WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.045
Volume 4, Issue 4, 1801-1808. Research Article ISSN 2277– 7105

A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL OF DICLOFENAC OR DEXAMETHASONE IN THE COMBINATION OF TRAMADOL FOR PAIN RELIEF AFTER CAESAREAN SECTION

Kaveh Behaeen*[1], Sholeh Nesioonpour[1], Reza Akhondzadeh[1], Shaghayegh Mousavian[1]

[1]Department of Anesthesiology, Pain Research Center, Ahwaz Jundishapur University of Medical Sciences, Ahwaz, Iran.

Article Received on
15 Fab 2015,

Revised on 10 March 2015,
Accepted on 02 April 2015

***Correspondence for Author**
Kaveh Behaeen
Department of Anesthesiology, Pain Research Center, Ahwaz Jundishapur University of Medical Sciences, Ahwaz, Iran.

ABSTRACT

Background*:** Pain relief after caesarean section (CS) leads to early ambulation and good early mother–child bounding. Best to our knowledge there is no published study assessing the combination of opioid +NSAID vs. opioid +steroid (anti-inflammatory) drugs to diminish post-caesarean section pain. In the present study we assessed the pain-relieving quality of combination tramadol with diclofenac vs. dexamethasone on post-caesarean section pain management. ***Method*:** Eighty eligible pregnant female who were candidate for elective C/S were randomly assigned to two groups to receive tramadol 100mg IV with diclofenac 75mg IM group (TDF) vs. tramadol 100mg IV with dexamethasone 8mg IV group (TDX) post-operatively. All patients underwent spinal anesthesia. Pain severity was quantified according to visual analogue scale (VAS), ranging 0: no pain to 10: worst pain that could not tolerate, and recorded on[2, 4, 8, 12], and 24 hours post C/S operation. Each patient given extra analgesic pethidine (0.2mg/kg) if needed (VAS 3 or more). The first time that patients complaint from pain and request analgesic drug and total amount of pethidine was recorded. ***Results: The first time that patients complained from pain were 105 ± 15 min in (TDF) group and 90 ± 20 min in (TDX) groups ($p<0.05$). The mean of the time that patients request extra analgesic drug pethidine were 130 ± 10 min in (TDF) group and 110 ± 12 min in (TDX) group ($p<0.05$). The mean of total VAS score at 4h and 8h after surgery were significantly lower in (TDF) group ($p=0.04$). ***Conclusion*:** It was shown that combination of tramadol with diclofenac can significantly

diminish post caesarean section pain and reduce the usage of pethidine post operatively.

KEYWORDS*:* caesarean section, pain, diclofenac, dexamethasone, tramadol, satisfaction.

INTRODUCTION

One of the undesirable complications of surgery is postoperative pain that may lead to serious morbidities like agitation, hypertension, mood changing, mother post-delivery depression, tachycardia[1] Postoperative pain management leads to patient satisfaction, earlier patient ambulation and mobilization, reduce risk of GI discomfort post-operative nausea and vomiting (PONV), ileus, infection, thromboembolic disorder (DVT), less post-op complication thus shortened hospital staying so reduced hospital costs.[1-2-3-4]

The aim of pain management is reduce post-surgical complication, while providing adequate analgesia and help to rehabilitation. Today we have various methods to provide adequate post-op pain relief including analgesic drugs, acupuncture[3], aromatic therapy[5], Transcutaneous Electric Nerve Stimulation (TENS)[6], Low-Level Laser[1], PCA device[7], That needs multidisciplinary teams with multimodal analgesia..[2-7] The major goal to pain management is provide less dependence on opioids and avoid their adverse effects.[8] Opioids are potent drugs for pain control such as Pethidine and tramadol but with side effect like nausea, vomiting, pruritus, urinary retention, respiratory depression, physical dependence and addiction.[9-10]

Anti-inflammatory drugs have also antipyretic and analgesic effect, when added with opioids have synergic effect, so with lower doses of opioids we have adequate analgesic effect for longer time and decrease adverse side effects.[11-12]

For caesarean section, the combination of Non-steroidal anti- inflammatory drugs (NSAIDs) and morphine is administrated broadly.[13] Diclofenac, a non-selective NSAID, has been illustrated to decrease morphine use by 33% to 47% and improve postoperative pain relief and reduce morphine-associated side effects.[13,14]

When diclofenac is not suitable or contraindicated for pain management fallowing caesarean section, allergic reaction to NSIADs and bleeding tendency, dexamethasone might be substituted as it was shown.[15]

Thus, diclofenac or dexamethasone might be effective in controlling post-C/S pain in

combination with an opioid via a multimodal approach.

METHODS

After approval this randomized, double blind, prospective study by the human research ethic committee of Ahwaz Jundishapur University of Medical Sciences, Iran (ethical code 1392.241) and Ahwaz Imam *Khomeini hospital's pain* research center, Inclusive criteria: all eligible & volunteer pregnant nulipar and gravid 1 (multipar) women whom were escatule for elective C/S, ASA class I or II ,in the range of 18 - 30 years old age, were approached for entry into this study. Exclusion criteria: preterm labor (less than 37weeks), asthma, cardiovascular disease, Preeclampsia, history of seizure, general anesthesia, any significant history of pain disorders like fibromyalgia and addiction, psychologic diseases , psychosomatic disorders and mood disturbance , patient incorporate.

The study group was allocated using computer random number generation. Randomization numbers were kept in a sealed document in the hospital department until the end of the trial. All patients were given informed & written consent and receive one of two postoperative analgesic drug regimens: tramadol (Alborz Pharmacy Co. Iran) 100mg IV with diclofenac (Daropakhsh pharmacy CO. Iran) 75mg IM or Tramadol 100mgIV with dexamethasone (Daropakhsh pharmacy CO., Iran) 8mg IV.

All patients anesthetize with spinal block using 12.5 mg bupivacaine(Darou Darman Pars Pharmacy CO, Iran) ,in the sitting position using a 25-gauge spinal needle by one anesthesiologist at L3-4 space. They were given an IV infusion of Ringers Lactate (10-20ml/kg) based on clinical status. They monitored by ECG, saturation of oxygen, pulse oxymetry and non-invasive blood pressure. All patients received 6liters/min O2 via face mask during operation.

After intrathecal injection, the blood pressure was measured every 5 min until the end of caesarean section. A reduction in systolic blood pressure over 20% base line preoperative values treat by administration of 5mg ephedrine(repeated on demand) or bradycardia under 60 beats/min treat by 0.5mg atropine. after delivery each patients receive one of two postoperative analgesic drug regimens based on one's own groups: tramadol 100mg IV + diclofenac 75mg IM (TDF) group or tramadol 100mg IV + dexamethasone 8mgIV (TDX) group.

In post-operative period one trained nurse who was blind to the study groups assessed the

pain severity using VAS score, at 2,4,8,12 and 24 hours after operation. Each patient given pethidine (0.2mg/kg) if VAS 3 or more. The first time that patients complaint from pain and asked for analgesic drug and total amount of pethidine was recorded.

RESULTS

According our study mean age of participants was 25.3±6.1 years. This were 24.9±5.6 years in TDX groups and 25.8±6.2 years in TDF groups (p>0.05).

The mean of the first time that patients compliant from the pain post-operatively were 90 ±20min in TDX groups and 105 ±15 min in TDF groups (p=0/045). (table 2).

The mean of the first time that patients request for receiving extra analgesic petidine were 110 ±12min in TDX and 130 ±10min in TDF groups (p=0/039).(table 2).

The mean VAS score were 4.5 ±1.5 in TDX and 3.82 ±1 in TDF groups (p=0.035).

The mean of VAS score at 2h,4h,8h,12h,24h after operation were 3.5 ±1 in 2h, 6.35 ±4 in 4h , 5.90 ±2 in 8h, 4.15 ±1 in 12h, 3.3 ±1 in 24h in TDX group .the respective values in TDF group were: 3.0 ±1 in 2h , 5.1 ±2 in 4h , 4.12 ±1 in 8h , 3.80 ±1 in 12h, 3.1 ±1 in 24h. (p=0.03).(figure 1).

The VAS score of 4h and 8h after operation were significantly different between groups with respective p values of 0.025 and 0.042.(table 1) &(figure 1).

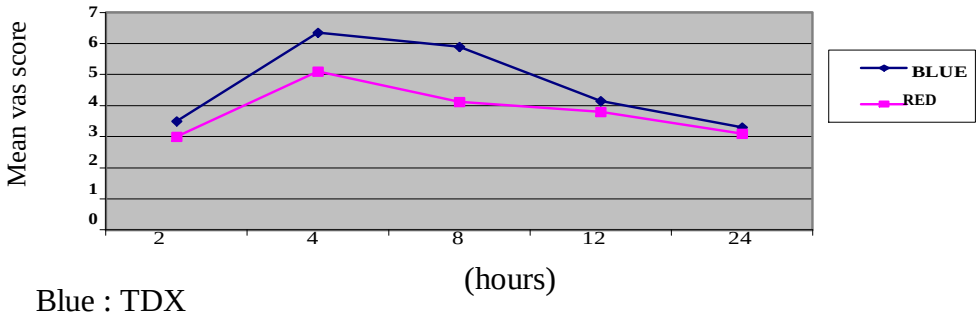
Finally the total amount of administrated pethidine was significantly lower in TDF group (42±5mg) versus TDX group(59±4mg) (pV:0.033) .(table 2).

Table 1. The means of VAS Score in TDX and TDF groups

* =$p<0.05$

Groups	2	4	8	12	24	Overall
TDX(Blue)	3.5 ±1	6.35±4	5.9 ±2 *	4.15 ±1	3.3 ±1	4.5±1.5
TDF(Red)	3.0 ±1	5.1 ±2 *	4.12 ±1	3.8 ±1	3.1 ±1	3.82 ±1

Figure one. Trend of VAS score during first 24



Blue : TDX

Red: TDF

Table 2. The mean of time that patients complain from the pain and request for extra analgesic and total pethedine dose

	TDX	TDF	P
First time patients complaint from the pain post – operatively	90 ±20 min	105 ±15 min	0.045*
First time patients asked for analgesic	110 ±12 min	130 ±10 min	0.039*
Total amount of used pethedine in 24 hours	59 ±4*mg*	42 ±5*mg*	0.033*

* =$p<0.05$

DISCUSSION

According to our study those patients whom treated with tramadol+diclofenac (TDF) group suffer less pain in the first day post-operatively in comparison with tramadol+dexamethasone(TDX) group and the total amount of administrated extra IV analgesic pethidine was significantly lower in (TDF) group.(figure 1& table 2)

The first time that patients complained from the pain post-operatively and request extra analgesic were significantly longer in TDF group.(table 2) the overall VAS score and the score of 4h and 8h after CS were significantly lower in TDF group. .(figure 1)

It shows TDF treatment was superior than TDX in post C/S pain management.

Post C/S pain has two components(somatic: due to surgical incision) and(visceral: due to uterine contractions).according to data analysis it shows diclofenac has good effect for subsidies visceral pain and opioid was good for treat somatic pain so a combination of both might lead to better pain management and patient satisfaction than each one alone.[8]

Present study has shown that patients given a combination of diclofenac and tramadol used 28% less Pethidine usage compared to patients given dexamethasone and tramadol in the first 24 h after caesarean section.

This opiate-sparing characteristic of diclofenac was reported by other studies and estimated up to 30 percent that was as like as our findings.[13,14,16,17] Sahar et all. Study showed that combination of diclofenac and morphine would lead to substantial pain reduction and lower post operative opioid administration in comparison with paracetamol and morphine[13] Wilder-Smith et.all study showed combination of 100mg tramadol with 75mg diclofenac was superior to tramadol alone for post-operative pain management.[18] Also using non selective NSAIDs fallowing surgery is still controversial due to the potential risk of bleeding disorders.[12] None of our 40 participants in the diclofenac group had any complication due to post C/S bleeding ,this result is found in another study with diclofenac after c/s as well[19] So further studies are needed to assess the potential risk of bleeding after non selective NSAIDs administration for post C/S pain management or use of COX-II inhibitors as an alternative for non-selective NSAIDs when the risk of bleeding complication is high. In our study, none of 40 patients who had received diclofenac developed uterine atony. Also no adverse effect was detected in our mothers and their neonates. On the other hand poor post-operative pain management in the mother would lead to adverse effect on the milk production and subsequently detoriate neonatal feeding.

CONCLUSION

Our study showed that administration of 75mg diclofenac (IM) with 100mg tramadol (IV) seems better post-CS pain management and lower opioid usage without occurrence of any bleeding complication.

ACKNOWLEDGEMENT

We acknowledge the vice chancellor of Deputy of Research and Technology Affairs of Ahvaz Jundishapour University of Medical Sciences. We are indebted to all physicians, staff , nurses and patients who participated in this study. This article based on Shaghayegh Mosavian clinical trial research study granet no: pain-9203 Irct no: 1392.241.

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