Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Obstetrics and Gynecology Research

Journal homepage: www.ijogr.org

Original Research Article

A randomized controlled trial of intravenous paracetamol and intravenous tramadol for labour analgesia

Meghna Marwah[1], **Kavita Mandrelle**[1,*], **Dootika Liddle**[2]

[1]*Dept. of Obstetrics and Gynaecology, Christian Medical College and Hospital, Ludhiana, Punjab, India*
[2]*Dept. of Anaesthesia, Christian Medical College and Hospital, Ludhiana, Punjab, India*

ARTICLE INFO

Article history:
Received 09-04-2023
Accepted 24-05-2023
Available online 24-08-2023

Keywords:
Labour analgesia
VAS
Intravenous paracetamol
Intravenous tramadol

ABSTRACT

Background: Labour pain is among the most excruciating pain experienced by women. Pain relief during labour is expected to reduce maternal stress, improve maternal and perinatal outcome. Paracetamol and tramadol are easily available, inexpensive and easy administeration. The present study compared the efficacy of intravenous paracetamol and intravenous tramadol for labour analgesia.

Materials and Methods: A randomized controlled trial was conducted in the Department of Obstetrics and Gynaecology, Christian Medical College, Ludhiana including 130 patients divided into two groups. Group A received 1000 mg of intravenous paracetamol and Group B received 100 mg of intravenous tramadol hydrochloride for labour analgesia in active phase of labour (>/= 4 cm cervical dilatation). Pain intensity was assessed by Visual Analogue scale (VAS) before; after 1 and 3 hours of drug administration. Duration of labour, mode of delivery, drug-delivery interval, maternal side effects and neonatal outcomes were also assessed.

Results: Total 130 patients with 65 in each group were included. Pain intensity was assessed and it was observed that Mean VAS score was significantly lower after 1 and 3 hours of drug administration in Group A than Group B. Mean duration of 1^{st} stage of labour (210.79+-70.49 minutes) and mean drug delivery interval (4.34 hours) was significantly lower in Group A than Group B (246.95+/-76.09 minutes; 5.17 hours). Maternal side-effects were observed more with tramadol than paracetamol.

Conclusion: Intravenous paracetamol is more effective labour analgesic with lesser VAS score, shorter duration of labour, drug delivery interval and with few maternal side-effects.

1. Introduction

Labour pain is defined as uterine contractions that bring about demonstrable effacement and dilatation of the cervix.[1] There are three stages of labour, first stage is from onset of true labour pains till complete dilatation of cervix. Second stage of labour is from full dilatation till the expulsion of fetus. Third stage of labour includes separation, descent and expulsion of the placenta.[2] Mechanism of labour pain during 1^{st} stage of labour is Visceral pain which is due to dilatation of cervix and distension of lower uterine segment carried by slow conducting C fibres from spinal level T10-L1.[3] Mechanism of pain during 2nd stage of labour is somatic pain which is due to distention of pelvic floor, vagina and perineum by rapidly conducting A delta Fibres from spinal level S2-S4.[3] Labour pain is due to result of many complex interactions, physiological and mental, excitatory and inhibitory which reduces uteroplacental blood flow leading to altered fetal homeostasis.[4] There are two techniques for labour analgesia. The non-pharmacological techniques include of psycho prophylaxis, reassurance and

* *Corresponding author*.
E-mail address: meghnamarwah31@gmail.com (K. Mandrelle).

https://doi.org/10.18231/j.ijogr.2023.054

transcutaneous electric nerve stimulation (TENS). The pharmacological techniques include opioids like pethidine, tramadol, morphine, fentanyl, butorphanol, pentazocine and regional analgesia. The gold standard and most commonly used obstetric analgesia is regional analgesia which include pudendal nerve block, paracervical block and neuraxial blocks (epidural Anaesthesia, subarachnoid block, combined spinal and epidural block). These altered local analgesia techniques have revolutionized obstetric anaesthesia.[5]

1.1. Paracetamol (Acetaminophen)

It is a diethyl active metabolite of phenacetin. It has very good analgesic – antipyretic action with negligible anti-inflammatory action. It acts by inhibiting the synthesis of (centrally appearing) prostaglandins (COX) in the central nervous system (CNS) and peripherally blocking off pain impulse generation.[6] It has serotonergic (5HT) mechanism and cannabinoid agonism mechanism contributing to its analgesic effect.[7] Various studies have proved that intravenous paracetamol as powerful analgesic agent which is less expensive, and requires no special monitoring.[8] It has a favourable safety profile with no hazard of congenital anomalies.[9] Studies have documented protection and efficacy of intravenous paracetamol as a labour analgesic.[10]

1.2. Tramadol HCl

It is a centrally acting atypical opioid analgesic. It is used for labour analgesia in developing nations as it is cheaper, requires no special tracking and has proved its protection and efficacy. Side effects can be dizziness, nausea, sleepiness, dry mouth, sweating and lowering of seizure threshold.[11]

However, the gold standard is regional analgesia which include pudendal nerve block, paracervical block and neuraxial blocks (Epidural anaesthesia, subarachnoid block, combined spinal and epidural block). These altered local analgesia techniques have revolutionized obstetric anaesthesia.[5]

2. Aim and Objectives

1. To compare the efficacy of intravenous paracetamol and intravenous tramadol for labour analgesia.
2. Primary objective: To measure the difference in VAS score in both the groups before administration of drug, 1 hour and 3 hours after administration of respective drugs.
3. Secondary objective: To record the duration of 1^{st} and 2^{nd} stage of labour, mode of delivery, drug-delivery interval, maternal side effects and neonatal outcomes in terms of APGAR scores and NICU admissions.

3. Materials and Methods

1. The study was conducted in the Department of Obstetrics and Gynaecology, Christian Medical College, Ludhiana, Punjab, a tertiary care centre in North India.
2. Duration of study- 18 months (15^{th} November 2020 to 15th May 2022).
3. Type of study- A Randomized Controlled Trial-Double blinded.
4. The sample size – 130 patients, 65 in each group, who satisfied inclusion and exclusion criteria.

3.1. Inclusion criteria

All primigravidae with singleton, term pregnancy (>/= 37 weeks) and cephalic presentation admitted in labour room for delivery.

3.2. Exclusion criteria

1. Malpresentation.
2. Multigravidas
3. Multiple pregnancy.
4. Previously scarred uterus (Uterine scar due to previous lower segment caesarean section, Myomectomy, Hysterotomy).
5. Preterm labour.
6. Major degree of placenta-previa.
7. History of drug allergy.
8. Cardio vascular disorders.
9. Fetal distress prior to active phase of labour.
10. Patients who deliver within 3 hours of drug administration.
11. Patients who refused participation.
12. Patients who received analgesia in latent phase of labour.

A double blinded randomized controlled trial was conducted in a total of 130 antenatal patients admitted in labour room ward with singleton term pregnancy and cephalic presentation in active phase of labour. Patient was informed about the trial in her own vernacular language and randomized in two different groups on the basis of block randomization 1:1. An informed consent was taken from each participant. Demographic data along with the detailed history, general physical examination, systemic examination and obstetric examination was done for all the participants at the time of admission. Progress of labour during latent phase of first stage of labour was monitored every 30 minutes for the assessment of uterine contarctions and fetal heart rate and 4 hourly monitoring was done for maternal temperature, pulse and blood pressure. All antenatal patients once in active phase of labour, (cervical dilatation >/= 4 cm) were randomized into two different groups (65 patients in each group) on the basis of block randomization. In Group

A, patients received 1000 mg of intravenous paracetamol (Molace GB) in 100 ml of normal saline over 15 minutes. In Group B, patients received 100 mg of intravenous tramadol hydrochloride (Supridol) in 100 ml normal saline over 15 minutes, Drugs were given in active phase of labour with cervical dilatation between 4-6 centimeters.

The preparation of drug was done by three designated staff members members (each staff for every shift in Labour ward), who were trained to prepare and administer the study drugs as per the randomisation code during active phase of labour (cervical dilatation between 4 cm to 6 cm). Double blinding was done in the study, neither the investigator nor the study participant were aware of the drug administered. These drugs are routinely given in labour room wards, hence no other department was involved for blind preparation of analgesia.

Pain intensity before drug administration and pain relief after 1 hour and 3 hours of drug administration were measured by Visual Analogue scale (VAS) score. The VAS Score was divided as mild pain (0 cm to 4 cm), moderate pain (4.1 cm to 8 cm) and severe pain (8.1cm to 10 cm).

Labour was monitored using a WHO Modified Partogram. Duration of stages of labour were recorded and compared in both the groups.

1. Duration of active phase of first stage of labour was recorded in minutes from 4 centimetres till full cervical dilatation.
2. Duration of second stage of labour (from full cervical dilatation till expulsion of fetus) and third stage of labour (from expulsion of fetus till the expulsion of placenta with membranes) were also recorded in minutes.
3. Drug - delivery interval was also recorded in minutes from the time of drug administration till expulsion of fetus.
4. Mode of delivery (normal vaginal delivery, caesarean section and instrumental delivery) was noted and compared in both the groups.

Blood loss was noted in third stage as well as for two hours post delivery in both the groups. Blood loss more than 500 ml in vaginal delivery and more than 1000 ml in caesarean section was considered as increased bleeding.

A repeat dose of analgesic drug was given after 6 hours of administration of first dose if required. Patients opting for epidural analgesia after drug administration were noted and excluded from further evaluation.

Maternal side effects of the drugs such as – nausea, vomiting, increased bleeding (PPH) and allergic reactions were observed during labour as well as postpartum for two hours.

Neonatal outcomes in both the groups were assessed in terms of weight of the baby at birth (in Kgs), APGAR Score at 1 minute and 5 minutes which is further divided as Normal APGAR[7–9] and Abnormal APGAR [Moderate perinatal asphyxia (APGAR Score 4-6) and Severe perinatal asphysia (APGAR Score 0-3)]; need of Neonatal Intensive Care Unit (NICU) admission and any neonatal. The neonates were observed from birth till two hours after delivery.

4. Result

A total of 130 primigravidae antenatal patients with term singleton pregnancy and cephalic presentation were divided into two different groups- Group A and Group B (based on block randomisation 1:1), each group including 65 patients. The descriptive variables were reported as Mean (SD) for continuous variables, frequencies for categorial variables. The P value <0.05 was considered significant. All statistical analysis were performed using SPSS (Statistical Packages for Social Sciences, version 21.0. Armonk, NY: IBM corp.).

Three patients opting for epidural analgesia after drug administration were excluded to avoid crossing over.

4.1. Demographic variables

1. There were total 130 study cases with the mean age of patients in Group A and Group B as 26.20 ± 4.02 years and 25.37 ± 3.74 years.
2. The mean gestational age of the patients who received paracetamol (Group A) and tramadol (Group B), was similar that is 38.48 ± 0.92 weeks and 38.67 ± 0.84 weeks of gestation respectively.
3. Three (3) patients opted for epidural analgesia who received IV Paracetamol (Group A) and none in the patients receiving IV Tramadol (Group B) and they were excluded from further evaluation to avoid crossing over. Therefore, total of 127 patients were involved in final evaluation of study.

4.2. Mean VAS Score at different intervals

The relief in pain intensity was assessed by VAS score before; after 1 and 3 hours of drug administration. The mean VAS score after 1 hour of drug administration was significantly lower in Group A (6.38±0.818) than Group B (7.338±0.88). p= 0.001. Similarly, after 3 hours of drug administration, Group A (7.861±1.2) had significantly lower mean VAS score than Group B (9.11±0.748). p= 0.001.

Table 1: Demographic variables

Variables	Group A (n=65)(IV Paracetamol) Mean ± SD	Group B (n=65) (IV Tramadol) Mean ± SD
Age (years)	26.20 ± 4.02	25.37 ± 3.74
Gestational Age (weeks)	38.48 ± 0.92	38.67 ± 0.84

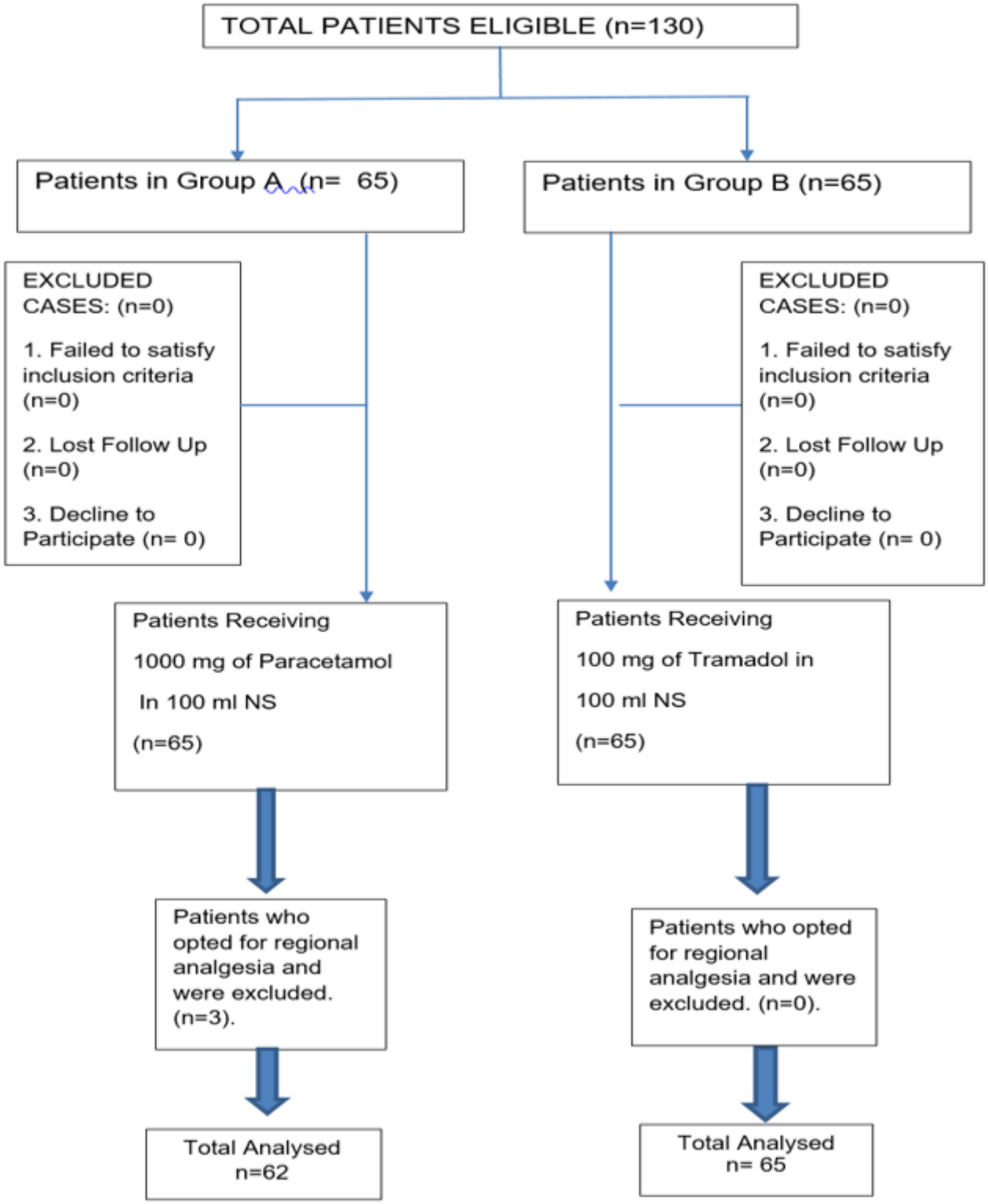

Fig. 1: Consort

Table 2: Mean VAS (Visual Analogue Scale) score before, after 1 hour and after 3 hours of drug administration in Group A (IV Paracetamol) and Group B (IV Tramadol)

VAS (Visual Analogue Scale) SCORE	(IV Paracetamol)Group A (n=62)* Mean ± SD	(IV Tramadol)(Group B) (n=65) Mean ± SD	P value
Before the administration of drug	8.66±0.88	8.6±0.68	0.912
1 Hour after the drug administration	6.38±0.818	7.33±0.88	0.001
3 Hours after the drug administration	7.86±1.2	9.11±0.75	0.001

*Three patients who opted for epidural analgesia in Group A were excluded from the study

4.3. Mean duration of labour

Majority of the patients in Group A (46.8%) had active phase of first stage of labour lasting for 101-200 minutes while only 27.7% patients in Group B had same duration. Maximum patients in Group B (49.2%) had active phase of first stage lasting for 201-300 minutes. The mean duration of active phase of first stage of labour was significantly shorter (210.79±70.49 minutes) in Group A as compared to Group B (246.95±76.096 minutes).

Whereas it was observed that mean duration of second stage was longer in Group A (47.86+/- 31.42 mins) than Group B (38.53+/-24.71 mins) but it was statistically not significant.

Drug delivery interval (duration of drug administration till the delivery of baby) during both the normal vaginal delivery and caesarean section was recorded. In this duration of second stage was not necessarily included as patients were undergoing both the vaginal as well as the caesarean section delivery. Three patients who opted for epidural analgesia after the administration of analgesic drug were excluded. Therefore, it was observed that mean drug delivery interval was significantly lower in patients of Group A (4.34 hours) than Group B (5.17 hours) and it was statistically significant.

The study observed that 87% patients in Group A and 84.6% in Group B had vaginal delivery where as 12.9% in Group A and 15.5% in Group B underwent Caesarean sections. It was observed that the mode of delivery was not affected by the analgesic drug administered.

No maternal side effects were seen in Group A whereas a few patients in Group B had nausea (15.4%) and vomiting (6.15%) after the administration of drug. P value= 0.001.

It was observed that neither of the drugs affect the birth weight, APGAR score at one and five minute and the number of NICU admissions of neonates.

Majority of neonates born to patients in Group A (75.8%) and Group B (85.5%) had no neonatal complications which was statistically significant (P value= 0.003). Therefore, it demonstrates that neonatal complications were not related to the analgesic drug used.

5. Discussion

Paracetamol (acetaminophen) is now the most commonly used drug worldwide, available over the counter, used in almost all age groups as first line treatment for pain and pyrexia and forms step one of WHO analgesic ladder. The exact mechanism of action is not fully elucidated. A number of central mechanisms including effects on prostaglandin production, and on serotonergic, opioid, nitric oxide, and cannabinoid pathways and a combination of interrelated pathways are involved. It is centrally acting inhibitor of COX and/ or serotonergic system thus inhibiting prostaglandin synthesis. Various studies have shown the effectiveness and safety of intravenous paracetamol as an analgesic agent in varied spectrum of clinical conditions such as musculoskeletal pain, tension type headaches, migraines and across variety of surgical procedures. It is inexpensive, easy to administer, requires no special monitoring, have useful opioid-sparing effects with minimal side-effects.

Tramadol hydrochloride (synthetic analogue of codeine) has a unique pharmacological profile. It combines the mechanism of action of opioids and tricyclic antidepressants. It is a weak μ-opioid receptor agonist and inhibits transmission of pain impulses and alters pain perception. Also, it reduces the reuptake of norepinephrine and serotonin in the descending spinal inhibitory system and thereby enhancing the effectiveness of the inhibitory pathway. It causes less maternal and fetal respiratory and cardiovascular depression common to other opioids. Along with the ease of its administration it is considered as a good alternative to epidural analgesia in rural Indian setup with less resources.

Our study is one of a kind to compare intravenous paracetamol with intravenous tramadol for labour analgesia.

In the present study, the mean age of patients in Group A and Group B was 26.2 years and 25.37 years with a standard deviation of 4.02 and 3.74 respectively. These findings are in accordance with the study done by Kaur J et al.[12] with mean age of 26.76± 4.12 years in Group A and 26.0± 3.4 years in Group B. The study done by Garg N et al.[13] also had similar mean age in both the groups that is 24.71± 3.62 years and 23.18± 2.37 years respectively. The mean gestational age of patients at the time of study was almost similar in both the

Table 3: Comparison of mean duration of various stages of labour and drug delivery interval in Group A (IV Paracetamol) and Group B (IV Tramadol)

Mean Duration	(IV Paracetamol) Group A	(IV Tramadol) Group B	p value
First stage of labour	210.79±70.49 mins (3.5 hours)	246.95±76.09 mins (4.1 hours)	**0.013**
Second stage of labour	47.86±31.42 mins	38.53±24.71 mins	0.13
Third stage of labour	5.9±2.7 mins	6.0±2.4 mins	0.886
Drug – delivery interval	260.37±81.68 mins (4.34 hours)	310.19±120.56 mins (5.17 hours)	0.007

groups that is 38.48 weeks and 38.67 weeks. It was similar in accordance with Garg N et al.[13] and Kaur J et al.[12]

In the present study, the mean duration of active phase of first stage of labour was 210.79 ±70.49 minutes in Group A and 246.95± 76.09 minutes in Group B and was statistically significant. Therefore, it shows that patients receiving Injection Paracetamol had a significantly shorter duration of active phase of first stage of labour after drug administration than Injection Tramadol. The findings of the present study correlates with Garg N et al.,[13] Mohan H et al.[14] and Kaur J et al.[12] which also showed that patients in Group A had significantly shorter duration of active phase than Group B.

However, the mean duration of second stage of labour was longer (47.86 ± 31.42 minutes) in Group A than (38.53 ± 24.71 minutes) Group B, however it showed no significant difference among them.

The present study showed that Group A patients had significantly shorter drug to delivery interval (mean) as compared to patients in Group B. The findings of the present study correlates with various studies conducted Garg N et al.,[13] Das BP et al.[15] and Kaur J et al.[12] which also showed a significantly shorter duration of drug to delivery interval in the patients receiving Injection Paracetamol than Injection Tramadol. Maximum patients delivered vaginally whereas rest of them underwent Caesarean sections in Group A (87% and 12.9%) and Group B (84.6% and 15.5%) respectively. Studies by Garg N et al.,[13] Aimakhu CO et al.[16] and Kaur J et al.[12] also had maximum normal vaginal deliveries in both the groups as compared to Caesarean sections. It was observed that the choice of analgesic drug did not affect the mode of delivery. In this study, before drug administration, both the groups had severe intensity of pain with similar (mean) VAS Scores (8.66 ± 0.8 and 8.67 ± 0.68 respectively). Whereas, We found that Group A patients had a significant decrease in pain intensity at 1 and 3 hours after drug administration according to the mean VAS score in Group A (6.38 ± 0.81 and 7.861 ± 1.2) than Group B (7.3 ± 0.88 and 9.1 ± 0.74). The findings of the present study are in accordance with Das BP et al.[15] and Kaur J et al.[12] where pain intensity (VAS Score) at 1 and 3 hours after drug administration was also significantly lower in Paracetamol group than tramadol group. This demonstrates that intravenous paracetamol is a more effective labour analgesic drug than intravenous tramadol. In the present study, patients in Group B had significant side effects such as nausea (15.4%) and vomiting (6.1%) whereas patients in Group B noted no side effects. These findings are in accordance with the study of Garg N et al.[13] which also showed that side effects of vomiting was seen more commonly with patients receiving Tramadol whereas nausea was more common in patients receiving Paracetamol. Majority of the neonates had birth weight between 2.5 kg to 3 kg. The mean birth weight in Group A (2.95 ± 0.31 kg) and Group B (2.96 ± 0.30 kg) was almost similar and the difference between them was not statistically significant. The findings of the present study correlated with Garg N et al.[13] which also showed that majority of the neonates had birth weight between 2.5 kg to 3.5 kg and mean birth weight among both the group was not statistically significant. In the present study, only a few patients in Group B (3.08%) had APGAR at one minute between 4-6 leading to moderate birth asphyxia and rest of the neonates had normal APGAR scores irrespective of the analgesic given. The difference among the two groups was not significant. These are similar to the study by Kaur J et al.[12] where APGAR score was comparable among the two groups and no significant neonatal adverse outcome was noted.

In the present study, most of the neonates in Group A (90.3%) and Group B (84.6%) did not require NICU admission and had no significant neonatal complications.

6. Conclusion

It is observed in the study that VAS scoring was significantly lesser after 1 hour and after 3 hours in women who received paracetamol compared to tramadol, therefore it is more effective labour analgesic drug. The mean duration of active phase of first stage of labour and mean drug delivery interval were significantly lower in patients receiving paracetamol than tramadol as analgesic drug. The present study concluded that intravenous paracetamol is a better analgesic in terms of pain relief when compared with intravenous tramadol.

7. Source of Funding

None.

8. Conflict of Interest

None.

References

1. Archie CL. The course and conduct of normal labour and delivery. In: Decherney AH, Nathan L, Goodwin TM, Laufer N, editors. Current Diagnosis & Treatment Obstetrics & Gynaecology. McGraw-Hill Education; 2007. p. 203–11.
2. Steer P, Flint C. ABC of labour care: physiology and management of normal labour. *BMJ*. 1999;318(7186):793–6.
3. Rowlands S, Permezel M. Physiology of pain in labour. *Baillieres Clin Obstet Gynaecol*. 1998;12(3):347–62.
4. Chandnani K, Sainee HB. Pain relief in labour: tramadol versus pentazocine. *Int J Reprod Contracept Obstet Gynecol*. 2013;2(2):186–9.
5. Pandya ST. Labour analgesia: recent advances. *Indian J Anaesth*. 2010;54(5):400–8.
6. Aronoff DM, Oates JA, Boutaud O. New insights into the mechanism of action of acetaminophen: its clinical pharmacologic characteristics reflect its inhibition of the two prostaglandin H2 synthases. *Clin Pharmacol Ther*. 2006;79(1):9–19.
7. Smith HS. Potential analgesic mechanisms of acetaminophen. *Pain Physician*. 2009;12(1):269–80.
8. Arslan M, Celep B, Çiçek R, Kalender H, Yılmaz H. Comparing the efficacy of preemptive intravenous paracetamol on the reducing effect of opioid usage in cholecystectomy. *J Res Med Sci*. 2013;18(3):172–7.
9. Rebordosa C, Kogevinas M, Horváth-Puhó E, Nørgård B, Morales M, Czeizel AE, et al. Acetaminophen use during pregnancy: effects on risk for congenital abnormalities. *Am J Obstet Gynecol*. 2008;198(2):178.
10. Abdollahi MH, Mojibian M, Pishgahi A, Mallah F, Dareshiri S, Mohammadi S, et al. Intravenous paracetamol versus intramuscular pethidine in relief of labour pain in primigravid women. *Niger Med J*. 2014;55(1):54–7.
11. Beakley BD, Kaye AM, Kaye AD. Tramadol, pharmacology, side effects, and serotonin syndrome: a review. *Pain Physician*. 2015;18(4):395–400.
12. Kaur J, Sharma S, Singh N, Madan A. Role of intravenous acetaminophen infusion for analgesia during active labour. *Int J Clin Obstet Gynaecol*. 2019;3(3):145–9.
13. Garg N, Vanitha VG. A Randomized Controlled Trial of Intravenous Paracetamol and Intravenous Tramadol for Labour Analgesia. *Obstet Gynaecol Res*. 2019;2(2):3–13.
14. Mohan H, Ramappa R, Sandesh M, Akash BK. Intravenous paracetamol infusion versus intramuscular tramadol as an intrapartum labor analgesic. *Contracept Obstet Gynecol*. 2015;4(6):1726–30.
15. Das BP, Ali J, Baruah A. Comparative study between intravenous paracetamol and intramuscular tramadol as labour analgesic. *Int J Sci Res*. 2016;5(10):1675–9.
16. Aimakhu CO, Saanu OO, Olayemi O. Pain relief in labour: a randomized controlled trial comparing intramuscular tramadol with intramuscular paracetamol at the University College Hospital. *Trop J Obstet Gynaecol*. 2017;34(2):91–8.

Author biography

Meghna Marwah, PG Resident https://orcid.org/0009-0006-8032-4671

Kavita Mandrelle, Professor and Head https://orcid.org/0000-0002-4074-6371

Dootika Liddle, Professor https://orcid.org/0000-0003-3897-6028

Cite this article: Marwah M, Mandrelle K, Liddle D. A randomized controlled trial of intravenous paracetamol and intravenous tramadol for labour analgesia. *Indian J Obstet Gynecol Res* 2023;10(3):259-265.