

Original Paper

Comparing the Effects of Paracetamol and Pethidine on First-stage Labor Pain Relief and Their Maternal and Neonatal Complications



Masoumeh Khammar¹ , Zohreh Ghorashi^{2*} , Azita Manshoori³ 

1. Midwifery (MSc), Departments of Midwifery, School of Nursing and Midwifery, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.

2. Assistant Professor, Departments of Midwifery, School of Nursing and Midwifery, Geriatric Care Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.

3. Assistant Professor, Department of Obstetrics and Gynecology, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran..

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ABSTRACT

Introduction: The pain relief effect of Paracetamol, as a safe analgesic drug in labor, compared to Pethidine, as a well-known analgesic drug, need to be more evaluated.

Objective: This study aims to compare the effects of Paracetamol and Pethidine on the first-stage labor pain relief and neonatal and maternal complications.

Materials and Methods: This single-blind, parallel group, randomized clinical trial conducted on 100 nulliparous pregnant women referred to a maternity hospital in Rafsanjan Iran in 2018 who were selected using a convenience sampling method and by assigned into two groups Paracetamol (n=49, receiving 100 mg intravenous Paracetamol) and Pethidine (n= 51, receiving 50 mg intravenous Pethidine) using the minimization method. The drugs were administered when there was at least a 4-cm cervical dilation. Maternal complications and infant's 1 and 5-min the Apgar scores and ability to breastfeed were evaluated. Pain intensity measured by the Visual Analogue Scale (VAS) and compared using two-way repeated measures ANOVA before and 30 minutes, 1, 2, 3 and 4 hours after drug administration.

Results: There were no significant differences between the two groups in term of age, body mass index, and gestational age, and no significant difference in pain intensity in any groups among the time points. Maternal complications were significantly lower in the Paracetamol group than in the Pethidine group; however, the difference was statistically significant only in terms of nausea (P=0.04). Infants' breastfeeding ability was significantly better in Paracetamol group than in the Pethidine group (P=0.04). The results of two-way ANOVA showed that the mean VAS score was not significantly different between the two groups.

Conclusion: Paracetamol can alleviate the first-stage labor pain similar to Pethidine, but with fewer maternal and neonatal complications.

* Corresponding Author:

Zohreh Ghorashi, Assistant Professor.

Address: Departments of Midwifery, School of Nursing and Midwifery, Geriatric Care Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.

Tel: +98 (343) 4255900

E-mail: zghorashi@yahoo.com

Highlights

- Most pregnant women during the labor process seek analgesic drugs.
- Pethidine is an analgesic drug for labor pain; however, it has well known side effects on the mother and the newborn.
- Paracetamol is an effective analgesic drug in labor with less side effects.

Plain Language Summary

The use of analgesics during childbirth is now part of standard care in many countries around the world. There are many medications for labor pain relief, each with their own risks and benefits. The aim of this study was to compare the effectiveness of Paracetamol and Pethidine in alleviating the labor pain and its side effects in nulliparous pregnant women, divided into two groups; one received 100 mg of Paracetamol and other received 50 mg of Pethidine. In both groups, pain intensity was measured at 5 time points during labor. The maternal and neonatal side effects of both drugs were evaluated. There was no significant difference in pain intensity among the five time points in any groups. Maternal side effects were significantly higher in the pethidine group than in the paracetamol group. The ability of infants to breastfeed was better in the Paracetamol group than in the pethidine group. The results indicated that Paracetamol had sufficient potential to control the pain of the first stage of labor similar to pethidine, but with fewer maternal and neonatal side effects.

Introduction

The physiologic process of childbirth is associated with acute pain in the first and second stages of labor [1]. The severe pain during childbirth may affect the maternal psychological health, delivery progress, and the fetal and neonatal health. Therefore, providing adequate analgesia in the first and second stages of labor is one of the basic principles of modern obstetrics & midwifery. Using appropriate analgesia during labor should have the least side effects. Pethidine is considered as one of the most widely used analgesics which works as an antinociceptive through the ascending and descending receptors and neurons of the hypothalamic basal ganglia, limbic region, and brain cortex [2]. Pethidine and its active metabolite which is called “Norpethidine”, have numerous side effects on the mother and the fetus, especially if multiple doses are given during labor. Despite the widespread use of Pethidine for labor pain relief worldwide, maternal complications such as nausea (44%), vomiting (18%), central nervous system weakness, and drowsiness are common (11%) [3] as well as fetal complications including respiratory distress, reduced ability to breastfeed, and reduction of heart rate variability [4].

Paracetamol is one of the most commonly used medication to treat pain [5]. A recent study has shown that Paracetamol reduces labor pain without significant maternal and fetal complications [6]. Paracetamol was used for the first time in 2014 to control labor pain. Its analgesic effect was very significant during the first 30 minutes after intravenous injection in first stage of labor. No fetal and maternal complications were reported [7]. Another study that compared the analgesic effects of Paracetamol and Pethidine for labor pain relief showed a significant reduction of pain in both groups 15 minutes, 1 and 2 hours after administration. None of the mothers who had received Paracetamol showed side effects, while the frequency of side effects in the Pethidine group was 64% [8].

Although Paracetamol is administered in some maternal settings, the use of Paracetamol is not globally common for labor pain relief [9]. Limited studies have been conducted on Paracetamol use in labor and its analgesic effects during the first and second stages of labor [6-8]. On the other hand, the side effects of Pethidine during labor cannot be neglected. Therefore, this study aims to compare the effects of Paracetamol and Pethidine used in the first and second stages of labor in nulliparous women.

Methods and Materials

In this single-blind randomized clinical trial with parallel groups, 100 pregnant and nulliparous women who referred to a maternity hospital in Rafsanjan, Iran for childbirth and were in the first stage of labor were enrolled by a convenience sampling method, and were assigned into two groups: Paracetamol (n=49) and Pethidine (n=51). With $\alpha=0.05$, $\beta=0.2$, estimating the Standard Deviation (SD) of pain intensity in paracetamol group ($\sigma^2=1.17$) and in pethidine group ($\sigma^2=0.97$) based on a previous study [6], and considering minimum pain intensity in two groups to be clinically significant ($\Delta=0.6$ and $K=1$), the sample size was estimated at 50 people for each group. Inclusion criteria were: Being nulliparous, pregnancy with a single fetus and cephalic presentation, absence of any developmental abnormalities or fetal anomalies according to prenatal ultrasound results, and maternal demand for pharmacologic methods of labor pain relief. Exclusion criteria were fetal distress and the need for emergency cesarean section. The first participant was allocated to Paracetamol group at random. Minimization method with regard to maternal age, body mass index (BMI), and gestational age was used for random allocation of samples in two groups.

Sampling and allocation were carried out by the first researcher. The sampling process carried out from September 2018 to March 2019. After signing consent form and allocation, 9 women from the Paracetamol group and 10 women from the Pethidine group were excluded due to obstetric complications such as fetal heart rate problems leading to cesarean section and the unwillingness to continue participation (Figure 1). Standard routine cares were provided to all mothers, such as fetal heart monitoring at the time of arrival and controlling fetal heart rate every half hour as well as an obstetrician visit. Intervention performed when there was ≥ 4 cm cervical dilation. The patients were unaware of the type of medication they were receiving.

In the Paracetamol group, 100 mg of Paracetamol was infused in 100 mL of Ringer's lactate serum for 15 minutes. In the Pethidine group, 50 mg of Pethidine was diluted in 5 mL of distilled water and was intravenously and slowly injected over 2 minutes [8]. All used drugs were already available and we did not order them. The drugs administered by an obstetrician in both groups just at a single dose. In both groups, pain intensity in first stage of labor was measured before, 30 minutes, 1, 2, 3 and 4 hours after drug administration based on the Vi-

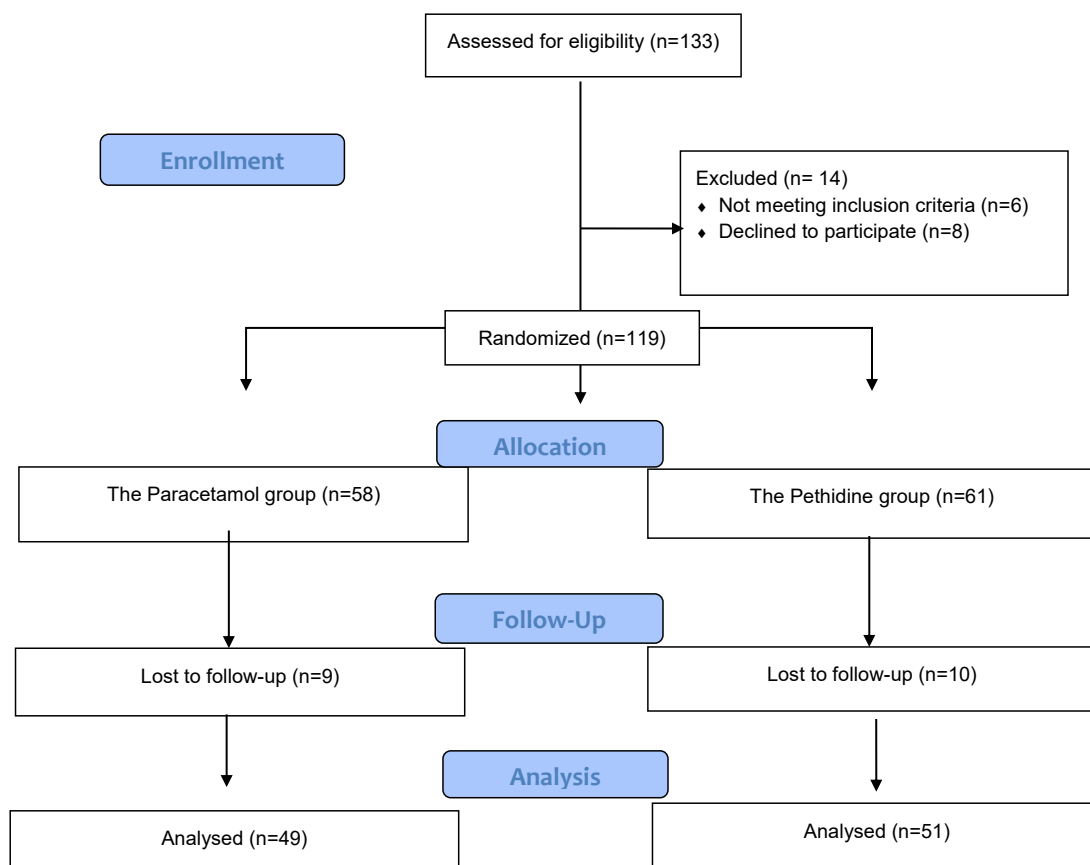


Figure 1. CONSORT diagram

sual Analogue Scale (VAS) using a 10-cm ruler with zero (no pain) and 10 (intolerable pain) marked at each end [10]. In Iran, the validity of this scale has been confirmed which has a correlation coefficient of $r=0.88$ [11]. The duration of first labor stage and the possible side effects of drugs during labor were also recorded in a relevant checklist. Maternal complications included nausea, vomiting, drowsiness, and respiratory depression. These variables were observed 4 hours after administration of drugs. Neonatal complications included Apgar scores of 1 and 5-min and ability to breastfeed. These complications were evaluated 15 minutes after birth.

At the end, all collected data were analyzed in SPSS v. 21 software. Independent T test was used to compare the quantitative variables of age, anthropometric parameters, duration of first labor stage, and VAS score before drug administration between the two groups. Mann-Whitney U test was used to compare the median of gestational age and the 1 and 5-min Apgar scores after birth (considering abnormal distribution of data). Two-way repeated measures ANOVA was used to compare VAS scores at 30 minutes, 1, 2, 3 and 4 hours after drug administration. Fisher's exact test was also used to

compare maternal and neonatal outcomes of the two drugs. Significance level was set at 0.05.

Results

Participants were 100 nulliparous pregnant women (49 in the Paracetamol group and 51 in the Pethidine group) who were in the first phase of labor seeking to use labor pain relief methods. There were no significant differences between the two groups in term of age, BMI and gestational age (Table 1).

The mean and SD of VAS score before drug administration in the Pethidine group was higher than in the Paracetamol group. Independent t-test results (Table 2) showed that this difference was statistically significant ($P=0.02$). Therefore, this variable was included in the data analysis as a confounding variable to minimize its effect on data analysis

The results of independent t-test showed no significant difference in VAS scores in any groups among five time points ($P<0.05$). The results of two-way repeated measures ANOVA (Table 3) showed that the mean VAS

Table 1. Age, Body Mass Index (BMI), and gestational age of women in the two study groups (n=100)

Variables	Mean±SD		P
	Paracetamol (n=49)	Pethidine (n=51)	
Age(y)	23.38±4.88	24.27±4.20	0.33*
BMI (Kg/m ²)	29.15±3.04	29.48±3.36	0.61*
Gestational age (week)	39.00±1.15	38.84±1.07	0.38**

*Independent T test; **Mann-Whitney U

Table 2. Mean pain scores at different times before and after intervention in two study groups

Time	Mean±SD		P
	Paracetamol (n=49)	Pethidine (n=51)	
Before	7.83±1.28	8.45±0.39	0.02
After 30 minutes	6.63±1.34	6.40±1.26	0.16
After 1 hour	6.68±1.20	5.90±0.99	0.71
After 2 hours	6.89±0.87	6.90±0.99	0.45
After 3 hours	7.15±0.83	7.30±0.94	0.76
After 4 hours	7.42±0.60	7.80±0.63	0.12

*Independent T test

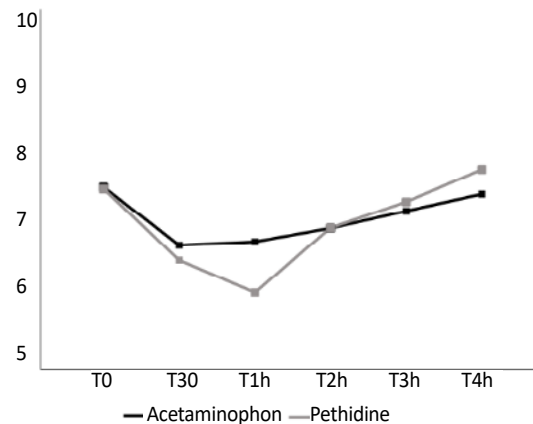


Figure 2. Comparing the change in pain intensity between the two groups at different time points (before and after intervention)

Table 3. Comparison of pain severity changes in different measurement times in the two groups

Pain score	df	Mean Square	F	P*
Pretest score	1	61.23	50.04	0.0001
Time	1	24.89	20.34	0.0001
Group	1	0.227	0.185	0.67
Time×group	-	-	6.14	0.002

*Two-way repeated measures ANOVA

scores between the Paracetamol and Pethidine groups were not significantly different, but there was a significant difference between the two groups in terms of time-group interaction effect (P=0.002). This indicates that the slope of change in pain intensity was different between the Pethidine and Paracetamol groups at different time points (Figure 2).

In comparing the maternal side effects of two drugs, results showed that the frequency of nausea, vomiting, drowsiness, and respiratory depression in the Paracetamol group were lower than in the Pethidine group, but this difference was statistically significant only in nausea (Table 4). There was no statistically significant difference in the 1 and 5-min the Apgar scores of

Table 4. Frequency of maternal complications in two study groups

Maternal Complication		No. (%)		P*
		Paracetamol	Pethidine	
Nausea	Yes	9(18.4)	19(37.3)	0.04
	No	40(81.6)	32(62.7)	
Vomiting	Yes	6(12.2)	11(21.6)	0.28
	No	43(87.8)	40(78.4)	
Drowsiness	Yes	1(2)	7(13.7)	0.06
	No	48(98)	44(86.3)	
Respiratory depression	Yes	0(0)	1(1.96)	0.99
	No	49(100)	50(98.04)	

*Fisher’s exact test

newborns between the two groups, but their ability to breastfeed was significantly better in the Paracetamol group than in the Pethidine group ($P=0.04$).

Discussion

This study compared the Paracetamol and Pethidine effects in the first stage of labor on pain relief, and maternal and neonatal complications in nulliparous women. The results showed that pain score significantly decreased in the both groups 30 minutes, 1, 2, 3 and 4 hours after administration compared to its pretest score. Both Paracetamol and Pethidine were able to relieve labor pain in the first stage of labor. This is consistent with the results of other studies on the analgesic effect of Paracetamol and Pethidine in the first stage of labor [9, 12, 13]. Mean VAS score was not significantly different between the two groups of Paracetamol and Pethidine; however, the slope of pain intensity change was different at different time points. Mothers who received Pethidine experienced more pain relief in the first hour (especially in the first 30 minutes) than those who received Paracetamol. However, in other time points, pain intensity decreased in both groups similarly. There was no significant difference in the mean VAS score in any groups among five time points. The ability of Pethidine for pain reduction in the first hour of administration was higher compared to Paracetamol, but Paracetamol had similar analgesic effects in other time points. These differences were not statistically significant. These finding indicates a relatively similar ability of Paracetamol and Pethidine in controlling labor pain.

The difference between the pain relief effects of Pethidine and Paracetamol has been shown in other studies in favor of Paracetamol [12-14]. In the present study, the pain relief effects of the two drugs at different time points were not significantly different. Some studies have revealed the pain relief ability of Paracetamol similar to Pethidine [15, 16] or less than Pethidine [17]. However, the side effects of Pethidine are well known and more significant in comparison with Paracetamol [18-20]. In this study, nausea, vomiting, and drowsiness of mothers were higher in the Pethidine group. However, the difference was statistically significant only in nausea. In addition, there was a case of respiratory depression in the Pethidine group that was clinically stressful and risky.

Our findings confirm the use of Paracetamol as an appropriate drug to relieve labor pain. However, the sample size was small (100 nulliparous women). Further studies are recommended to use a larger sample size to

compare Pethidine and Paracetamol effects in multiparous women. This study was a single-blind clinical trial and the drug administrator was informed of the type of intervention in each group. Moreover, there was not a control group. We used available drugs for our intervention; we did not prepare them.

Paracetamol can decrease first-stage labor pain similar to Pethidine, with fewer maternal and fetal complications. However, more studies are required to recommend the use of paracetamol in all cases.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the ethics committee of [Rafsanjan University of Medical Sciences](#) (Code: IR.RUMS.REC.1397.168) and registered by Iranian Registry of Clinical Trials (ID: IRCT2019202042595N1). Written informed consent was obtained from all participants.

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Authors' contributions

Methodology and data analysis: Zohreh Ghorashi; data collection: Masoumeh Khammar, Azita Manshoori; Writing original draft: Masoumeh Khammar; Final review: All Authors.

Conflict of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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