6%)	5 (3.1%)	0.008**
No	143 (89.4%)	155 (96.9%)	
Maternal satisfaction			
Good	150 (93.8%)	152 (95.0%)	0.627
Poor	10 (6.3%)	08 (5.0%)	

Discussion

Different studies have been conducted to compare the efficacy, safety and tolerability of analgesics and their routes of administration. Most of these modalities like epidural and intrathecal analgesics came under the domain of anaesthesia, require meticulous patient monitoring and are not widely available.

Nalbuphine has been used intravenous or intramuscularly for pain relief in abdominal surgeries such as hysterectomies and caesarean sections due to its faster onset of action and longer duration.[14] But its association with sedation and drowsiness is more as compared to other opoids due to the mixed agonistic and antagonistic effect. But in this study oral tramadol was effective in relieving pain at 4 and 12 hours post-operatively, with side effects profile also comparable among both groups. In another study conducted in India by Solanki et al[15] for post operative pain relief in orthopedic surgeries comparing intravenous nalbuphine and tramadol showed the higher requirement of rescue analgesia in intravenous tramadol group. But onset of drug action and duration of analgesia after first dose was similar in both groups. The duration of analgesia was longer in nalbuphine group after third dose as intravenous tramadol was not as effective in reducing pain similar to that of our study in which the pain reduction was statistically significant in nalbuphine group at the 8 hours post operatively.

Davis et al[16] conducted a study in 2005 comparing oral analgesia oxycodone and acetominaphen with the morphine patient controlled analgesia device in the post operative caesarean patients. In this study pain assessment done at 6 (p=0.04) and 24 hours (p=0.004) post operatively was significantly reduced in the oral analgesic group. But the nausea was more at 24 hour in oral analgesic group that was in contrast to our study which may be attributed to different type of opoid. Oral opoid oxycodone is chiefly in use in obstetrics unit of Australia and New-Zealand for post operative caesarean pain relief with minimal effect on lactation.[17] But the excretion of drug into breast milk was not considered in our study. Tramadol safety for breastfeeding mothers was proven in a review article in which the post operative patients were given tramadol in a dose of 100 mg every 6 hourly and the breast milk excretion was minimal about less than 2.5 % of maternal dose/ body weight in kg/ day. No neonatal adverse events like neonatal sedation and neurological side effects were reported to date about tramadol as compared to oxycodone and codeine. Maximum

recommended dose of oral tramadol is about 400 mg per day.[7] In our study, we used about 250 mg per day.

Studies on oral tramadol are limited in post operative caesarean patients. Wilder-Smith et al[18] conducted a study on intramuscular tramadol and diclofenac when given in combination has better pain relief and time to first analgesic demand was reduced. While in our study fixed dose analgesia protocol was followed. Sedation, drowsiness and nausea were assessed on rating scale and they were not significant in these patients as that of our study.

In a study conducted in Italy, post surgical patients with inguinal hernia repair, hemorrhoidectomy, and varicose veins surgery were randomized into tramadol/paracetamol group and codeine/paracetamol group. The mean pain scores were significantly lower in the tramadol group at 1, 6, 12, 24 and 48 postoperative hours. Rescue analgesia requirement was 18.2% in codeine group and 5.5% in tramadol group, that was in contrast to our results in which reversion of analgesia and rescue analgesia was significantly higher in tramadol group versus intravenous nalbuphine group.[19]

Single dose oral tramadol in different doses has been used for post operative pain relief in peadiatric surgeries. One of the trial by Finke et al[20] have found significant pain relief when oral tramadol was used in a dose of 2mg/kg body weight. The rescue analgesia given either as intravenous morphine or oral oxycodone dose was reduced about half at this dose (p=0.006). Minor side effects have been noted that were insignificant similar to that of our results. In another meta-analysis about oral tramadol versus codeine or placebo in post surgical and dental extraction patients showed few adverse effects (headache, nausea, vomiting and somnolence) in post surgical patients compared to dental patients.[21] This is in accordance to the results of our study. Oral tramadol is commonly used in dental surgeries for pain relief such as third molar tooth extraction due to decrease sedation, low potential of causing drug dependance and respiratory depression.[22]

Strength and Limitations: The strength of this research is that it is a unique study of its own kind, conducted first time in our country comparing oral and intravenous opoid in post operative caesarean patients. Study design is randomized controlled which is an additional advantage. The limitation is that the blinding of nursing staff and professionals was not done. The drug level excreted in breast milk was not measured.

Conclusion

Oral tramadol and intravenous nalbuphine are equally efficacious in reducing post operative caesarean pain especially at the 4 and 12 hours as assessed by VAS scoring. The pain scores at 8 hours was less than 4 in both groups indicating effective pain relief however was significantly reduced in intravenous nalbuphine group. Oral tramadol is easy to administer, less invasive, no expertise required, tolerable and side effects are comparable with intravenous analgesia. Tramadol whether in oral or intravenous form produces less maternal sedation due to weak opoid effect and less excretion in breast milk and the ability of neonate to eliminate that much amount of parent drug and the metabolite via renal excretion makes the drug safer for neonate as well.

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