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Plasma exchange therapy in HELLP syndrome: A single-center experience

HELLP sendromunda plazma değiştirme tedavisi: Tek merkez deneyimi

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Background/aims: *The aim of this study was to investigate the effectiveness of plasma exchange therapy in patients with various forms of hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome.* ***Methods****: During a three-year period, 13 patients with HELLP syndrome were treated with one or two sessions of plasma exchange after delivery. Diagnosis of hemolysis, elevated liver enzymes, and low platelets syndrome was made according to Sibai's criteria, and the severity of illness was categorized according to platelet counts. Among patients, nine were in class-1 and the remaining four were in class-2. Patients with very high levels of aspartate aminotransferase (AST) (>2000 U/L) and lactate dehydrogenase (LDH) (>3000 U/L) were defined as fulminant type (2 cases).* ***Results:*** *Rapid improvement in platelet counts was observed after treatment with plasma exchange. All patients survived except the two fulminant hemolysis, elevated liver enzymes, and low platelets syndrome cases.* ***Conslusion****: In our study, plasma exchange therapy was effective in patients with severe hemolysis, elevated liver enzymes, and low plateletssyndrome, but fulminant cases did not appear to respond to this therapy.*

Key words: Plasma exchange, HELLP syndrome

Amaç: *Bu çalışmanın amacı değişik formdaki hemoliz, artmış karaciğer enzimi, düşük trombosit sayısı sendromlu hastalarda plazma değiştirme tedavisinin etkinliğini araştırmaktır.* ***Yöntem:*** *3 yıllk periyodda, 13 hemoliz, artmış karaciğer enzimi, düşük trombosit sayısı sendromlu hasta, doğumlarını takiben tek yada iki seans plazma değiştirmeyle tedavi edildi. hemoliz, artmış karaciğer enzimi, düşük trombosit sayısı sendromu tanısı Sibai'nin kriterlerine göre yapıldı ve hastalığın şiddeti trombosit sayısına göre sınıflandırıldı. Hastaların, dokuzu klas-1 ve kalan dördü klas-2 idi.Yüksek ALT (>2000 IU/L) ve LDH (>3000 IU/L) değerlerine sahip iki hasta, fulminant tip olarak tanımlandı.* ***Bulgular:*** *Plazma değiştirme tedavisinden sonra trombosit sayısı hızla düzeldi. Fulminant hemoliz, artmış karaciğer enzimi, düşük trombosit sayısı sendromlu 2 hasta haricinde tüm hastalar sağ kaldı.* ***Sonuç:*** *Çalışmamızda, şiddetli hemoliz, artmış karaciğer enzimi, düşük trombosit sayısı sendromunda plazma değiştirme tedavisi etkili bulundu, fakat fulminant vakalar bu tedaviye cevap vermedi.*

Anahtar kelimeler: Plazma değiştirme, HELLP sendromu

INTRODUCTION

In the spectrum of patients with severe pre-eclampsia, there is a potentially lethal complication called 'HELLP syndrome' (hemolysis, elevated liver enzymes, and low platelets). Laboratory features of HELLP syndrome are considered to be secondary to microangiopathic hemolytic anemia, hepatic dysfunction and thrombocytopenia (1).

Laboratory features of microangiopathic hemolysis, liver function abnormalities and thrombocytopenia are presented with fragmented red cells and polychromasia on the peripheral blood smear, increased serum lactate dehydrogenase (LDH), increased serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT), and platelet count less than $100x10^3/\mu L$ (2). Because LDH reflects both the extent of hemolysis and hepatic dysfunction, it is one of the most important laboratory tests together with platelet count for disease assessment and surveillance. The most severe morbidity and mortality associated with HELLP syndrome is encountered when platelet count falls below $50x10^3/\mu L$ (3). The disease process usually resolves in 24 to 48 hours after delivery of the placenta, at which time the hepatic and hematologic systems begin to recover.

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Although delivery of the placenta with elimination of the residual gestational decidua is the eventual goal of the management, some patients require transfusion of blood products and most benefit from corticosteroid therapy, but a few patients are refractory to these conservative methods (4). Though treatment of these unresolved cases with plasma exchange has been used with some success thus far, further studies are required to evaluate this approach.

MATERIALS AND METHODS

Thirteen patients with HELLP syndrome were consecutively admitted to the Obstetric and Gynecology Unit in Gaziantep University School of Medicine between February 2002 and August 2005. Diagnosis of HELLP syndrome was made on the basis of at least three of the following criteria: microangiopathic hemolysis (abnormal peripheral smear, LDH>600 U/L), elevated liver enzymes (AST>70 U/L), and low platelet count (<150x10^3/μL) (5). The severity of HELLP syndrome is categorized according to platelet counts as: severe, <50x10^3/μL; moderate, 50-100x10^3/μL; and mild, >100x10^3/μL (6). Platelets, serum AST and ALT and LDH levels were determined with standard laboratory methods. Pregnancies were delivered vaginally or by cesarean section. We prefer cesarean section in patients with an unripe cervix under 34 weeks of gestation. All patients received conservative treatments such as antihypertensives, anti-epileptic drugs and corticosteroids, etc. All patients were treated also with one or two plasma exchanges using an apheresis device (Haemonetics 3p, Braintree, USA) in the postpartum period. Plasma exchange was started and was exchanged within 24 hours after delivery, especially in patients with severe HELLP syndrome. Vascular access was via antecubital or subclavian vein. One total plasma volume was exchanged daily with fresh frozen plasma (FFP) during pheresis. A written informed consent was obtained from all patients.

RESULTS

The mean maternal and gestational ages were 27±7 years and 33±4 weeks, respectively. Five patients were primi- and eight patients were multigravida. Clinical features and general laboratory findings of all cases are summarized in Table 1. Among them, nine had class-1 syndrome and the remaining four had class-2 according to Martin's criteria (6). Four cases were preeclamptic (no: 3-6) and seven were eclamptic (no: 2, 7, 9-13) on admission. Five patients underwent cesarean section but the remaining eight delivered vaginally. Only two fetal deaths occurred due to abruption. Although the majority of cases survived, two of them died due to multi-organ failure, with the involvement of the liver and renal systems (mortality rate: 15.3%). Both deaths were in patients with the fulminant form of HELLP syndrome. One patient had intracranial bleeding and three patients underwent hemodialysis because of acute renal failure. Two sessions of plasma exchange were performed on two patients and only one session in the remaining. Adverse reactions to plasma exchange including chills, urticaria and paresthesias were observed in some patients (n: 4), but were not severe enough to stop the procedure. Rapid improvement in platelet counts was seen 48 hours after the treatment with plasma exchange (Figure 1). Eleven patients were followed for three months and found healthy.

Table 1. Main clinical and laboratory findings of all patients with HELLP syndrome

Case no.	Age	Type of delivery	Week of pregnancy	Hb g/dl	Platelet x10^3/μL	LDH U/L	ALT U/L	AST U/L	Maternal outcome
1	33	CD	29	9.3	52	1134	1665	28555	Healthy
2	18	CD	33	8.4	40	1662	293	595	ARF
3	28	VD	38	10.8	54	1800	766	1754	Healthy
4	30	VD	33	12	38	1390	75	156	Healthy
5	19	CD	40	7.4	37	9685	1800	2527	Deceased
6	42	VD	36	10	45	1720	1670	3117	ARF
7	33	CD	31	10.7	35	1363	207	211	ICB
8	21	VD	34	9.3	34	2669	368	820	ARF
9	38	VD	33	7.5	26	8820	1294	2189	Deceased
10	26	VD	37	8.8	68	2306	60	182	Healthy
11	25	VD	26	10.5	27	3097	549	705	Healthy
12	29	VD	30	6.2	33	2259	376	1017	Healthy
13	21	CD	36	10.8	61	5910	409	754	Healthy

CD: Cesarean delivery, VD: Vaginal delivery, ARF: Acute renal failure, ICB: Intracranial bleeding, Hb, LDH, ALT, AST, and platelet values were at the time of diagnosis

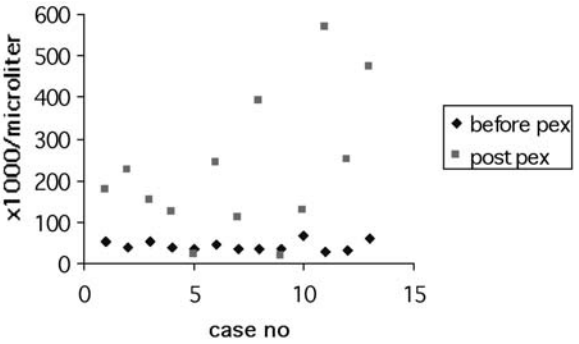

Figure 1. Platelet counts of patients before and after plasma exchange (pex: plasma exchange)

DISCUSSION

Many aspects of HELLP syndrome are still controversial, such as diagnosis, classification and management (7, 8). Diagnostic criteria of HELLP syndrome are inconsistent because different cut-off values for laboratory tests are observed in the literature. In this study, the cut-off values for LDH, platelet count and AST have been used by many authors, and all cases fulfilled diagnostic criteria of HELLP syndrome (2, 5). Delivery in all cases was carried out because six of them were beyond 34 weeks of gestation and the remaining seven were in unstable condition (severe HELLP) or with acute renal failure (9). During the postpartum period, the majority of cases will show resolution of the disease within 72 hours of delivery; however, some patients, especially those with the persistent form of the disease, will not improve or will even get worse. Some authors have suggested that such cases might benefit from plasma exchange (10). The exact mechanism of the effect of plasma exchange in HELLP syndrome is not known, but in general plasma exchange removes plasma factors, if any, and substitutes new elements by refreshing the patient's own plasma. Lattuada et al. (11) observed reduced metalloprotease activity in patients with HELLP syndrome but as no autoantibody or ultralarge von Willebrand (vWB) factor multimers are detected, a completely different mechanism from thrombotic thrombocytopenic purpura (TTP) was proposed. Hsu et al. (12) found elevated serum levels of human chorionic gonadotropin (hCG) and soluble E-selectin in patients with HELLP syndrome, which means placental and vascular endothelial dysfunction may play a role in the pathogenesis of HELLP syndrome. Eser et al. (13) reported that recovery time of platelets, AST, ALT and LDH was shorter in patients with HELLP syndrome treated with plasma exchange than in the control group. This finding may imply that HELLP syndrome has a 'plasma factor'.

Maternal mortality rate in HELLP syndrome is variable (1-23%) due to severity of disease, delayed diagnosis and presence of multi-organ involvement (14, 15). The mortality rate in HELLP syndrome cases treated with plasma exchange is restricted to a few studies in the literature (10, 13). Eser et al. (13) reported no deaths in 29 patients with HELLP syndrome treated with plasma exchange, whereas mortality rate was 23% in the control group. In another study, two deaths were observed in 18 patients with HELLP syndrome treated with plasma exchange (10). In our study, there were two maternal deaths. These two cases were in class-1 HELLP syndrome and additionally had high LDH and AST values (Table 1). According to Catanzarite et al. (16), patients with high values of AST (>2000 U/L) and LDH (>3000 U/L) in HELLP syndrome carry high risk for mortality (fulminant HELLP) (16).

In conclusion, plasma exchange is effective in patients with severe HELLP syndrome, but fulminant cases do not appear to respond to this therapy; this approach needs further evaluation.

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