CLINICAL STUDY

The Effects of Plasma Volume Expanders to Renal Function and Urine Output in Severe Preeclampsia

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Abstract

Objective: To investigate the effect of fresh frozen plasma (FFP) infusion in the postpartum period on urine output, serum blood urine nitrogen (BUN) and creatinine levels in women with severe preeclampsia.

Materials and Methods: Clinical records of patients who were diagnosed with severe preeclampsia were reviewed between the 2001-2004. From a total of 134 cases, records of 52 patients with oliguria were evaluated. Following delivery, patients whose urine output was less than 0.5 ml/kg per hour following the 3 consecutive hours were accepted as oliguric. Subjects received FFP were classified as FFP group (n=29). The control group (n=23) consisted of subjects who were infused with crystalloid solution only. Serum BUN, creatinine levels and urine output in a 24 hour period were recorded in the two groups. Changes in blood levels of BUN and creatinine and urine output were compared between the two groups after the 24th hour.

Results: In the FFP group, there was no difference in BUN levels between basal and that after FFP infusion (p=0.305). However, serum creatinine levels decreased following FFP infusion (p=0.017). In the crystalloid group, there was no statistically significant change for BUN and creatinine levels after the 24 hour period of crystalloid infusion (p=0.09 and p=0.46 respectively). Also at the end of the 24 hour period, BUN and creatinine levels were not significantly different between the two groups (p=0.24 and p=0.29 respectively). Mean urine output was 1498±568 ml/24 h in FFP group and 1368±447 ml/24 h crystalloid group (p=0.67).

Discussion: Fresh frozen plasma, as a plasma volume expander to enhance intravascular volume and urine output in the postpartum period, does not provide additional benefit for improvement of oliguria in women with severe preeclampsia.

Keywords: fresh frozen plasma, severe preeclampsia, oliguria, creatinine

Özet

Şiddetli Preeklamptik Hastalarda Plazma Volüm Genişleticilerin Böbrek Fonksiyonu ve Atılan İdrara Etkileri

Amaç: Bu çalışmada, şiddetli preeklamptik olgularda postpartum dönemde ortaya çıkan oligüri varlığında, taze donmuş plazma (TDP) infüzyonunun idrar çıkışı ve böbrek fonksiyonları üzerindeki etkilerinin değerlendirilmesi amaçlanmıştır.

Materyal ve Metot: 2001-2004 yılları arasında kliniğimize başvuran ve şiddetli preeklampsi tanısı alan toplam 134 hastanın kayıtları retrospektif olarak incelendi. Bu hastalarda postpartum birbirini takip eden 3 saat boyunca saatlik idrar çıkışı 0.5 ml/kg/saat'in altında olması oligüri olarak kabul edildi. Postpartum dönemde oligüri gelişen ve bu nedenle kristaloid ve TDP infüzyonu yapılan 29 hasta, Grup I ve sadece kristaloid infüzyonu yapılan 23 hasta, kontrol grubu olarak (Grup II) belirlendi. Hastaların oligüri tanısı aldıkları anda ve postpartum 24. saatteki kan üre azotu (BUN), kreatinin değerleri ve 24 saatlik idrar çıkışları kaydedildi.

Sonuçlar: İlk grupta, plazma volüm genişletici uygulamadan önce ve sonraki BUN değerleri arasında anlamlı fark saptanmadı (p=0.305). Serum kreatinin değerlerinde ise TDP infüzyonu sonrasında azalma olduğu görüldü (p=0.017). TDP infüzyonu yapılmayan ikinci grupta ise kristaloid infüzyonu sonrasında BUN ve kreatinin değerleri arasında anlamlı bir azalma izlenmedi (sırasıyla p=0.09 ve p=0.46). Yirmi dördüncü saat sonunda gruplar arasında serum BUN ve kreatinin değerleri arasında anlamlı bir fark görülmedi (p=0.24 ve p=0.29). Ortalama 24 saatlik idrar çıkışı; TDP infüzyonu yapılan grupta 1408±368 ml, kristaloid infüzyonu yapılan grupta ise 1368±447 ml idi (p=0.67).

Tartışma: Postpartum dönemde; oligüri gelişen şiddetli preeklamptik olgularda, intravasküler volümü artırmak ve idrar atımını düzeltmek için plazma volüm genişletici olarak taze donmuş plazma kullanımının etkisiz olduğu bulunmuştur.

Anahtar sözcükler: taze donmuş plazma, oligüri, şiddetli preeklampsi, kreatinin

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Introduction

Preeclampsia is a multisystem disorder unique to pregnancy. Hypertensive disorders are seen in about 7-10% of human pregnancies. Despite advances in medical practice, preeclampsia and eclampsia remained as a leading cause of maternal mortality throughout the world. Exact physiopathological mechanisms underlying preeclampsia have not been understood. However, insufficient trophoblastic invasion of maternal vessels and endothelial dysfunction secondary to endothelial injury are the well known hypothesis to explain the mechanism of this disease (1). Glomerular filtration rate increases by 40-60%, resulting in fall of serum levels of creatinine, blood urine nitrogen (BUN) and uric acid in normal pregnancy (2,3). However, in the case of preeclampsia, renal blood flow decreases secondary to vasoconstriction and impaired glomerular filtration causes oliguria. Increased capillary permeability, secondary to endothelial injury contributes to relative volume deficit in the preeclamptic patients (4,5).

Following delivery, the effect of plasma volume expanders for the correction of oliguria is not clear. The purpose of this study was to investigate the effect of fresh frozen plasma (FFP) as plasma volume expander on urine output, serum BUN and, creatinine levels as basic markers of kidney functions in women who had severe preeclampsia with oliguria.

Materials and Methods

Clinical records of patients who were referred to Department of Obstetrics and Gynecology between the years 2001 and 2004 with the diagnosis of severe preeclampsia were reviewed. Patients who had a history of antihypertensive drug use for chronic hypertension, diabetes mellitus, and cardiac or renal disease were excluded from the study. Also patients who had chronic hypertension with superimposed preeclampsia were excluded. All subjects were between the 24 and 40 weeks of gestation.

We administered corticosteroids to enhance lung maturation between the 24 and 34 weeks of gestation by intramuscular Betamethasone (Celestone, Schering-Plough, Germany) two doses of 12 mg with twenty-four hours interval. Intravenous magnesium sulphate ($MgSO_4$) infusion (4-6 g slow intravenous (i.v.) infusion in 20 minutes as loading dose and followed with 1 g per hour i.v. infusion) was initiated following the decision of delivery to prevent or treat of eclampsia. $MgSO_4$ infusion was stopped at the end of the 24 hours following the delivery. During the oliguric periods, serum $MgSO_4$ levels were assessed and infusion stopped until the improvement of urine output. In the postpartum period, blood pressure, pulse and urine output were monitored intensely. Patients whose urine output was less than 0,5 ml/kg per hour following the 3 consecutive hours after infusion were accepted as of oliguric. Group I (FFP group) consisted with subjects who received FFP as a volume expander. Subjects who were infused only crystalloid solutions (Lactated Ringer Solution, 125 ml per hour) were accepted as Group II (Crystalloid group). In the FFP group, to preserve renal blood flow and to decrease the fluid loss to third space, we utilized 4 units of FFP as plasma volume expander. Volume expansion was the only indication for plasma infusion, not postpartum bleeding or consumption coagulopathy. Also constant crystalloids (Lactated Ringer Solution, 100 ml per hour) were infused synchronously. In the FFP group, the crystalloid infusion amount was less than crystalloid group due to co-incidental FFP infusion. Diuretics were not used to increase the urine output. Crystalloid infusion was stopped following the 24 hours of infusion in both groups.

Antihypertensive drugs were initiated when systolic and diastolic blood pressures exceeded 160 mmHg and 105 mmHg, respectively. Major antihypertensive drug choice was intravenous infusion of nitroglycerin and captopril tablets to avoid possible interactions between the $MgSO_4$ and nifedipine. We did not choose alpha methyldopa due to weak antihypertensive effect in the early postpartum period. Following the cessation of $MgSO_4$ prophylaxis, slow releasing tablets of nifedipine, or alpha methyldopa were used.

Urine output, serum creatinine and blood urine nitrogen (BUN) levels were compared with basal levels at 24 hours after the diagnosis of oliguria in both groups. We did not apply for approval from the local ethics committee due to the retrospective design of this study.

Demographic and general characteristics were compared by two-tailed Student's *t* test. Also non-parametric Mann-Whitney test and Wilcoxon test were used to determine treatment effect by SPSS 11 software (SPSS Inc, Chicago Ill). P value <0.05 was considered to be statistically significant.

Results

A total 134 hypertensive pregnant women who were classified as severely preeclamptic were reviewed retrospectively. However, only 52 of them had our inclusion criteria and follow-up data. The FFP group consisted of 29 women who received FFP as plasma volume expander and the crystalloid group consisted of 23 women who did not receive any plasma volume expander. Baseline characteristics are shown in Table 1. Age, gravida, parity, and gestational weeks at delivery, birthweight, frequency of antihypertensive drug requirement were not different between groups ($p>0.05$). In the FFP group, 4 of 29 (13.7%) patients, and in the crystalloid group, 9 of 23 (39.1%) patients delivered by vaginal route ($p=0.038$).

The FFP group received magnesium sulphate infusion longer than the crystalloid group (31.68±13.6 h vs. 24.73±4.14 h, $p=0.019$). Following the diagnosis of oliguria, in both groups basal BUN and creatinine levels were estimated (Table 2). Urine output, BUN and creatinine levels were determined twenty-four hours later again. Only one patient from the FFP group had eclamptic convulsions at the postpartum period. In the FFP group, there was no difference in BUN levels between the basal and those attined after FFP infusion ($p=0.305$). However, creatinine levels decreased following FFP

Table 1. Mean+SD baseline characteristics of FFP group and crystalloid group

	FFP group (n=29)	Crystalloid group (n=23)	*P* value
Age (years)	29.21±4.96	29.52±6.96	0.85
Gravida	2.51±1.97	2.86±2.07	0.56
Parity	0.93±1.22	1.52±1.19	0.22
Rate of vaginal delivery (%)	13.7 (n=4)	39.1 (n=9)	0.038*
Gestational weeks at delivery (weeks)	32.87±3.17	33.92±3.97	0.29
Birthweight (g)	1908.96±830.30	2432.04±1091.53	0.055
Total duration of magnesium sulphate (h)	31.68±13.16	24.73±4.14	0.019*
Antihypertensive drug requirement	11 (%37.9)	9 (%39.1)	0.084
Time period from admittance to delivery (h)	40.48±34.21	38.43±20.74	0.80

*Statistically significant
Values are expressed as mean.

(p=0.017). In the crystalloid group, there was no statistically significant changes for BUN and creatinine levels following the 24 hour period of crystalloid infusion (p>0.05). Also at the end of the 24 hour period, BUN and creatinine levels were not statistically different between the two groups (p=0.24 and p=0.29 respectively). Mean urine output was 1498±568 ml/24 h in the FFP group and 1368±447 ml/24 h in the crystalloid group (p=0.67).

Discussion

Although the clinical diagnosis of preeclampsia is sometimes difficult, there is no question that this disorder is unique to pregnancy. It is characterized by poor perfusion of many organs (including feto-placental unit), and is completely reversible following the termination of pregnancy. Defective trophoblastic invasion and endothelial dysfunction due to endothelial injury plays a central role in the pathogenesis of preeclampsia (6,7). Endothelial dysfunction can alter both vascular responses and intravascular coagulation in a manner consistent with pathophysiological abnormalities present in preeclampsia. Hypovolemia is an important feature of preeclampsia. However, to realize that this hypovolemia is relative; the circulating volume is expanded in comparison to non-pregnant state but less so than in normal pregnancy. Reduced organ perfusion causes decreased glomerular filtration rate, oliguria, proteinurea, decreased excretion of BUN, creatinine, uric acid which indicates kidney involvement in preeclampsia (8). Once delivery is accomplished, spontaneous diuresis usually begins within 24 hours in most cases of preeclampsia and eclampsia (1,2,4).

Oliguria and fluid management in the preeclamptic patient might be an important problem following the delivery. Crystalloid infusion at the rate of 60-120 ml per hour for correction of oliguria is the first step intervention for prevention of oliguria. Low dose dopamine infusion (2 µgram/kg/min) to correct oliguria is another option (9). However, this group of patients should be monitorized by central venous access (10). The use of low dose dopamine in a labor setting can improve urine output in postpartum preeclamptic women with oliguria who had not responded to a single fluid challenge (11). However, this approach is still controversial (12). Even though it is agreed that plasma volume decreases in preeclamptic patients, the use of fluid is controversial. Excessive fluid load could lead to congestive heart failure and perhaps cerebral edema (13). Fresh frozen plasma as a volume expander could be utilized to increase the influx of extravascular fluid into vascular compartment. In literature, there are several reports about plasma volume expanders in severe preeclamptic patients remote from term to prolong pregnancy (14). However, Duley et al. (15) reported that this strategy does not improve maternal or fetal outcome in women with early preterm hypertensive complications of pregnancy. Also this conclusion was supported by Ganzevoort et al. (14). Our aim was to prevent volume overload by continuous crystalloid infusion and to prevent fluid loss. However we did not find any difference in urine output between these two groups. Only creatinine levels were decreased following the infusion of fresh frozen plasma significantly. The major handicap of this retrospective study is the higher abdominal delivery rate in the FFP group. Blood loss secondary to abdominal delivery might be another factor that contributed to hypovolemia and hypoperfusion of kidneys.

In conclusion, data about plasma volume expanders to improve urine output in the postpartum period is limited. The use of plasma volume expanders to enhance intravascular volume does not provide additional benefit for improvement of oliguria.

Table 2. BUN, creatinin levels and, urine output before and after the plasma volume expander infusion

	FFP group Baseline (0 Hour)	Postinfusion (24th hour)	*p**	Crystalloid group Baseline (0 Hour)	24th hour	*p**
Blood Urine Nitrogen (mg/dl)	37.60±19.62	35.96±20.76	0.305	28.57±20.67	31.06±17.42	0.094
Creatinin (mg/dl)	0.97±0.35	0.90±0.39	0.017	0.78±0.22	0.77±0.23	0.465
Urine Output (ml)	----------	1498±568		----------	1368±447	0.67

Values are expressed as median.
*p<0.05

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