

# Determination and Comparison of the Effect of Ibuprofen and Acetaminophen on Postpartum Hypertension in Pregnant Women with a History of Preeclampsia

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## ABSTRACT

**Background & Objective:** The aim of this study was to determine which of the two drugs of ibuprofen, as a common non-steroidal anti-inflammatory drugs (NSAID), and acetaminophen would have the least effect on postpartum hypertension in patients with preeclampsia.

**Materials & Methods:** Clinicodemographic data including age, gestational age at delivery, body mass index, parity, and route of delivery, were collected through interviews with patients and reviewing patient records. In this double-blind clinical trial, among 84 patients included in the study, 42 patients were randomly assigned to the acetaminophen (650 mg every 6 to 24 hours) and 42 patients into the ibuprofen (600 mg every 6 to 24 hours) group.

**Results:** The two groups were not significantly different in terms of mean age ( $P = 0.322$ ), body mass index ( $P = 0.950$ ), route of delivery ( $P = 0.657$ ), parity ( $P = 0.818$ ), and mean systolic ( $p = 0.530$ ) and diastolic blood pressure ( $P = 0.691$ ). Following the intervention, the duration of blood pressure control ( $P = 0.182$ ), mean systolic blood pressure ( $P = 0.371$ ), and mean diastolic blood pressure ( $P = 0.13$ ) were not significantly different in the acetaminophen and ibuprofen groups. There was no significant difference between the two groups in terms of the number of patients and the dosage of opioids used.

**Conclusion:** The results revealed that in patients with preeclampsia, acetaminophen and ibuprofen to control postpartum pain have a similar impact on blood pressure.

**Keywords:** Ibuprofen, Acetaminophen, Hypertension, Pregnant Women, Preeclampsia



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## Introduction

Blood pressure disorders are the most common pregnancy complications (5-10%), which are responsible for 15% of maternal mortalities. The diagnosis of gestational hypertension is made in women whose blood pressure reaches 140/90 mmHg or higher for the first-time during pregnancy with no proteinuria. Preeclampsia is a pregnancy-specific syndrome that can affect almost any part of the body. Hypertension typically occurs after the 20<sup>th</sup> week of pregnancy and is associated with proteinuria (1). The symptoms of severe preeclampsia include headache, visual disturbances, epigastric pain, and nausea and vomiting (2).

Eclampsia refers to the onset of seizures in women with preeclampsia in whom seizures cannot be attributed to other causes. A very severe and specific form of preeclampsia is HELLP syndrome, which includes hemolysis, elevated liver enzymes, and decreased platelet counts (2). The risk factors for preeclampsia include nulliparity, obesity, multiple gestation, maternal age over 35, and African-American ethnicity (3, 4). Preeclampsia often affects young and nulliparous women, while older women are more at risk for chronic hypertension with the increased risk of preeclampsia. The incidence of preeclampsia is strongly influenced by race and ethnicity, and as a result, the genetic background plays a role in it (5).

Chronic and continuous uses of nonsteroidal inflammatory drugs (NSAIDs), especially cyclooxygenase inhibitors, increase the risk of hypertension in healthy and non-pregnant individuals and sometimes even have neutralizing effects on hypertensive drugs in patients with hypertension (6, 7). The possible mechanisms for such effects include NSAIDs-mediated disruption of aldosterone metabolism (8), sodium retention, inhibition of vasodilation by prostaglandins (9, 10), and production of vasoactive arachidonic acid metabolites through the production and induction of cytochrome p-450 (11).

In this regard, various types of NSAIDs are widely used to control postpartum pain in normotensive women because they are associated with high efficacy (12, 13). These drugs are even stronger than acetaminophen and greatly reduce the need for opioids after cesarean delivery (14-16). In addition, analgesic alternatives to cyclooxygenase inhibitors are associated with potential risks. Postpartum use of opioids may increase the susceptibility to dependence on these drugs, which is associated with depression and suppression of the infant's central nervous system during lactation.

Although acetaminophen is a non-opioid alternative that reduces the use of opioids after cesarean section, its use is contraindicated in cases of severe elevations in liver enzymes common in preeclampsia (17, 18). The aim of this study was to compare ibuprofen, as a common NSAID, and acetaminophen to determine which has the least effect on postpartum hypertension in patients with preeclampsia.

## Methods

This was a double-blind interventional study that included 84 (two groups of 42) pregnant women aged over 18 years with a history of preeclampsia during pregnancy at the time of cesarean section. The Clinicodemographic information of the patients, including age, gestational age at delivery, body mass index (BMI), parity, and route of delivery, were extracted through interviews with the patients and review of patient records.

The first group was treated with ibuprofen (IBU) at a dose of 600 mg every six to 24 hours, and the second group was treated with acetaminophen (ACE) at a dose of 650 mg every six to 24 hours. The patients' blood pressure was evaluated hourly for 24 hours after delivery. Labetalol or nifedipine were administered in cases with blood pressure greater than 150/110 mmHg, and the time of normalization of blood pressure following treatment with antihypertensive drugs was recorded in the two groups.

Intravenous blood samples were extracted daily and the status of creatinine, alanine transaminase (ALT), aspartate transaminase (AST), and other serum biomarkers was assessed. Also, if necessary, opioids were prescribed to control postpartum pain, and the

prescribed dose was recorded in the two groups. The results were expressed as mean and standard deviation (mean  $\pm$  SD) for quantitative variables and as a percentage for stratified qualitative variables. *T*-test or analysis of variance (ANOVA) was run to compare quantitative variables, and Chi-square test was used to compare qualitative variables. The analyses were performed in SPSS version 23, and a *P*-value of less than 0.05 was considered significant.

The study protocol was verified by the ethical committee of Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1399.1244).

## Results

The mean age of mothers in the ACE and IBU groups was  $30.42 \pm 6.40$  and  $31.76 \pm 5.84$  years, respectively. There was no significant difference between the two groups in terms of mean maternal age ( $P = 0.322$ ). The mean BMI in the ACE and IBU groups was  $36.30 \pm 7.48$  and  $36.40 \pm 7.99$  kg/m<sup>2</sup>, respectively. There was no significant difference between the two groups in terms of mean BMI ( $P = 0.950$ ; [Table 1](#)).

In the ACE and IBU groups, 15 (51.7%) and 14 (48.3%) mothers were nulliparous, and 27 (49.1%) and 28 (50.9%) mothers were multiparous, respectively. There was no significant difference between the two groups in terms of parity ( $P = 0.818$ ). In the ACE and IBU groups, 24 (48%) and 26 (52%) mothers had vaginal delivery, respectively, while 18 (52.9%) and 16 (47.1%) mothers had cesarean section, respectively. There was no significant difference between the two groups in terms of the route of delivery ( $P = 0.657$ ).

The mean systolic blood pressure of the patients before the intervention in the ACE and IBU groups was  $181.95 \pm 14.17$  and  $179.92 \pm 15.24$  mmHg, respectively. There was no significant difference between the two groups in terms of mean systolic blood pressure ( $P = 0.530$ ). The mean diastolic blood pressure of the patients before the intervention in the ACE and IBU groups was  $150 \pm 11.10$  and  $105.92 \pm 10.18$  mmHg, respectively. There was no significant difference between the two groups in terms of mean diastolic blood pressure ( $P = 0.691$ ).

Post-intervention, the mean systolic blood pressure in the ACE and IBU groups was  $164.04 \pm 14.15$  and  $166.92 \pm 15.18$  mmHg, respectively. The two groups did not differ significantly with respect to mean blood pressure ( $P = 0.371$ ). Mean diastolic blood pressure in the ACE and IBU groups was  $95.02 \pm 9.12$  and  $98.07 \pm 9.13$  mmHg, respectively. The two groups were not significantly different in terms of mean blood pressure ( $P = 0.13$ ). The duration of blood pressure control in the ACE and IBU groups was  $60.09 \pm 10.29$  and  $56.73 \pm 12.48$  hours, respectively. There was no significant difference between the two groups in terms of the duration for blood pressure control ( $P = 0.182$ ; [Table 2](#)). ([Table 3](#)) indicates the number of patients

who needed pain control and opioid use, and (Table 4) displays the amount of opioid used. As can be noted, there was no significant difference between the two groups in terms of the number of patients and the amount of opioid used.

Finally, three patients from the IBU group were readmitted to control blood pressure, while in the ACE group one patient was readmitted to control blood pressure. There was no significant difference between the two groups in terms of readmission ( $P = 0.21$ ).

**Table 1.** Demographic data of the studied population in two groups of intervention

Variables (Mean $\pm$ SD)	Intervention		P-value
	Ibuprofen	Acetaminophen	
Maternal age	5.84 $\pm$ 31.76	6.40 $\pm$ 30.42	0.322
BMI*	7.99 $\pm$ 36.40	7.48 $\pm$ 36.30	0.950
SBP*	15.24 $\pm$ 179.92	14.17 $\pm$ 181.95	0.530
DBP*	10.18 $\pm$ 105.92	11.10 $\pm$ 150	0.691

\*BMI: Body Mass Index, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure

**Table 2.** Comparison of post-intervention mean systolic and diastolic blood pressure between the two groups

Variables (Mean $\pm$ SD)	Intervention		P-value
	Ibuprofen	Acetaminophen	
SBP	15.18 $\pm$ 166.92	14.15 $\pm$ 164.04	0.371
DBP	9.13 $\pm$ 98.07	9.12 $\pm$ 95.02	0.13

\* SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure

**Table 3.** Comparison of the number of patients between the two groups who used opiates to control pain

Postpartum days	Intervention		p-value
	Ibuprofen N (%)	Acetaminophen N (%)	
First day	13 (54.2 %)	11 (45.8 %)	0.629
Second day	19 (52.8 %)	17 (47.2 %)	0.659
Third day	17 (65.4 %)	9 (34.6 %)	0.059

**Table 4.** Comparison of the dosage of opioids used between the two groups

Postpartum days	Intervention		p-value
	Ibuprofen (mg $\pm$ SD)	Acetaminophen (mg $\pm$ SD)	
First day	8.17 $\pm$ 22.04	8.42 $\pm$ 18.76	0.073
Second day	8.88 $\pm$ 29.47	10.61 $\pm$ 28.30	0.586
Third day	10.04 $\pm$ 37.73	15.38 $\pm$ 40.45	0.081

## Discussion

In this study, we investigated the effect of ibuprofen, as a common NSAID, and acetaminophen on postpartum hypertension in patients with preeclampsia. In this study, which was performed as a double-blind intervention among 84 patients, 42 patients were treated with ibuprofen at a dose of 600 mg every six to 24 hours and 42 patients were treated with

acetaminophen at a dose of 650 mg every six to 24 hours. We found no significant difference between the two groups in terms of mean maternal age, BMI, parity, route of delivery, and systolic and diastolic blood pressure.

Following the intervention, the duration of blood pressure control and the mean systolic and diastolic blood pressure after the intervention were not significantly different between the two groups. There was no significant difference between the two groups in terms of the number of patients and the amount of opioid used. Among the patients, three and one patients from the IBU and ACE groups were readmitted to control blood pressure, respectively. There was no significant difference between the two groups in terms of readmission.

Nonsteroidal anti-inflammatory drugs are widely used to control postpartum pain in normotensive women because they are associated with high efficacy, but chronic and continuous use of NSAIDs, especially cyclooxygenase inhibitors, elevates the risk of hypertension in healthy non-pregnant individuals, and sometimes it may even have neutralizing effects on hypertensive drugs in patients with hypertension.

In human samples, the results related to the effect of NSAIDs on postpartum blood pressure have been associated with conflicting results. Prescribing higher doses of NSAIDs will also reduce the rate of postpartum breastfeeding. In a study by Anastasio, Campbell (19), it was reported that NSAIDs administration did not affect the mean blood pressure compared to those without NSAIDs. On the other hand, acetaminophen is a non-opioid alternative that reduces the use of opioids after cesarean section, but its use is contraindicated in cases of severe elevations in liver enzymes common in preeclampsia.

Our findings were in line with those of a number of previous studies. The studies by Vetri (20) and Wasden, Ragsdale (21), which were consistent with our study in terms of retrospective design, showed no association between postpartum NSAIDs use and persistent BP greater than 150/100 mmHg, mean arterial pressure, diagnosis of high blood pressure, or length of hospital stay. Our findings were inconsistent with the results of Vigil-De Gracia, Solis and Ortega (22), who conducted an open-label, randomized controlled trial. In that study, it was reported that women with severe preeclampsia who were given ibuprofen after vaginal delivery had a much higher

incidence of hypertensive episodes than in the acetaminophen-treated group (63.1% vs. 28.6%), but severe hypertension did not differ between the two groups (24.5% and 14.5%, respectively). In Vigil et al.'s study, the researchers did not report whether hypertension was stable and whether it led to the use of drugs to control blood pressure or prolonged hospital stay.

Furthermore, in the study of Blue, Murray-Kreza (23) where, like our study, patients were treated with ibuprofen 600 mg or acetaminophen 650 mg every six hours, no difference was noted between the two groups in terms of duration of severe postpartum hypertension. There was also no difference between the two groups in terms of time of resolution of blood pressure above 150/100, mean postpartum blood pressure, maximum systolic and diastolic blood pressure after childbirth, frequency of use of antihypertensives to control blood pressure, duration of postpartum hospital stays, intrapartum antihypertensive drugs use, or postpartum opioid dose. Their results were consistent with our findings.

## Conclusion

The results of this study revealed that acetaminophen and ibuprofen were not superior to each other in controlling postpartum hypertension in patients with preeclampsia, and the time required to control blood pressure in both medications was similar.

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## Conflict of Interest

There are no conflicts of interests.

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