INTRAVENOUS PARACETAMOL INFUSION VERSUS INTRAMUSCULAR PETHIDINE AS LABOUR ANALGESICS

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ABSTRACT

Background

Labour is one of the most painful and stressful events in life. The intensity of pain experienced by women in labour has been found to affect the progress of labour, fetal well-being and maternal psychology. Intramuscular pethidine is one of most common drugs used for labour analgesia. Paracetamol may be used as alternative to pethidine as labour analgesia.

Objective

To compare the efficacy and adverse effects of intravenous paracetamol versus intramuscular pethidine hydrochloride as analgesia in the 1st stage of labour.

Patients and Methods

This is a single-blinded prospective-randomized study conducted in Sulaimani maternity teaching hospital over a period of six months starting from the 1st of December 2017 till 31st of May 2018. The study included 200 primigravidae women with term uncomplicated pregnancy in their active phase of labour. After taking informed consent, the women were randomly distributed into two groups, one hundred women received 1000mg paracetamol by intravenous infusion, and the other one hundred women received 100 mg pethidine intramuscularly. The primary outcome was the efficacy of the drug to provide adequate analgesia in labour. Pain intensity before administering drug was recorded by Mc Gills pain intensity scale, then at the 1sthr, and in the 3rdhr after drug administration. The secondary outcomes included the presence of adverse maternal effects, mode of delivery and fetal Apgar scores at 1st and 5th minutes.

Results

The mean of pain score was low in both groups after 1h of drug administration but it was significantly lower in the pethidine group. Also at 3h of drug administration the mean pain score was significantly much lower in pethidine group compared to the paracetamol group (p -value=0.001). The maternal and neonatal side effects were significantly higher in the pethidine group compared to the paracetamol group (P value= 0.001)

Conclusions

Intramuscular pethidine is more effective than intravenous paracetamol in relieving pain during the 1st stage of labour. But the use of paracetamol causes less maternal and neonatal side effects than pethidine.

Keywords: *Labour pain, analgesia, Intramuscular pethidine, Intravenous paracetamol.*

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INTRODUCTION

More than 95% of women report pain in labour. Pain is an important part of the physiology of normal labour, it is usually intermittent, and accompanies uterine contractions [1]. It affects maternal psychology and course of labour causing apprehension, anxiety, and stress [2] .

Since childbirth can be extremely painful, the provision of pain relief (analgesia) during labour is a humanitarian duty and a vital component of a positive maternal experience [3]. In fact, the American College of Obstetricians and Gynecologists (ACOG) states that maternal request is a sufficient indication for pain relief during labour, and analgesics should not be withheld [4]. Many methods of relieving pain in labour and various coping strategies have been advocated, ranging from non-clinical supportive measures (for example, the positions adopted by women and the extent of their mobility during labour) to complex pharmacological interventions like epidural analgesia. It is important that whatever method is used to ameliorate maternal discomfort, it should be both effective in meeting the needs of the individual woman and safe for both the mother and her baby. The choice of technique, agent, and dosage is based on many factors including patient preference, medical status and presence of contraindication [5].

Opioids are the most commonly used systemic medications for labour analgesia, and although they do not typically provide complete analgesia, they do allow the parturient to better tolerate labour pain. In addition, they are easily accessible worldwide, and easy to administer in most facilities as their use does not usually need any specialized equipment or personnel [6]. Meperidine (Pethidine) is a synthetic opioid and it is the most commonly used opioid in the obstetric setting. [3] It acts mainly like other opioids" through the μ1 and μ2 opioid receptors in the central and peripheral nervous system. It is metabolized in the liver to produce nor-meperidine (nor-pethidine) a pharmacologically active metabolite which is a potent respiratory depressant.

The nor-pethidine crosses the placenta and is excreted into breast milk by passive diffusion, equilibrating between materno-fetal compartments in 6 minutes. Pethidine reaches its maximum effect after 30–40 minutes and can be re-administered after 3–6 hours. Its elimination half-life in neonates is around 23 hours because of the neonate's immature elimination pathways, while in adults the elimination half-life of pethidine is only 3 hours [7]. The recommended method of administration is through intramuscular rout (IM). The individual dose for adults is 25–150 mg when administered IM and 50 mg with intravenous administration[7]. Maternal side effects are similar to those of other opioids, namely respiratory depression, delayed gastric emptying, nausea, vomiting, sedation and hypotension [8]. Fetal and neonatal complications related to the total dose and dose to delivery time. Maximal fetal uptake of pethidine occurs 2 to 3 hours after maternal IM administration and studies have shown that infants born within this time have increased risk of respiratory depression [7]. The optimal time for delivery of the baby following a dose of pethidine is either within the first hour or after the fourth hour of administration. If pethidine is used within 4 hours of delivery of the baby, the pediatrician should be informed and asked to attend the delivery in case any neonatal respiratory support is needed. Hence, whilst pethidine can be given easily, good attention to timing and access to assistance are still required [8].

Paracetamol (acetaminophen) is an effective non-narcotic analgesic. It has been widely used for over a century as an effective analgesic and antipyretic agent with tolerable side effects. Its efficacy and tolerability are well established and, in contrast with other analgesics, it has a favourable safety profile. It can be administrated per oral, IV, IM, or rectally [9].

The mechanism of action is thought to be the high plasma concentrations achieved with intravenous acetaminophen, which drive it across the blood brain barrier, inhibiting central prostaglandin synthesis, and also it has a serotonergic mechanism. Pain relief is reached within 15 minutes of intravenous acetaminophen administration [10, 11]. It is metabolized through conjugation with glucoronic acid and sulfate to be excreted into the urine. A small fraction (<4%) is metabolized by cytochrome P450 to a reactive intermediate (N-acetyl benzoquinone imine) which is toxic for the hepatocytes and, under normal conditions of use, is rapidly detoxified and eliminated in the urine after conjugation with cystein.

Paracetamol is a safe analgesic and at therapeutic doses, it is associated with fewer adverse effects than either opioids or non-steroidal anti-inflammatory drugs. Healthy adults taking regular doses of up to 4,000 mg a day show little evidence of toxicity. Serious skin rashes may rarely occur, and too high dose can result in liver failure. It appears to be safe during pregnancy and breast-feeding [12] . Intravenous paracetamol is currently approved by the U.S. Food and Drug Administration (FDA) for use to treat fever, mild to moderate pain,

and moderate to severe pain when used with adjunctive opioids analgesics [13].

There is a paucity of studies assessing its intrapartum use. It has been shown that the metabolism of paracetamol is unchanged in pregnant woman, and increasing towards term in the fetus, with absent reports of fetal insult when used in the standard dose in healthy women at term [14]. If proved to be an effective analgesic agent in labour, paracetamol being inexpensive and simple to administer could be a boon agent of obstetric analgesia in developing countries [15].

For assessing the pain intensity, the McGill pain Questionnaire are probably the most frequently used self-rating instruments for the measurement of pain in clinical and research settings. It composed of multiple items assessing the intensity, quality, and behavior of pain. The short form McGill pain Questionnaire is available for use in specific research settings when the time to be obtain information from patients is limited and when more information of intensity of pain is desired (16).

The aim of this study is compare the efficacy of intravenous paracetamol infusion versus intramuscular pethidine hydrochloride as analgesics in the 1st stage of labour as well as comparing the maternal and fetal side effects of both drugs.

PATIENTS AND METHODS

This is a single-blinded prospective-randomized study conducted in Sulaimani maternity teaching hospital over a period of six month starting from the 1st of December 2017 till 31st of May 2018. The study included two hundred primigravidae with singleton uncomplicated pregnancy, gestational age between 37- 40 weeks, who were admitted to the labour word with spontaneous onset of labour in their active phase of the 1st stage. Exclusion criteria includes: gestational age < 37 or > 40 weeks, induced labour, multiple pregnancy, medical disease complicating pregnancy (e.g. Hypertension, Diabetes, asthma, thyroid and heart diseases).

After taking full history and performing proper general and obstetrical examination and after taking informed consent, the women were randomly distributed in two groups. The paracetamol group (100 women) and Pethidine group (100 women). Women in the paracetamol group received a 100 ml intravenous infusion containing 1000 mg of paracetamol in a single dose over 15 min., while women in the Pethidine group were given 100 mg Pethidine by IM. Injection in the upper and outer quadrant of gluteal region with a 2-ml syringe. The progress of labor was monitored using a partogram and the fetal heart rate was monitored by intermittent auscultation with sonic-aid. The Pain intensity before administering the drug was recorded by McGill pain intensity scale (Table1).

Then at the 1st and the 3rd hours after drug administration to assess response to the analgesics. Any need for additional analgesia was recorded. The women were followed up throughout labour till the end of the 3rd stage. Maternal side effects (including nausea, vomiting dizziness and respiratory depression) as well as any fetal heart rate abnormality and the mode of delivery were all recorded. Also the neonatal condition at birth including the Apgar score at 1st and 5th minutes, any respiratory depression requiring resuscitation and the need for admission to neonatal care unit were all recorded and compared between the two groups.

Table 1. McGill's pain intensity scale [16]

McGill's scale	pain intensity
0	No Pain
1	Mild pain
2	Discomfort
3	Distressing
4	Horrible
5	Excruciating

Statistical analysis

The data presented in tabular forms showing the frequency distribution of different variables among the both groups of patients (Pethidine and Paracetamol group). Chi-square tests were used to compare the categorical data between these two groups of patients (Demographic and clinical characteristics) as well as pain. The vital signs (Pulse rate, systolic and diastolic blood pressure) before and after medication of both groups were compared using independent t test. P-value of 0.05 was used as a cut off point for significance of statistical tests.

RESULTS

A total of two hundred primigravidae were included in the study (100 women in each group). Regarding the demographic characteristics of the studied women, the mean age for women in pethidine and paracetamol groups was 23.9± 4.4 and 24.1 ±4.2 years respectively. The mean BMI for the Pethidine group was 29.98 kg/m^2 and for the Paracetamol group was 29.88 kg/m^{2,} while the mean gestational age for women in both groups was 38.9 wks.

Regarding cervical dilatation in cm, the mean for pethidine group was 5.1 ±0.95 and for the paracetamol group was 5.2±1.02 cm. There was no statistically significance difference between the two groups in all above demographic parameters (P-value > 0.05) as shown in Table (2).

The pain intensity was observed by using McGill's pain intensity scale (table 1).

Before drug administration: In Pethidine group, 84% had score 3 (distressing) and 16% had score 4 (horrible). In Paracetamol group, 80% had score 3 and 20% had score 4, there was no statistically significant difference between both groups in pain intensity (P-value =0.59)

After 1 hr. of drug administration: in Pethidine group 11 women had score 1 (mild pain), 59 women had score 2 (discomfort), and 29 women had score 3 (distressing).

While in paracetamol group no any women had score 1, 31 women had score 2, and 69 women had score 3. The difference was statistically highly significant (p -value < 0.001)

one case of the Pethidine group ended by caesarean section before reaching the end of 1st hour (so excluded from statistical analysis).

Three hours after drug administration: in Pethidine group only 1 woman had score 1, while 46 women had score 2 and 46 women had score 3. In Paracetamol group no any women had score 1, 2 women had score 2, and 91 women had score 3. The difference in the two groups was also statistically highly significant (p-value< 0.001) (Table 3). Seven cases in each group ended by caesarean section before reaching the end of the 3rd hr. So the remaining number after 3 hr. was 93 women in each group.

The number of women who requested additional analgesia after 3 hours was significantly higher in the paracetamol group compared to the pethidine group {70 (75.26%) versus 40 (43.01%), P value= 0.001} as shown in table (4):

For the maternal vital signs (pulse rate, systolic and diastolic blood pressure) before and after drug administration, a statistically significant difference was observed between the two groups with regard to the changes in pulse rate and blood pressure before and after drug administration (as shown in table 5).

Regarding side effects, 35% of women in pethidine group complained from nausea compared to 9% in Paracetamol group, 19% of women in Pethidine group complained from vomiting, compared to 4% in Paracetamol group, and 20% of women in Pethidine group complained from dizziness compared to 2% in Paracetamol group. The difference between the two groups was statistically significant (P value = 0.001). as shown in figure (1). No one of women in both groups developed respiratory depression.

Regarding fetal heart rate abnormality and meconium stained liquor during labour, no significant difference observed between the two groups. Also the mode of delivery was not significantly different (18% of the women in the Pethidine group delivered by caesarean section compared to 16 % in the paracetamol group. The difference in the two groups was statistically not significant (P value = 0.59) (Table 6).

The Apgar score of the fetuses in the 1st minute, there were significantly more fetuses in the pethidine group had low Apgar score compared to fetuses of the paracetamol group (6%with Apgar of 4-5 and 23% with Apgar of 6-7 in the pethidine group versus 1% and 9% for the paracetamol group respectively). P value = 0.003 (Table 7).

Also in the 5th minute more fetuses in the pethidine group had Apgar score of 6-7 compared to the paracetamol group (10% versus 1%). The difference in the two groups was also statistically significant (p value=0.005). Ten babies were admitted to the neonatal care unit, 5 of them the cause of admission was low Apgar score (4 of them from pethidine group & 1 from paracetamol group), and from those 5 cases 4 discharged in the same day & 1 diagnosed as birth asphyxia.

The other 5 cases that need admission to NCU for other causes like meconium stain liquor & for suspecting of congenital abnormality

Table 2. The demographic and clinical characteristics of women in both groups.

Demographic and clinical characteristics		Pethidine group	Paracetamol group	P-value
Age (years) Mean±SD		23.9± 4.4	24.1 ±4.2	0.73
Occupation	House wives Employee Student	77 12 11	70 16 14	0.67
BMI(kg/m2) Mean±SD		29.98 ±1.37	29.88 ±1.44	0.63
Cervix dilatation(cm) Mean±SD		5.1 ±0.95	5.2 ±1.02	0.43
Gestational age(weeks) Mean±SD		38.8± 1.02	38.9± 1.01	0.89

Table 3. Pain intensity before and after drug administration in both groups.

Pain Scores		Pethidine group	Paracetamol group	P value
Pain Score before medication	Score 3	84	80	0.59
	Score 4	16	20	
Pain Score after one Hour	Score 1	11	0	< 0.001
	Score 2	59	31	
	Score 3	29	69	
Pain Score after three Hours	Score 1	1	0	< 0.001
	Score 2	46	2	
	Score 3	46	91	

Table 4. The number of women who requested additional analgesia in both groups.

Request for additional analgesia	Pethidine group No (%)	Paracetamol group No (%)	P- value
Requested	40 (43.01)	70 (75.26)	0.001
Not requested	53 (56.99)	23(24.43)	0.001
Total	93 (100)	93(100)	

Table 5. Comparing vital signs premedication, after 1 hr, and after 3 hr in both groups.

Vital signs	Mean (± SD)		P value
	Pethidine group	Paracetamol group	
Pulse rate before medication	86.2(4.8)	86.4 (4.9)	0.74
Pulse rate after one hour	92.8(5.3)	88.4 (4.1)	< 0.01
Pulse rate after three hours	92.4(4.5)	88.5 (3.9)	< 0.01
SBP before medication	117.3 (5.2)	118.0(6.2)	0.39
SBP after one hour	112.5 (6.6)	116.9 (6.2)	< 0.01
SBP after three hours	113.0 (5.5)	116.4 (5.0)	< 0.01
DBP before medication	77.0(4.7)	76.2 (4.8)	0.22
DBP after one hour	72.4 (5.4)	74.8 (4.4)	0.01
DBP after three hours	72.0 (4.6)	74.5 (4.2)	< 0.01

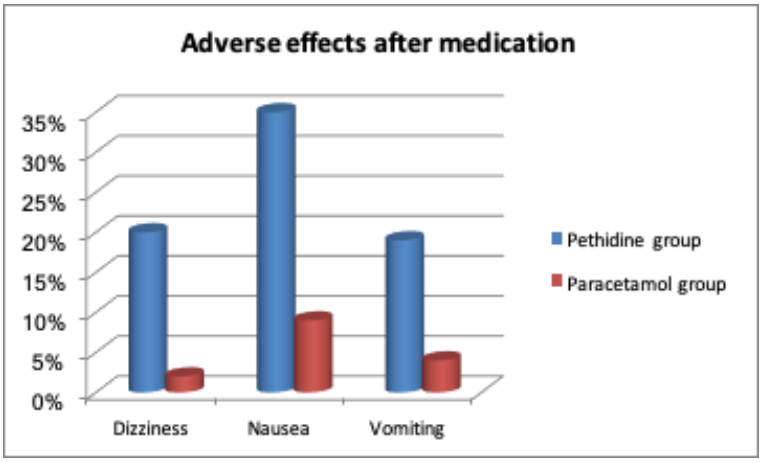

Figure 1. Maternal side effects after medication in both groups.

Table 6. Intrapartum abnormalities and mode of delivery in both groups.

Parameter	Pethidine group No (%)	Paracetamol group No (%)	P-value
Fetal heart abnormality			
Yes	11(%)	6 (%)	0.2
No	89 (%)	94 (%)	
Meconium stained liquor			
Yes	4(%)	6 (%)	0.52
No	96 (%)	94 (%)	
Mode of delivery			
Caesarean section	18 (%)	16 (%)	0.73
Normal vaginal delivery	82 (%)	84 (%)	

Table 7. Apgar score in the 1st and 5th min in both groups.

Apgar score		Pethidine group	Paracetamol group	P value
1st minute	Four- Five	6%	1%	0.003
	Six- seven	23%	9%	
	Eight - Nine	71%	90%	
5th minute	Six - Seven	10%	1%	0.005
	Eight - Ten	90%	99%	

DISCUSSION

Labour is one of the most painful and stressful events in life. It is well known that labour pains evoke a generalized neuroendocrine stress response, causing marked physiologic changes. The intensity of pain experienced by women in labour has been found to affect the progress of labour, fetal well-being and maternal psychology. As a result, satisfactory analgesia influences the course of labour positively and most women request analgesia [(2)].

In the present study both Pethidine and paracetamol were found to be effective in reducing the severity of pain during labour but Pethidine was significantly more effective. This result agreed with A.E.H. Elbohotyv et al. (2012) [(17)] they studied intravenous infusion of paracetamol versus intravenous pethidine as an intrapartum analgesic in the first stage of labor, they found as recorded by the VAS score, there was significant pain reduction at 1h & at 3h in both groups (P=0.001). The reduction in pain was significantly greater in the Pethidine group.

In paracetamol group about 31 % women had substantial relief of pain which lasted for >1 h. This might be explained that peak analgesic effect of paracetamol is seen at 1 h. This result agreed with Lallar et al. (2014) [(18)] who found Intravenous Paracetamol Infusion versus Intramuscular Tramadol for the pain score by McGill scale at 1 h but disagreed with it with regard to pain score at 3 h, they found that paracetamol group had a significant decrease in pain intensity 1 h after intravenous paracetamol administration as compared to intramuscular tramadol group. About 75% women in the paracetamol group had substantial relief of pain for at least for 1h & about 50% at 3h.

Also this result agreed with Ankumah et al. (2012) [(19)] who found that the primary outcome of IV paracetamol versus Morphine for Analgesia in Labor was similar in both groups within 120 minutes of initial treatment, but more women receiving intravenous paracetamol required rescue analgesia.

About the analgesic effect of the Pethidine in the present study, more than 70 % had decrease in mean pain score at 1 h after drug administration and > 50 % had lower mean pain score at 3h, while in Paracetamol group mean pain score decrease in31% at 1 h & 2.1% at 3 h, (p=0.001) this finding agreed with Abdollahi, et al.(2014) [(15)] Intravenous paracetamol versus intramuscular pethidine in labour pain for the low mean in pain score at 1 h and disagreed for the pain score at 3 h, that the estimated pain score based on verbal questioning from mothers at the end of delivery using VAS of pain, was significantly lower in paracetamol group comparing to that of the pethidine group. But it agreed with Maryam Khooshideh1 and Ali Shahriari (2009) [(20)] Who found more than 50% of women rating analgesia as either good or excellent after administration of pethidine in the first stage. And the pethidine seemed to be a better alternative than tramadol for analgesia in second stage of labour.

In comparing the mode of delivery, maternal side effects and neonatal side effects of the two drugs in the present study, finding showed that 65 % of women in Pethidine group had 1 or more of the following symptoms (dizziness, blurred vision, tachycardia, nausea, vomiting, and significant change in blood pressure), while in Paracetamol group about 16 % (P value =0.001). In addition, fetal heart rate variability was recorded in Pethidine group more than Paracetamol group but it was not significant (P-value =0.2). Also the Apgar score at 1st minute was significantly lower in Pethidine than that of the paracetamol group (P-value=0.005). This is agreed with A.E.H. Elbohoty et al. (2012) [(17)] who recorded maternal and fetal adverse effects only in the pethidine group, in which (64%)

had 1 or more of the following symptoms (dizziness, blurred vision, dryness of the mouth, vomiting, nausea, tachycardia, and change in blood pressure), in addition, fetal bradycardia was recorded in 2 women.

Also this result agreed with Maryam Khooshideh1 and Ali Shahriari (2009) [20] about the maternal side effects that there was a significantly higher incidence of nausea and vomiting and dizziness in Pethidine group compared with Tramadol group. But disagreed with it for the neonatal side effects in which all neonates (100%) had an Apgar score above 7 at one and five minutes. Also disagreed with Abdollahi, et al. (2014) [15] that there were no significant drug complications, and Apgar scores of neonates were similarly normal in both groups of the study.

Also the Finding of the present study for the maternal & neonatal side effects after paracetamol administration agreed with Lallar et al.2014 [18] who found, the mean Apgar score of neonates in the paracetamol group at 1 and 5 minutes was near to normal. In addition, in the paracetamol group, nausea and vomiting was recorded in very little cases.

Finally, about the mode of delivery, in the present study no significant difference found between the two groups with regard to the number of those delivered by cesarean section, this finding agreed with Abdollahi et al. (2014) [15] and A.E.H. Elbohoty et al. (2012) [17] they also found no significant difference in the mode of delivery between the two groups.

In conclusion, Paracetamol can provide analgesia in the first stage of labour, but the analgesic efficacy of paracetamol was not found to be as good as pethidine. Paracetamol may be preferred over pethidine as it is simple to administer and associated with less maternal and neonatal side effects.

REFERENCES

1. Felicity Plaat, Analgesia, Anesthesia and Resuscitation. In: Keith Edmonds, Editor. Dewhurst's textbook of Obstetrics & Gynecology, 8th Ed. Wiley-Blackwell; 2012. P: 356.

2. Lowe NK. The nature of labour pain. American Journal of Obstetrics and Gynecology 2002; 186: 16–24.

3. Othman M, Jones L, Neilson JP. Non-opioid drugs for pain management in labour: an overview of systematic reviews. Journal of Evidence-Based Medicine. 2012, May;5 (2):101-2.

4. Goetzl LM. ACOG Practice Bulletin. Clinical Management Guidelines for Obstetrician-Gynecologists Number 36, July (2002). Obstetric analgesia and anesthesia. Obstetrics and gynecology. (2002) Jul; 100(1):177-91.

5. Anim-Somuah M, Smyth R, Howell C. Epidural versus non-epidural or no analgesia in labour. Cochrane Database of Systematic Reviews. 2005, Issue 4. [DOI: 10.1002/ 14651858.CD000331.pub2].

6. Hughes SC, Levinson G, Rosen MA, Shnider SM, editors. Shnider and Levinson's anesthesia for obstetrics. Lippincott Williams & Wilkins; 2002: 92.

7. Hughes SC, Levinson G, Rosen MA, Shnider SM, editors. Shnider and Levinson's anesthesia for obstetrics. Lippincott Williams & Wilkins; 2002: 94.

8. Chu A, Ma S, Datta S. Analgesia in labour and delivery. Obstetrics, Gynecology and Reproductive Medicine. 2017 Jun 1; 27(6):184-90.

9. Bektas F, Eken C, Karadenz O, Goksu E, Cubuk M, Cete Y. Intravenous paracetamol or morphine for the Treatment of Renal Colic: A Randomized, Placebo-Controlled Trial. Ann Emerg Med 2009; 54: 568–574.

10. Singla NK, Parulan C, Samson R, Plasma and cerebrospinal fluid pharmacokinetic parameters after single-dose administration of intravenous, oral, or rectal acetaminophen. Pain Pract. 2012;12(7):523–532

11. Moller PL, Sindet-Pedersen S, Petersen CT, Juhl GI, Dillenschneider A, Skoglund LA. Onset of acetaminophen analgesia: comparison of oral and intravenous routes after third molar surgery. Br J Anaesth. 2005;94(5):642–648

12. Hyllested M, Jones S, Pedersen JL et al. Comparative effect of paracetamol, NSAIDs or their combination in postoperative pain management: A qualitative review. Br J Anaesth 2002 ; 88: 199–214.

13. Fox ER, Jones VM, Beckwith MC. Acetaminophen Injection: A Review of Clinical Information Including Forms Not Available in the United States. Journal of pain & palliative care pharmacotherapy. 2012. Jun 22;26(2):115-7.

14. Isbister GK, Bucens IK, Whyte IM. Paracetamol overdose in a preterm neonate. Arch Dis Child Fetal Neonatal Ed. 2001; 85: 70–

15. Abdollahi MH, Mojibian M, Pishgahi A, Intravenous paracetamol versus intramuscular pethidine in relief of labour pain in primigravid women. Niger Med J 2014;55(1):54–57

16. Melzack R, J. The McGill pain Questionnaire: appraisal and current status. Guilford press; (2001).

17. Elbohoty AE, Abd-Elrazek H, Abd-El-Gawad M, Salama F, El- Shorbagy M, Intravenous infusion of paracetamol versus intravenous pethidine as an intrapartum analgesic in the first stage of labour. Int J Gynaecol Obstet. 2012; 118:7-10

18. Lallar M, Anam HU, Nandal R, Singh SP, Katyal S. Intravenous paracetamol infusion versus intramuscular tramadol as an intrapartum labour analgesic. J Obstet Gynaecol India 2015;65(1):17–22

19. Ankumah NA, Tsao M, Hutchinson M, Pedroza C, Mehta J, Sibai BM, et al. Intravenous acetaminophen versus morphine for analgesia in labor: a randomized trial. American journal of perinatology. 2017 Jan;34(01):38-43.

20. Khooshideh M, Shahriari A. A comparison of tramadol and pethidine analgesia on the duration of labour: a randomized clinical trial. Australian and New Zealand Journal of Obstetrics and Gynecology. 2009 Feb 1;49(1):59-63.