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The Efficacy of Intravenous Paracetamol Injection to Reducing Labor Pain: A Randomized Clinical Trial Study

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ABSTRACT

Background & Objective: Labor pain is one of the most severe pains that a woman may experience, so it is important to research the methods to reduce this pain. Paracetamol infusion is an efficient and available remedy to alleviate labor pain in an active phase. This study was conducted to assess the efficacy of intravenous paracetamol injection on reducing labor pain.

Materials & Methods: In this double-blind randomized clinical trial study, the number of 110 nulliparous pregnant women who were candidates for vaginal delivery were included in the study. After the onset of the active phase of labor, the control group received only 300 cc normal saline and the intervention group received 300 cc normal saline plus one gram of paracetamol. The maternal pain score, duration of the first and second stages of labor, delivery type and Apgar score were compared between two groups. Repeated measure ANOVA was used for comparison of means of the VAS score between groups based on repeated observations.

Results: The mean age of the patients was 25.09 ± 4.2 years (18-35 years). The mean length of the first stage (2.85 vs. 3.52 hours, P = 0.001) and second stage (38.77 vs. 43.44 minutes, P = 037) in the intervention group was significantly lower than the control group. Moreover, the mean score of pain was significantly lower in the paracetamol group at all times than the control group (P <0.05).

Conclusion: The prescription of intravenous paracetamol not only reduces pain during labor in women but also reduces the duration of different stages of labor, increases patients' satisfaction with natural childbirth, and reduces the demand for Cesarean.

Keywords: Paracetamol, Active labor, primi gravida Primary Gravid, Reducing pain, Side effect, Newborn' Apgar

Introduction

Pain is an inevitable part of the delivery process. According to the International Association of Pain, pain is unpleasant and the mental-emotional experience is associated with tissue damage **(1)**. Labor pain is known as the most severe pain and it can be a terrible experience during a woman's life. Labor pain is a severe pain that increases rapidly and is affected by physiological, psychological, social, cultural and environmental factors **(2, 3)**.

Pain, anxiety and stress stimulate the sympathetic system; and cause the increase in catecholamines such as epinephrine, norepinephrine and stress hormones such as cortisol and beta-endorphins. At the same time as catecholamines are increased, alpha-stimulated receptors are stimulated and vascular contraction and increased muscle tonicity occur in the uterus. As a result, it reduces blood flow to the uterus and increases the blood pressure in the mother. In addition, increased catecholamines reducethe passage of blood from mother to fetus, limit oxygen supply for fetal consumption, reduce effective contractions of the uterus and slow down the course of delivery, and increase metabolism and oxygen consumption in mother **(4, 5)**.

The pain and prolonged delivery are among the most important factors in encouraging women to have cesarean delivery, which not only require more specialized facilities and higher costs, but also have more compilcations for mothers **(6)**. Various methods are used to reduce labor pain in different parts of the world **(7-10)**. To reduce postpartum pain, drugs such as paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) were added to opioid drugs after delivery **(11-13)**.

Paracetamol is a non-opioid drug that affects the central nervous system (CNS) and essentially acts by inhibiting central cyclooxygenase (COX) and activating serotoninergic pathways in the spinal cord **(14)**. The injectable formulation contains 10 mg of effective ingredient per ml and should be injected intravenously.

Considering the lower side effects of paracetamol in patients and also, the effects of labor pain and the prolonged period of delivery to encourage mothers to have cesarean, this study was conducted to assess the efficacy of intravenous paracetamol injection on reducing labor pain".

Methods

In this double-blind randomized clinical trial study, the number of 110 nulliparous pregnant women who were candidates for vaginal delivery in Ayatollah Mousavi Hospital, Zanjan were included into the study.

Nulliparous pregnant women aged between 18 and 35 years old who were candidates for vaginal delivery, with the absence of congenital uterine and fetal disorders, pregnancy age in the range of 37-42 weeks of gestation, with the embryo cephalic presentation, has the pain score above 4, not received any narcotic drugs or other analgesics methods, and estimated fetal weight less than 4 kg were included to the study. Patients with multiple pregnancy, polyhydramnios, intrauterine growth restriction (IUGR), pre-eclampsia, chronic blood pressure, placenta previa, gestational diabetes, medical or surgery problems during pregnancy, and BMI>35 were considered as exclusion criteria. Moreover, patients with severe hypersensitivity to paracetamol or hypoxia and fetal distress during admission were excluded from the study.

This study was approved by the Ethics Committee of Zanjan University of Medical Sciences. To conduct the study, 110 eligible nulliparous pregnant women, after describing the purpose of the study and getting informed consent, were included in the study. We used convenience sampling method for choosing participant. Included patients were randomly divided into two equal groups (55 patients in each group) through balanced block randomization (block size: 4). After the onset of the active phase of labor (4-4 dilation), the control group received only 300 cc normal saline and the intervention group received 300 cc normal saline plus one gram of paracetamol.

In this study, the researcher was aware of the treatment group allocation of patients, but the patients and the person assessing the patient's pain, were unaware of the patient's allocation. Therefore, the study had a double-blind design.

The maternal pain was evaluated by using VAS score by the trained midwife for all patients, and the mother's pain was recorded every hour. Blood pressure was also measured on a regular basis every hour and documented in the relevant checklist. Moreover, the duration of the first and second stages of labor was recorded. The Apgar score and delivery type were other variables that were recorded by the research team.

For statistical analysis, results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. Continuous variables were compared using the student t-test for comparison between two groups. Repeated measure ANOVA were used for comparison of means of VAS score between groups based on repeated observations. Data were analyzed using SPSS version 23.0 (IBM, Armonk, New York, USA) and P values less than 0.05 were considered statistically significant.

Results

Figure 1 shows the CONSORT flow chart. The number of 137 patients were assessed at the enrollment phase and a total of 110 patients met eligibility criteria and were randomized into intervention (n=55) and control group (n=55), respectively. In continue, two patients were dropped from follow-up in the control group and one patients discontinued the intervention in intervention group, and finally 54 patients in the paracetamol group and 53 patients in the control group were entered to the final analysis.

The mean age of the patients was 25.09±4.2 years (18-35 years), mean age of pregnancy was 39.17±0.88 weeks (37- 41 weeks) and the mean BMI of them were 25.4±3.92 (32.44-18.48). Two groups were homogenous in regard to age, gestational age and BMI (P>0.05). The mean length of the first stage (2.85 vs. 3.52 hours, *P*=0.001) and second stage (38.77 vs. 43.44 minutes, *P*=037) in the paracetamol group was significantly lower than the control group. The mean scores of neonatal Apgar score and newborn weight were not significantly different between the two groups (P>0.05) (Table 1). Frequency of vaginal delivery in the two groups was not statistically significant (94.3% in the intervention group and 87% in the control group, *P*=0.18).

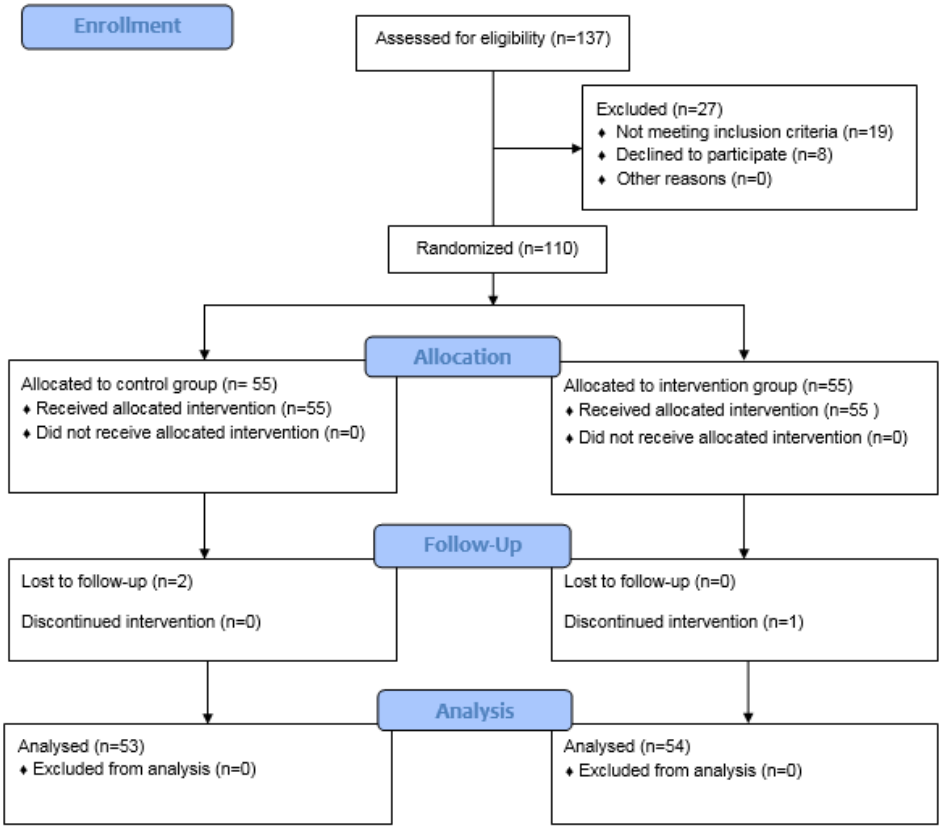

Figure 1. CONSORT flow chart

Table 1. Comparison of baseline characteristics between intervention and control groups

Variable	Intervention group	Control group	P-Value
Age (year)	24.57±4.81	25.62±3.67	0.21
BMI (kg/m^2)	25.62±4.07	25.17±3.78	0.56
Gestational age (week)	39.05±1.01	39.3±0.72	0.15
Apgar minute 1	8.81±0.47	8.88±0.37	0.39
Apgar minute 5	9.77±0.41	9.66±0.47	0.18
Neonate weight (gr)	3128.98±319.56	3070.81±193.28	0.26

The mean score of pain was significantly lower in the paracetamol group at all times than the control group (P <0.05) (Table 2 and Figure 2).

Table 2. Comparison of the mean VAS score in different times between two groups.

Time	Treatment group	Mean	SD	p-value*	F	P-Value**
Before injection	Paracetamol	9.57	0.71	0.55		
	Control	9.64	0.48			
After injection	Paracetamol	4.27	1.35	<0.001	52.96	<0.001
	Control	8.98	0.45			
First hour	Paracetamol	3.59	1.17	<0.001		
	Control	8.54	0.84			

Time	Treatment group	Mean	SD	p-value*	F	P-Value**
Second hour	Paracetamol	3.5	1.41	<0.001		
	Control	7.54	1.04			
Third hour	Paracetamol	3.53	1.33	<0.001		
	Control	7.65	0.9			
Fourth hour	Paracetamol	3.83	1.49	<0.001		
	Control	7.58	1.23			
Dilatation dilation4-6	Paracetamol	3.24	1.7	<0.001		
	Control	8.8	0.52			
Dilatation 6-8	Paracetamol	3.21	1.68	<0.001		
	Control	8.08	1.14			
Dilatation 8-10	Paracetamol	3.21	1.68	<0.001		
	Control	7.2	1.65			
End of delivery	Paracetamol	2.48	1.57	<0.001		
	Control	5.2	1.86			

*t.test, ** Repeated measure ANOVA

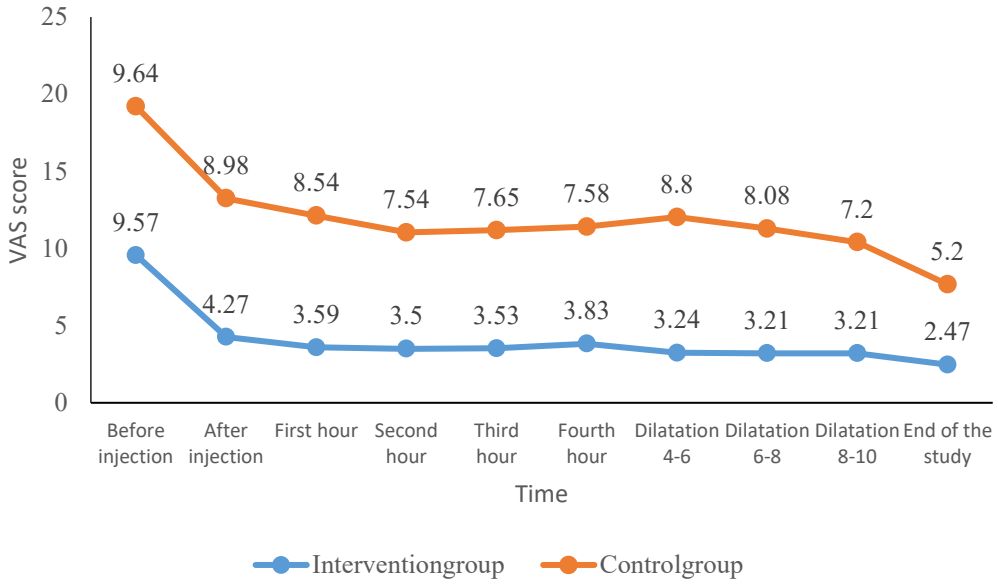

Figure 2. Comparison of the mean VAS score in different times between two groups.

The frequency of changes in blood pressure in the two groups did not show a statistically significant difference (P<0.05). High satisfaction in women receiving paracetamol was significantly more than control group (% 11.3 in 6.55%, P<0.001).

Discussion

The aim of this study was to evaluate the efficacy of intravenous paracetamol injection in relieving pain in an active phase of labor in Ayatollah Mousavi Hospital in Zanjan in 2017. The results of the study showed that the mean length of the first and second stage in the paracetamol group was significantly lower than that of the control group. It was also found that the mean score of pain was significantly lower in the paracetamol group at all times. Moreover, satisfaction in women receiving paracetamol was significantly higher than the control group.

The concomitant administration of opioids with non-opioids is widely used to increase the analgesic effect, and reduce opioid use and drug-related side effects after delivery **(15)**. Non-drug-related s include mainly NSAIDs (paracetamol) that have recently been shown

to reduce cesarean section pain and reduce the need for opioids **(14)**. However, few studies have suggested that paracetamol is used to reduce the pain of vaginal delivery. Our study showed that its use can reduce pain in the delivery. The drug passes through the placenta, but its safety for mother and fetus has been confirmed in various studies **(16)**. The analgesic efficacy and safety in various stages of operation is well illustrated **(17)**. If paracetamol is used, NSAID-related complaints such as bleeding and dyspepsia are not observed. In addition, its availability in form IV is an important feature that facilitates management in general anesthesia.

In studies to evaluate the analgesic effect of paracetamol to measure pain, the VAS score was used, as in our study. But Meenakshi et al. used McGill scale to compare the Methadone or Tramadol and paracetamol's antinociceptive effect. In this their study, there was no difference in the amount of pain before the injection of the drugs in the two groups. But one hour after injection in the paracetamol group, 4% of women had terrible pain and 29% had a painful discomfort, while in the tramadol group after 30 minutes, 30% had a terrible pain and 60% had painful pains. After three hours of injection, 26% of women in the paracetamol group had painful pain, while in the tramadol group, 51% had a terrible pain and 35% had painful pains **(18)**. Although the design of the study is not similar to our study, the results are consistent with our findings. It was found that paracetamol significantly reduces pain in different stages of labor.

A study by Kaur Makkar and colleagues showed that paracetamol, like tramadol, can be an effective analgesic in the active phase of labor, and there is less sedation and nausea and vomiting compared to tramadol **(19)**. The results of this study are in line with the findings of our study. Elbohoty et al. showed that paracetamol, in addition to reducing pain, had no side effects, which our study also showed no complications regarding paracetamol use **(20)**.

Many studies have been conducted to investigate the effect of paracetamol pain in various surgeries, all of which indicate a reduction **(21)** in postoperative pain **(22-25)**.

According to the studies, considering the usefulness and availability and low complications of paracetamol in reducing labor pain, it can be promoted in most countries to increase the desire for Vaginal delivery birth.

The present study had some limitations. The main limitation of this study was the lack of cooperation of patients due to the concern about the adverse effects of the drug on the mother and especially the fetus. However, this concern was reduced by explaining the safety of the drug and the importance of the subject in helping to provide effective strategies for controlling labor pain. Another limitation was another limitation was the non-cooperation of the mothers because the VAS scalehad to be measured at different times.

Conclusion

Regarding the results of this study, it can be concluded that intravenous paracetamol administration significantly reduced pain in women during the time of delivery. However, hemodynamic changes were not observed in these patients and there were no complications such as nausea, vomiting and instability of vital signs. Also, it was found that with the injection of paracetamol and reduction of pain in the course of labor, the duration of different stages of labor was significantly decreased. On the other hand, administration of paracetamol increased the satisfaction of patients from vaginal delivery and reduced the demand for cesarean section. Therefore, it can be concluded that paracetamol can be used as a simple, low-cost, and safe method as a supplement to control pain during and after vaginal delivery.

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Statement on informed Declarations

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Conflict of interest

The author claimed no conflict of interest.

Ethics approval and consent to participate

The ethics committees of Zanjan University of Medical Sciences approved this study with the ethical code.

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of the study are available from the corresponding author in SPSS form upon reasonable request.

Code availability

Not applicable

Authors' contributions

HG, FM and SF developed the research idea and proposal of the study, as well as writing the manuscript, data collection and analyzingthe data. All authors approved the final version of the manuscript.

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