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RESEARCH ARTICLE

COMPARATIVE STUDY BETWEEN INTRAVENOUS PARACETAMOL AND INTRAMUSCULAR TRAMADOL AS LABOUR ANALGESIA

***Abinaya. A., Latha. K and Jayashree V**

Department of Obstetrics and Gynaecology, Rajah Muthiah Medical College and Hospital, Annamalai University, Chidambaram, Tamil Nadu, India-608 002

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ABSTRACT

Objectives: The goal of the prevailing study was to assess the efficacy and safety of intravenous paracetamol (1 gm) as opposed to intramuscular tramadol (100 mg) as an intrapartum labour analgesic. **Materials and Methods:** This was a prospective study carried out in Department of Obstetrics and Gynaecology in Rajah Muthiah Medical College and Hospital from 2015-2017 on 60 antenatal mother in active labour, after receiving the ethical clearance and written knowledgeable consent. The first 60 consecutive parturients fulfilling the inclusion standards had been recruited into the study. Women had been then randomised to obtain both intravenous one thousand mg (1000mg) of Paracetamol (Group A, n=30) or intramuscular a hundred mg(100 mg) of tramadol (Group B, n=30). Both the groups had been observed and compared for time of onset of analgesia, pain intensity was recorded by using Mc Gills scale before ,one and three hour after drug administration, duration of labour, maternal cardio respiratory parameters, mode of delivery, fetal APGAR scores, neonatal outcome and side effects of drugs. **Results:** No difference in pain intensity was visible earlier than drug administration. There was significant pain reduction after 1 and 3 hours of paracetamol administration compared to tramadol. Total duration of labour from enrolment in study to delivery in the paracetamol group changed was 276 mins (4 hrs36 mins) ± 59.97 minutes and in the tramadol group it was 393 minutes (6hrs 33mins) ±74 mins which concluded duration of labour was shortened in paracetamol group. In the paracetamol group, nausea was seen in 6.67% accompanied by vomiting (3.33%). Nausea became most commonest side effect in the tramadol group (13.3%) followed by vomiting (10%). APGAR scores in both groups had been satisfactory. **Conclusion:** Intravenous paracetamol was more effective labour analgesic with fewer maternal side effects and shortens labour in comparison to intramuscular tramadol.

INTRODUCTION

Labour pain is among the maximum excruciating pain experienced by all women. Labour pain impacts maternal psychology and course of labor causing apprehension, tension, and strain. Pain during the primary stage of labour originates predominantly due to cervical dilatation and uterine muscle wall ischemia mainly due to lactate accumulation. During the late 1st stage and 2nd stage of labour, the vagina and perineum form extra sources of pain. The related increase in sympathetic activity results in elevated oxygen intake, minute ventilation all through contractions can result in respiratory alkalosis, and metabolic acidosis and left shift of maternal oxyhemoglobin curve accordingly which could lead to decreased oxygen being transferred to the fetus, prolonged labour and so unfavourable outcome. Thus, pain relief throughout labour is predicted to lessen maternal strain and improve maternal and perinatal outcome. Labour pain is due to a result of many complex interactions, physiological and mental, excitatory in addition to inhibitory. The pain if now not appropriately controlled may affect respiration, cardiovascular and gastro intestinal, urinary and neuro endocrine functions due to segmental and suprasegmental reflexes. Pain also reduces uteroplacental blood flow leading to altered fetal homeostasis.[1]

The non-pharmacological techniques of analgesia consist of emotional support, warm water bath, at ease beginning environment, psycho-somatic instruction, yoga, Acupuncture, Transcutaneous electric nerve stimulation (TENS), Hypnosis, Aromatherapy and Breathing exercises. The normally used and greater effective are pharmacological techniques which encompass opioids like pethidine, tramadol, morphine, fentanyl, butorphanol, pentazocine, though the regional analgesia is gold standard these days and most commonly used obstetric analgesia in developed countries. The more modern advances like mixed spinal epidurals, low dose epidurals, patient controlled intravenous, inhalational, and epidural analgesia, altered local analgesia techniques include pudendal block, paracervical block, lumbar sympathetic block, perineal

infiltration have revolutionized obstetric anesthesia[2]. But maximum of modern obstetric analgesia practices involve participation of expert anesthesiologist, high-priced equipment, and continuous monitoring centers which unfortunately will now not be available in developing countries wherein a majority of obstetric services are in the arms of midwives, educated nurses, and non-specialist medical doctors. In such situations, a method with minimal technicality is favoured. However, systemic opioids are associated with maternal (dysphoria, sedation, respiration depression, nausea and vomiting and not on time gastric emptying) and fetal adverse outcomes (fetal misery, early neonatal respiratory depression and behavioural and feeding troubles) for up to 6 weeks submit-delivery. These issues have brought about an exploration of an alternative non-opioid (Paracetamol) for maternal pain relief in labour.

Paracetamol, the mode of analgesic action of which has still now not been completely elucidated is concept to exert its analgesic activity through inhibiting the synthesis of prostaglandins in the central nervous system (CNS) (centrally appearing) drug and peripherally blocking off pain impulse generation[3,4]. Also it has serotonergic (5HT) mechanism and cannabinoid agonism mechanism contributing to its analgesic effect, has lately been made to be had as intravenous preparation[5]. Various studies have proved intravenous paracetamol as powerful analgesic agent that's safe, powerful, less expensive, and requires no special monitoring[6].

Paracetamol being cheaper and simple to manage could be as boon agent of obstetric analgesia in growing nations. Paracetamol is an effective non narcotic analgesic and antipyretic drug with tolerable aspect results when in comparison to other opioids and NSAIDs. Paracetamol has a favourable safety profile with no hazard of congenital anomalies[7]. The use of iv formulations throughout labour pain is excellent with improved bioavailability and earlier onset of action with higher mean IV c max (maximum plasma concentration of drug) and earlier time to maximum concentration (T-max), with much less intra subject variability, in comparison with other formulations. Studies have documented protection and efficacy of intravenous paracetamol as a labour analgesic[8].

Among systemic opioids, Tramadol HCl is a centrally performing robust opioid analgesic which interacts with Mu, delta and kappa opioid receptor in which it reveals purely agonist effects. It also has non opioid mechanism of action and these haven't had any adverse consequences on GIT/RS/CVS and CNS. Intramuscular tramadol HCl is generally used in labour analgesia in growing nations as it is cheaper, no special tracking is required and has been broadly studied and proved for its protection and efficacy in labour analgesia[9].

Thus widespread use of anti spasmodic helps to make sure regular progress of labour reduces the danger of dysfunctional labour and enables early identification of emerging obstetric trouble. The necessities of a satisfactory analgesic in labour are protection and powerful analgesia at some point of the painful periods of labour with no unpleasant maternal side effects and no depressant effect on the child or on the maternal cardiorespiratory system. The method used ought to be cheap, smooth to manage, produce desirable relief of pain however have to now not impair attention and co-operation. It have to be non poisonous to the mother and fetus. The approach ought to don't have any tocolytic action and must now not postpone labour. So we undertook this study with the aim to compare efficacy and safety of single dose 1000 mg intravenous paracetamol with 100 mg intramuscular tramadol hydrochloride as labour analgesia during active phase of labour.

MATERIALS AND METHODS

This study was a comparative prospective–randomised study conducted in Department of Obstetrics and Gynaecology in Rajah Muthiah Medical College and Hospital, Chidambaram 2015-2017. A random organization of sixty antenatal women in age group 20 to 35 years with term gestation with cephalic presentation in active phase of labour had been selected according to inclusion criteria and divided into 2 groups. Antenatal women with previous LSCS, scarred uterus (post myomectomy), multifetal gestation, fetal malpresentation, intrauterine fetal demise, antepartum hemorrhage, clinical diagnosis of CPD were excluded in this study.

GROUP A-30 women (15 primi+15 multi) in active labour received intravenous infusion containing a thousand mg (1000 mg) of paracetamol single dose over 15 minutes.

GROUP B-30 women (15 primi+15 multi) in active labour received one hundred mg(100 mg) intramuscular tramadol hydrochloride single dose in upper and outer quadrant of gluteal area with 2 ml syringe.

In all women included in this study had undergone detailed history, general, systemic and obstetric examination, vaginal examination had been done and all the required investigations completed. Labour was monitored using partogram. Pain intensity before administering drug recorded by means of Mc Gills pain intensity scale (table1). Measurement of pain relief was done after 1 and three hour of drug administration. Fetal monitoring performed with the use of a NST. Duration of labour, mode of delivery, neonatal outcome and drug delivery interval and side effects of drugs in both the groups have been noted.

Table 1 Mc Gills pain intensity scale

Mc Gills scale	Pain intensity
0	No pain
1	Mild pain
2	Discomfort
3	Distressing
4	Horrible
5	Excruciating

Statistical Analysis

Data had been defined as mean ± SD and percent. Metric data had been as compared through student's t test, whereas non metric information had been compared by means of chi square test and Mann-whitney U check. $P<0.05$ was taken into consideration as significant p value. Software used was Microsoft excel and stastical package for social sciences for data analysis (SSPS 21).

RESULTS

The mean age group of the women in paracetamol group was 24.86±4.06 years and in the tramadol group was 24.53±4.16 years. The difference was not statistically significant among the 2 study groups (p=0.755). (table 2)

The mean gestational age in paracetamol group was 39.35±1.73 weeks and in tramadol group was 39.33±1.22

weeks. The difference was not statistically significant between the two groups (p=0.962) (table 2)

The mean dilatation and effacement of cervix at enrolment in the paracetamol group had been 4.13±0.34 cms and 61.66±10.85% respectively. In the tramadol group, the mean dilatation and effacement of cervix had been 4.02±0.63 cms and 60.66±11.12% respectively without a statistically vast difference (p = 0.137, 0.726). (table 2)

Table 2

Parameters	GROUP A	GROUP B	P Value
Maternal Age	24.86±4.06 yrs	24.53±4.16 yrs	0.755(NS) *
Gestational Age	39.35±1.73 Weeks	39.33±1.22 weeks	0.962(NS) *
Cervical Effacement	61.66 ±10.85 %	60.66±11.12%	0.726(NS) *
Cervical Dilatation	4.13 ±0.34 cms	4.02 ± 0.63 cms	0.137(NS) *

* Non significant

Pain intensity before drug administration: Using Mc Gills pain scale, 9 women (30%) in the paracetamol groups had horrible pain, 18 women (60%) had distressing pain, and 3 women (10%) had discomfort at the point of entry into study. In the tramadol group, 10 women (33.3%) had horrible pain, 18 women (60%) had distressing pain, and 2 women (6.7%) had discomfort. The pain intensity was measured using McGills scale among the 2 groups before drug administration had been statistically insignificant (p = 0.881) (Table 3).

After 1 h of intravenous paracetamol administration, 1 women (3.3%) had horrible pain, four women (13.3%) had distressing pain, 22 women (73.4%) had discomfort, and 3 women (10%) had mild pain. In the tramadol group, 10 women (33.3%) had horrible pain, 18 women (60%) had distressing pain, 2 women (6.7%) had discomforting pain, and no women had mild pain after 1 h of drug administration. The difference between the two groups had been statistically significant. (p<0.001) (Table 3).

After 3 h of paracetamol administration, 4 women (13.3 %) had distressing pain, 17 women (56.7 %) had discomforting pain, and 9 women (30%) had mild pain.

In the tramadol group, 16 women (53.3%) had horrible pain, nine women (30%) had distressing pain, 2 women (6.7%) had discomfort, and 3 women (10%) had mild pain measured using Mc Gills pain intensity scale. The difference among the two groups had been statistically significant (p<0.001) (Table 3).

Women who had lower section caesarean section (LSCS) had been excluded for evaluation of pain and duration of labour.

The mean duration of active phase of rst stage of labour in the paracetamol group was 196mins (3hrs 16mins) ±56 minutes and in the tramadol group turned into 336 minutes (5hrs 36mins) ±75mins. The difference in mean duration of the active phase of rst stage of labour was statistically significant (p<0.001). (Table 4/fig 1)

The mean duration of the second stage of labour within the paracetamol group became 35.03±7.5 minutes and in the tramadol group it was 47.34 ±4.3 minutes. The mean duration of second stage of between the two groups. (p<0.001). (Table 4/fig 1)

The mean duration of 3 rd stage of labour in the paracetamol group was 5. 57±0.95 mins and within the tramadol group it was 10.34±1.79mins. The difference in the mean duration of third stage of labour was statistically significant between the two groups (p<0.001). (Table 4/fig 1)

Total duration of labour from enrolment in the paracetamol group was 276 mins (4hrs 36mins) ±59.97mins and in the tramadol group, it was 393 mins (6hrs 33mins) ±74 mins. The distinction was statistically significant among the two groups (p<0.001). (Table 4/figure 1)

Drug delivery interval in the paracetamol group was 233 mins (3hrs 53mins) ±44.13 minutes and within the tramadol group was 365 minutes (6hrs 5 mins) ± 53.15 mins. The difference was statistically significant between the groups (p<0.001).(table 5)

Table 3 Pain Intensity Measurement

Time	Pain intensity	Intravenous paracetamol group		Intramuscular tramadol group		p value
		n	%	N	%	
Before drug administration	Mild	0	0.0	0	0.0	0.881 (NS)*
	Discomfort	3	10.0	2	6.7	
	Distressing	18	60.0	18	60.0	
	Horrible	9	30.0	10	33.3	
After 1 h of drug administration	Mild	3	10.0	0	0.0	<0.001 (Sig)†
	Discomfort	22	73.4	2	6.7	
	Distressing	4	13.3	18	60.0	
	Horrible	1	3.3	10	33.3	
After 3 h of drug administration	Mild	9	30.0	3	10.0	<0.001 (Sig)†
	Discomfort	17	56.7	2	6.7	
	Distressing	4	13.3	9	30.0	
	Horrible	0	0.0	16	53.3	

* Not significant
†Significant

Table 4 Duration of Labour

Duration of labour	Group – A (IV Paracetamol - 1000mg)		Group – B (IM Tramadol – 100mg)		t-test value	P value
	Mean	Std. Deviation	Mean	Std. Deviation		
Ist	3.0621	0.56254	5.3610	0.74675	12.523	<0.001(S)†
IInd	0.3503	0.7510	0.4734	0.4369	7.596	<0.001(S)†
IIIrd	0.5571	0.0959	0.1034	0.17983	12.437	<0.001(S)†
Total Duration	3.9695	0.59978	5.9378	0.74011	13.824	<0.001(S)†

†Significant

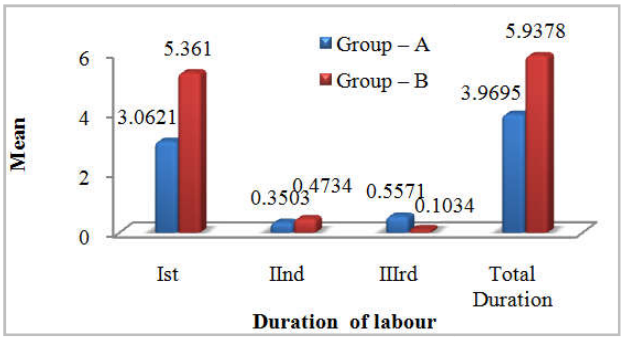

Figure 1

Table 5 Drug Delivery Interval

Group	N	Mean	Std. Deviation	t-test value	P value
Group – A (IV Paracetamol - 1000 mg)	30	3.5353	0.44131	16.831	<0.001(S) †
Group – B (IM Tramadol – 100 mg)	30	5.6583	0.53157		

†Significant

26 (86.7 %) women within the paracetamol group and 25(83.3%) in the tramadol group had spontaneous vaginal delivery. 3 (5%) women in each paracetamol and tramadol group had to undergo LSCS. There had been 2(6.7%) instrumental deliveries in paracetamol group and 4(13.3%) instrumental deliveries in tramadol group. No statistically significant difference in the mode of delivery had been determined between the two groups (p=0.601). (fig. 2)

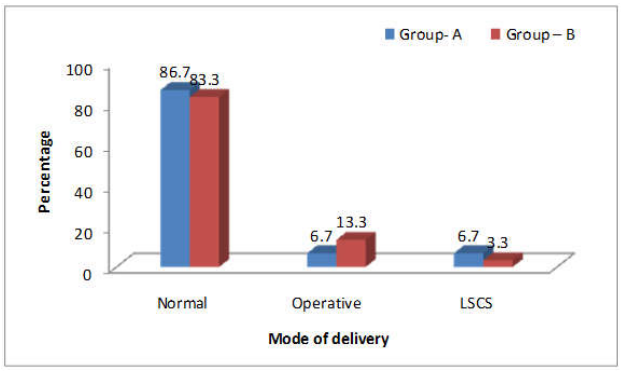

Figure 2 Mode of Delivery

In the paracetamol group, nausea seen in 6.67% followed by vomiting (3.33%). Nausea was commonest adverse effect within the tramadol group (13.3%) followed by vomiting (10%). No women in the paracetamol and the tramadol group had PPH and fetal tachycardia / bradycardia, respiratory depression.

Table 6 Maternal Complications

Maternal Complication	Group- A (IV Paracetamol – 1000 mg)		Group - B (IM Tramadol – 100 mg)	
	N	%	N	%
None	27	90.00	23	76.7
Nausea	2	6.67	4	13.3
Vomiting	1	3.33	3	10.00
PPH	0	0.00	0	0.00
Total	30	100.0	30	100.00

P value 0.370(not significant)

The variation in the nausea and vomiting were statistically insignificant among the 2 groups (p = 0.370) (Table 6)

The mean APGAR scoring of neonates in the paracetamol group at 1 min was 5.9 ± 1.17 and at 5 min was 7.8 ± 0.86. The mean APGAR score of the neonates in the tramadol group at 1 min was 5.8 ± 0.91 and at five min was 7.6 ± 0.66. The difference have been statistically insignificant (p = 0.714, 0.246). (fig. 3)

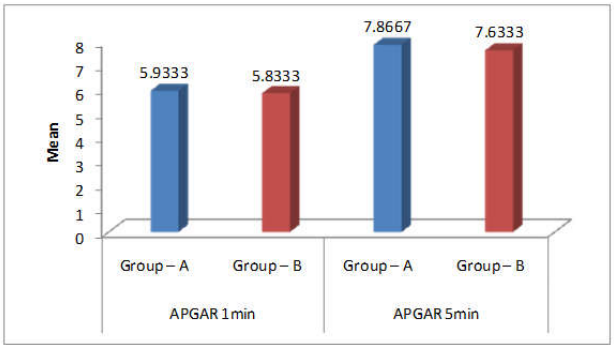

Figure 3 APGAR SCORE

The mean birth weight was 2.87 ± 0.43 kg within the paracetamol group and 2. 81 ± 0.31 kg in the tramadol group. The distinction were statistically insignificant among the 2 groups (p = 0.499). (fig. 4)

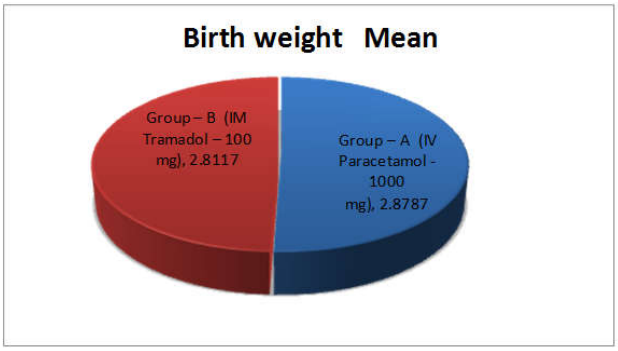

Figure 4

DISCUSSION

Paracetamol also known as acetaminophen or APAP (N-acetyl-para-aminophenol). Molecular system is $C_8H_9NO_2$. The probable mode of analgesic action of intravenous paracetamol was peripheral and central inhibition of COX and or interaction with serotonergic system. 1 gram of intravenous paracetamol had to be received only when women with body weight of more than 33 kg and when hepatic issues were ruled out. The dose needed should no longer be repeated within four hours and ought to no longer exceed 4gms in 24 hours.

Tramadol is a pethidine like synthetic 4 phenyl piperidine analogue of codeine. Molecular components is $C_{16}H_{25}O_2$ NHC. Tramadol has low affinity for opioid receptors and unlike different opioids, it is modestly potent opioid analgesic which interacts with mu, delta, kappa receptors wherein it exhibits purely agonists consequences. It inhibits reuptake of nor adrenaline and 5-hydrotryptonin[12]. It has no clinically tremendous respiratory depression at ordinary doses of 1-2 mg/kg body weight but concerns were voiced over excessive placental permeability of tramadol and side effects like nausea, vomiting and delayed gastric emptying that may result in hazard of aspiration where in case widespread anaesthesia is

required in an emergency situation.[10] Tramadol in solution contains tramadol hydrochloride 50 mg/ml in aqueous sodium acetate buffered solution without any preservatives, the Ph is 6 -6.8. The dose for parenteral management is 1.5-2 mg/kg.

The findings of present study propose that paracetamol group had a considerable decrease in pain intensity one and three hours after drug administration in comparison to intramuscular tramadol. About 75% women in paracetamol group has big alleviation of pain which lasted for atleast 3 hours. Meenakshi Lallar *et al* (2015)[10], Hema Mohan *et al*[11] (2015), Bishnu Prasad *et al*[12] (2013) also discovered to have pain alleviation after one and three hours of drug management. This might be defined by way of the reality that peak analgesic effect of paracetamol was seen at one hour and effect lasts for 4 to 6 hours. While intramuscular tramadol, the onset of action was within 10 minutes and action lasts for 2 to 3 hours.

There was a statistically substantial decrease in duration of first, 2nd and 3 rd stage of labour after intravenous paracetamol infusion compared to intra muscular tramadol. Jeetinder kaur Makkar *et al*[13] (2014) found vast lower in duration of first stage of labour. A exact analgesic will reduce the length of labour and prevent dysfunctional labour.

In a study carried out by Vijay Zutshi *et al*,[14] (2016) evaluated the efficacy of an intravenous infusion of 1000 mg of Paracetamol as an intrapartum analgesic. There was pain reduction at 1 and 2 hours in both groups ($p<0.001$). However, pain relief was more significant in Paracetamol group, specially at 1 hour. Duration of labour was shortened in paracetamol, without any maternal and foetal unfavourable effects. Intravenous Paracetamol was an efficacious nonopioid drug for alleviating labour pain without any significant maternal and foetal adverse outcomes

Drug to delivery interval as stated earlier was 3.53±0.44 hours in paracetamol and 5.65±0.53 hours in tramadol group respectively. A possible cause to explain this can be the reality that tramadol causes sedation although lesser than other opioids leading to lesser mobility of women in labour which could lengthen the labour. Also lesser pain relief as compared to paracetamol group might be cause for lengthened labour.

Operative delivery became 6.7% in group A and 6% in group B. Caesarean section was 6.7% in group A and 3% in group B. In a study by Karim *et al*[15], (2015) who evaluated the efficacy and adverse effects of an i.v. infusion of paracetamol in the active phase of labor as compared with sterile water (placebo) as a way for intrapartum analgesia. They found out that Paracetamol appears to be a safe and effective drug that can be used all through the intrapartum period.

In another study by Abdollahi *et al*[8] in 2014, evaluated intravenous paracetamol with intramuscular pethidine and it has been concluded that intravenous paracetamol was more effective, but no shortening of labour was observed with intravenous paracetamol and no difference in maternal and neonatal outcome.

In a study by Elbohoty *et al*[16] in 2012, intravenous paracetamol infusion was compared with intravenous pethidine as labour analgesia. It has been concluded that effectiveness of intravenous paracetamol and duration of action are similar in each drugs, but paracetamol was associated with fewer maternal adverse outcomes than pethidine and also shortened the duration of labour.

Sudha Patil *et al*[17] (2012) on studying the efficacy and safety of intramuscular tramadol in a hundred primigravida observed that onset of analgesia with tramadol was 15mins and the analgesic effect lasted for 4hours. The variant within the period of analgesia among special research with tramadol may be defined by the reality that CYP 2D6 activity influences tramadol's analgesic activity and enzyme displays genetic polymorphism, some sufferers being sluggish metabolisers and others being rapid.

Maryam Khooshideh *et al*[18] (2009) on comparing tramadol with pethidine observed tramadol to be a weaker analgesic than pethidine. These studies gives us an interpretation that paracetamol was probably a higher analgesic than tramadol.

Jeetinder Kaur Makkar *et al* [13] (2014) their study noted foetal bradycardia in five patients in tramadol group (17.2%) as compared to 2 in paracetamol group (6.6%). No maternal adverse outcomes were noted with paracetamol, confirming its beneficial safety profile. The mean Apgar scoring at 1 and 5minutes have been comparable between the 2 groups, indicating absence of any neonatal damaging results with the use of both of the 2 drugs.

In our study, neonatal outcome was beneficial with each paracetamol and tramadol. However adverse effects like nausea and vomiting were more common in tramadol group, however no other principal complications occured with any of the drugs.

CONCLUSION

Obstetric analgesia strives at making childbirth a satisfying and painless event. Findings from the existing study demonstrates that intravenous paracetamol is an efficacious non opioid drug for relieving labour pain than intramuscular tramadol. Paracetamol also shortens the duration of labour and has fewer maternal detrimental effects than tramadol; but neonatal outcome of both the drugs was favourable. So from our study, we conclude that intravenous paracetamol is easy, cost effective, feasible alternative as labour analgesics. In developing countries like India, with low socio economic resource settings, intravenous paracetamol can be used as an effective analgesia instead of intramuscular tramadol because of its better analgesic action, shortening of labour, and fewer maternal side effects. This turned into in accordance with the study of Malaise O which indicates that IV paracetamol has true efficacy and protection in labour analgesia. Also, the impact of paracetamol in reducing duration of hard work is beguiling and necessitates future studies, with ability benefits being, 1) a lower incidence of complications associated with extended labour (neonatal sepsis or maternal infection which include chorioamnionitis or puerperal sepsis) 2) tremendous in diminished foeto-placental reserve, lowering incidence of caesarean section3.) Reducing the time of parturition would be welcomed by means of women and health authorities with restrained medical resources especially in low income countries. Though it was said that reminiscences of pain fade constantly, this doesn't make it any more tolerable at the time. It is therefore simplest humane to try to relieve it and make labour more memorable for the women.

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