Original article

Efficacy of Postpartum Furosemide Therapy on Blood Pressure Recovery in Patients with Severe Preeclampsia: A Randomized Clinical Trial

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Abstract

Background: Hypertensive disorders are an important cause of maternal mortality and morbidity, and severe preeclampsia is the most common cause [Baha M. Sibia, AJOG (2012)]. The blood pressure rises progressively during the first 5 days after delivery, and it is due to mobilization of 6-8 liters of liquid, and 950 meq of accumulated sodium,from interstitial and extravascular space to intravascular space[Davison JM and Dunlop W, Seminars in Nephrology,4:198–207 (1984)].Severe rising of blood pressure may lead to complications, such as renal failure, pulmonary edema, eclampsia, intracranial hemorrhage, stroke, coma and death [Baha M. Sibia, AJOG (2012)].Therefore, postpartum anti-hypertensive therapy can prevent these complications and diminishes maternal mortality and morbidity rate. ***Objective***: This investigation was done to evaluate whether a short course of postpartum furosemide therapy in patients with severe preeclampsia accelerates blood pressure recovery, reduces antihypertensive drugs usage, prevents complications such as eclampsia and finally diminishes hospitalization. ***Study design***: In a randomized clinical trial, 90 patients with severe preeclampsia participated. After spontaneous onset of diuresis and discontinuation of sulfate magnesium, patients were randomly allocated to receive either no therapy or 20 mg oral furosemide daily for five days with oral potassium supplementation. Postpartum blood pressure, the need for antihypertensive therapy, rate of complications and duration of hospitalization between treatment and control groups were compared. ***Results***: Mean systolic blood pressure on the third day after delivery was not different significantly between treatment and control groups(127.9±10.2 compared with 130 ± 11.5 mm-Hg, P=0.36). Mean diastolic blood pressure on the third day after delivery was not different between two groups. Patients in treatment group required less antihypertensive therapy during hospitalization (26.7% compared with 33.3%, P=0.64) but the difference was not significant. Eclampsia occurred in two patients in control group and not occurred in treatment group. Duration of hospitalization was not affected by the intervention. ***Conclusion:*** Brief postpartum furosemide therapy in patients with severe preeclampsia may not be effective in postpartum blood pressure recovery and reducing the need for antihypertensive therapy. It may be useful to prevent complications such as eclampsia. Duration of hospitalization was not affected by the intervention.

Keywords: Severe preeclampsia; Furosemide; Postpartum hypertension.

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Introduction

Hypertensive disorders appear in 10% of all pregnancies[1]. Hypertension is a member of lethal triad in pregnancy along with bleeding and infection that has a significant role in maternal morbidity and mortality. 50% of maternal mortality due to hypertension is preventable[2] and 10% of it occurred after delivery[3]. Among hypertensive disorders in pregnancy, preeclampsia is the most life-threatening condition[4,5] that can lead to placentae abruption, convulsion, acute pulmonary edema, acute renal injury and death[6]. It may be followed by increased risk of cardiovascular complications in next years after delivery[7,8].

During pregnancy, 6 to 8 liters of water retained in extravascular space, and 950 mEq sodium

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accumulated too. After delivery this large amount of water and sodium, transfers from extravascular space to intravascular space[9], therefore blood pressure rises during the first five days, reaching maximum between three to six days after birth[10]. So, monitoring of postpartum blood pressure is emphasized[3].

Postpartum hypertension is due to iatrogenic causes too. Some drugs such as NSAIDS can lead to severe hypertension by retention of water and sodium and vasoconstriction[11]. Some women require different injections of ergot alkaloids for treatment of uterine atony. These drugs act on α receptors and can lead to hypertension, cerebral vasoconstriction and stroke. So, in patients with postpartum hypertension who receive these medications, we should discontinue them first[12].

Different antihypertensive drugs are used in pregnancy in hypertensive patients. Some of commonly used drugs in moderate to severe hypertension in pregnancy are methyldopa, clonidine, prazosin, propranolol, labetalol, nifedipine and hydralazine[13]. Diuretics such as furosemide are not used during pregnancy except in cases with pulmonary edema, because these medications reduce blood volume and blood pressure, result in uteroplacental insufficiency and fetal growth restriction[14].

It seemed diuretics are appropriate drugs in patients with fluid overload after delivery. They reduce blood volume and blood pressure by diuresis, so hypertensive crisis, complications and the need for antihypertensive therapy is decreased[15]. In recent years, many investigations were undertaken about gestational hypertension-preeclampsia, but the data about evaluation, management and complications of postpartum hypertension is limited[16].

Our goal in this study is to evaluate effectiveness of a brief course of postpartum furosemide therapy in lowering blood pressure, reducing the need for antihypertensive therapy, preventing complications such as eclampsia and diminishing hospitalization.

Materials and methods

The study was approved by the Department of Gynecology and Obstetrics of Qazvin University of Medical Sciences. The present study is a randomized controlled trial.All patients delivered of a pregnancy at or greater than 20 weeks of gestation and diagnosed with severe preeclampsia or hemolysis, elevated liver enzymes, low platelets syndrome(HELLP). The patients were admitted in Kosar hospital between March 21,2013 and March 20,2014. Exclusion criteria were gestational age less than 20 weeks, hypokalemia(K<3 mEq/L) on admission, taking diuretics or potassium supplements recently, any hemodynamic instability before or after delivery.

First of all,suitable patients in labor were chosen, and then we explained about the study to them and who agreed and signed the informed agreement, participated in the study. Information about patients such as age, gestational age, parity, weight, systolic and diastolic blood pressure on admission was written on a questionnaire form.

After delivery and discontinuation of intravenous magnesium sulfate and spontaneous diuresis, patients were randomly allocated to two groups by opening the next previously prepared sequential and numbered opaque study envelope. In the treatment group, patients were assigned to receive furosemide 20 mg/d for a total of 5 days during hospitalization and after hospital discharge. In the control group, patients received neither medication. Patients in both groups received similar postpartum nursing, including blood pressure assessment every 4 hours, daily weight measurement during hospitalization.

Anti-hypertensive drugs were begun for patients in two groups if systolic blood pressure was equal or greater than 160 mm-Hg and if diastolic blood pressure was equal or greater than 110 mm-Hg. Statistical analysis was performed using K2 Test, Student t Test, T paired Test and Anova. A p value of less than 0/05 was considered significant.

Data collection procedures

For data collection, a questionnaire form was prepared. After determining the patients according to the exclusion criteria, and who agreed to take part in the study and signed the informed agreement form, information was collected and filled in the form. The data was entered in a specific database, using the SPSS 16 statistical program. The data analysis was performed using K2 Test, T paired Test, Student t Test and Anova. P values for all tests were two tailed at a 5% level of significance. Study population were patients who were admitted in Kosar hospital in the year 2013. 90 patients(45 patients in each group) upon on sampling formula and 20% rate of failure to follow during hospitalization were selected.

Ethical issues

The original protocol of this study proposal has already obtained approval of the Committee for

Ethics in Research of the Qazvin University of Medical Sciences, under the number 8281. The protocol also was published in the Iranian Register Clinical Trials under the number 2014031717041N1.

Results

A total of 90 patients were eligible for the study and signed the informed agreement form to participate. Patients were randomly allocated to treatment and control group.The demographic characteristics of each group are shown in Table1.

Table 1. Demographics of teatment and control patient groups

Demographic	Treatment	Control	P
Maternal age (year)	30±6	28.6±6.9	0.32
Maternal weight (Kg)	78±12.7	81±14.6	0.38
Gestational age (week)	36±3.2	34.6±4.5	0.11
Parous (%)	53.3	55.6	1
Cesarean delivery (%)	69	80	0.33

Systolic and diastolic blood pressures on admission of patients and on the third day after delivery are depicted in Table 2 for groups of patients.

Table 2. Systolic and diastolic blood pressures on admission and third day after delivery in treatment and control patient groups (SBP, systolic blood pressure; DBP, diastolic blood pressure)

Blood pressure (mmHg)	Treatment	Control	P
SBP on admission	151.4±15.28	151.7±16.10	0.92
DBP on admission	97.5±10.31	95.1±10.79	0.27
SBP on the third day	127.9±10.27	130±11.53	0.36
DBP on the third day	82.84±7.66	82.57±7.22	0.86

Mean systolic blood pressure on the third day after delivery in treatment group was lower, compared with control group(127.97± 10.27 mm-Hg compared with 130.06± 11.53 mm-Hg, p=0.367) but the difference was not significant. Meandiastolic blood pressure on the third day after delivery between treatment and control group was not different(82.84± 7.66 compared with 82.57±7.22 mm-Hg, p=0.86).

Patients in treatment group required less antihypertensive therapy during hospitalization and at discharge(26.7% compared with 33.3%, p=0.64) but it was not significant. Length of hospitalization was not different between treatment and control group(5/04±1.16 compared with 5.07±1.14 days, p=0.93). There was no significant differences in weight lossbetween two groups(1.73±2.28 Kg in treatment versus 1.67±3.02 Kg in control group, p=0.94).

Eclampsia was occurred in two patients in control group and not occurred in treatment group. In two patients with eclampsia, developed severe systolic blood pressure(≥160 mm-Hg) and required additional antihypertensive therapy.

Discussion

Mean Systolic and diastolic blood pressure on the third day after delivery in patients with severe preeclampsia, was not different significantly between treatment and control groups. The rate of antihypertensive therapy was not different significantly between two groups. So, we concluded that brief furosemide therapy after delivery in patients with severe preeclampsia may not be useful in lowering blood pressure.As the differences between two groups were not statistically significant, more studies are needed.

Length of hospitalization seemed not to be shortened by this intervention. Weight loss on the third day after delivery was not different significantly between two groups. The course of postpartum furosemide therapy was only five days and the dosage of furosemide was low too, so if the duration and dosage of diuretic is higher, may weight loss and duration of hospitalization is influenced by this intervention.

Eclampsia had occurred in two patients in control group and not occurred in treatment group. Patients with eclampsia had severe systolic blood pressure after delivery and did required additional antihypertensive therapy for controlling blood pressure. So, postpartum furosemide therapy may be useful in preventing eclampsia in patients with severe preeclampsia.

In randomized clinical trial of postpartum preeclampsia management with furosemide by Ascarelli *et al.* in 2005[15], only patients with severe preeclampsia(n=70) who received furosemide, compared with controls, had significantly lower systolic blood pressure on postpartum day 2 and

required less antihypertensive therapy during hospitalization and at discharge. Neither length of hospitalization nor frequency of delayed postpartum complications was positively affected by the intervention. So results of our study were somehow in agreement with this study, but the number of patients with severe preeclampsia(n=90) in our study was greater, therefore our results are significant.

In comparative study of furosemide versus hydralazine for managing postpartum hypertension in severe preeclampsia by Zabihi Mahmoodabadi *et al.* in 2012[14], patients with severe preeclampsia who received furosemide, had significantly lower systolic blood pressure on postpartum fifth day, compared to those who received hydralazine and the author concluded furosemide is more effective on blood pressure mean reduction compared with hydralazine in patients with severe preeclampsia.

Treatment of patients with preeclampsia and eclampsia after delivery is still a questioning topic, because the blood pressure may rise and mortality such as stroke, pulmonary edema, intracranial hemorrhage, renal insufficiency may occur. So, it seems logical to use some drugs after delivery and reduce these complications. We think loop diuretics such as furosemide are appropriate drugs to reach this goal. Diuretics reduce blood volume and blood pressure by eliminating large volume of water that transfer from extravascular space to intravascular space after delivery. These drugs increase urinary sodium excretion too. Therefore, diuretics accelerate blood pressure recovery after delivery and may prevent eclampsia attacks and other complications such as intracranial hemorrhage, stroke, renal failure, and pulmonary edema.

Conflict of interest: The authors report no conflict of interest.

Author's contribution:

Data gathering and idea owner of this study: Dabaghi T, Shariati M, Laluha F, Barikani A

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Editing and approval of final draft Dabaghi T, Shariati M, Laluha F, Movahhed F, Barikani A

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