Original Article

Access this article online

Quick Response Code:

Website: www.ajts.org

DOI: 10.4103/ajts.AJTS_16_19

Role of plasma exchange in postpartum microangiopathies: An experience from a tertiary care center

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Abstract:

BACKGROUND: Postpartum microangiopathies are rare but are associated with high maternal and fetal mortality requiring early diagnosis and prompt treatment to improve the outcome.

AIMS AND OBJECTIVES: This retrospective study aims to assess the efficacy of plasma exchange (PE) therapy in postpartum thrombotic microangiopathies.

MATERIALS AND METHODS: We did retrospective analysis of all plasma exchange procedures performed in patients of postpartum thrombotic microangiopathies over a period of 1 year (2015-2016). Patient's pre- and post-plasma exchange hematological and biochemical parameters were recorded and compared for analyzing the response to the therapy. Patients were followed telephonically even after their discharge from the hospital.

RESULTS: Hematological and renal profile improved in 8 out of 9 patients after PE therapy. Survival after PE therapy was 40% in post partum atypical HUS and 75% in patients with HELLP syndrome at 4 months of follow up.

CONCLUSION: Early initiation of PE therapy in postpartum thrombotic microangiopathies can reduce morbidity and mortality associated with them.

Keywords:

Microangiopathy, plasma exchange, postpartum

Introduction

Plasma exchange (PE) has been successfully tried and recommended for various postpartum microangiopathies such as postpartum hemolytic uremic syndrome (HUS), thrombotic thrombocytopenic purpura (TTP), and HELLP syndrome as per the latest American Society for Apheresis (ASFA) guidelines.[1] Pregnancy being a hypercoagulable state is prone to the acute episodes of hemolytic anemia, thrombocytopenia, and acute renal failure.[2] Since laboratory profile of thrombotic microangiopathies is overlapping, hence it poses a great challenge to distinctly label the definite diagnosis in a particular patient. Furthermore, these conditions are associated with high perinatal or maternal morbidity and mortality[3] demanding early diagnosis and prompt treatment to improve the outcome. Here, we present our experience of PE in patients of postpartum HUS and HELLP syndrome referred to us from the department of Obstetrics and Gynaecology in our institute.

Materials and Methods

We did a retrospective analysis of our PE records over a period of 1 year (2015–2016) during which five cases of suspected postpartum HUS and four cases of HELLP

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Submission: 28-01-2019
Accepted: 21-07-2019
Published: 03-12-2019

How to cite this article: Hans R, Prakash S, Lamba DS, Sharma RR, Malhotra P, Suri V, *et al*. Role of plasma exchange in postpartum microangiopathies: An experience from a tertiary care center. Asian J Transfus Sci 2019;13:90-4.

syndrome (based on their laboratory and clinical profile) were referred to the department of Transfusion Medicine from the department of Obstetrics and Gynaecology of our tertiary care institute. These cases were referred to our institute from the peripheral regional health-care settings.

Plasma exchange intervention

PE procedures were performed on cell separator Cobe® Spectra (Terumo BCT, Lakewood, Colorado, USA) after priming the disposable kit with group-specific, crossmatched packed red blood cells due to low hemoglobin (<8 g/dl) of the patients. The replacement fluid used was fresh frozen plasma with a negative balance of 10% to prevent cardiac overload in the patients as these patients were oliguric or anuric. Procedures were done on daily (n = 3) or on alternate days (n = 6) depending on the clinical condition and hemodialysis requirements of the patients. Ionized calcium was monitored before the start of the procedure, and calcium infusion (1%) was given throughout the procedure. Preprocedure hematological, renal, and liver functions were noted, and these parameters were followed after each PE procedure for analyzing the response to the therapy. Patients were followed telephonically even after their discharge from the hospital.

Results

Patient characteristics of suspected postpartum hemolytic uremic syndrome patients

Of the five HUS patients, four were primigravida and one was multigravida. The age of patients ranged from 23 to 30 years. The details of antenatal and delivery outcome of these patients are shown in Table 1. The onset of clinical features suggestive of HUS was observed on day 2 in Cases I, II, and V and day 5 postabortion in Case III, and in Case IV, it was postpartum day 7. Patients were referred immediately to our institute with features of oliguria and thrombocytopenia.

Response to plasma exchange therapy and outcome of suspected hemolytic uremic syndrome patients

All patients showed improvement in their hematological and renal profile after PE, as shown in Table 2. However, only two patients (Case I and Case V) survived on follow-up. One patient (Case II) showed improvement in her biochemical and renal profile; however, she left the hospital against medical advice and on telephonic follow-up found to be expired. Another patient (Case III) underwent two PE procedures, but the patient expired after the second therapeutic plasma exchange (TPE) procedure due to septicemic shock as the patient left the hospital against medical advice. Case IV improved and was discharged; however, on follow up, the patient was found to be expired in a local hospital after getting some treatment for complaints of pain abdomen 1 week after discharge from the hospital.

Patient characteristics of suspected HELLP syndrome

Of four patients with HELLP syndrome, two were primigravida and the other two were multigravida. The age of patients ranged from 20 to 30 years. The details of antenatal and delivery outcome of these patients are shown in Table 3. HELLP syndrome was diagnosed in three of these patients during antenatal period, and one patient had uneventful history during antenatal phase. Patients were referred to our institute with complaints of oliguria, thrombocytopenia, and elevated liver enzymes within 1–5 days of the onset of these clinical signs and symptoms.

Liver transaminases (aspartate transaminase and alanine transaminase) were grossly deranged in these patients, whereas they were normal in suspected HUS patients. The details of laboratory profile of all patients are summarized in Table 4.

Table 1: Clinical profile of patients suspected of postpartum hemolytic uremic syndrome

Features	Case I	Case II	Case III	Case IV	Case V
Age (years)	30	24	30	27	23
Gravida	Primi	Primi	Multi (G6P4A1L4)	Primi	Primi
Mode of delivery	Term, Emg LSCS	Term, LSCS	Abortion at 28 Weeks	Term, LSCS	Term, LSCS
Status of baby	Alive and healthy	Alive and healthy	NA	Alive and healthy	Alive and healthy
Antenatal period	Uneventful	Uneventful	Uneventful	Uneventful	Uneventful
Onset of clinical signs and symptoms (postpartum/postabortion)	Day 2	Day 2	Day 5	Day 7	Day 2
Time between illness onset and PE	4 days	3 days	2 days	3 days	2 days
Presenting clinical features	Pedal and facial edema, low urine output	low urine output, bleeding from the urethra and ET tube, Jaundice	Generalized edema with low renal output	Clinical pallor with edema over the face and leg	Pallor, edema over the face and leg and low renal output
Hemodialysis (number of procedures)	2	ND	ND	3	8
Length of hospital stay (days)	20	10	7	14	19

LSCS=Lower segment caesarean section, ET=Endotracheal tube, ND=Not done, PE=Plasma exchange

Table 2: Pre- and post-plasma exchange pattern of laboratory (hematological and renal) profile of the patients

Case/PE procedures	Laboratory profile of suspected postpartum hemolytic uremic syndrome patients														Outcome
	Hematological profile										Renal profile				
	Hemoglobin (g/l)		Platelet count (10^9/L)		Lactate Dehydrogenase (µkat/L)		Bilirubin (mg/dl)		Peripheral Blood Film (%Schistocytes)		Serum urea (mmol/L)		Serum creatinine (µmol/L)		Urine output (ml/kg/h)		At 4 months of follow-up
	Pre-PE	Post-PE	Pre-PE	Post-PE	Pre-PE	Post-PE	Pre-PE	Post-PE	Pre-PE	Post-PE	Pre-PE	Post-PE	Pre-PE	Post-PE	Pre-PE	Post-PE	
Case I (4)	92	99	46	440	47.58	14.95	1.6	0.5	5	Nil	31.06	18.56	442	530.40	0.1	1	Alive
Case II (4)	69	76	80	61	169.30	16.03	1.3	0.3	6	Nil	40.70	28.56	362.44	335.92	0.1	0.2	Expired
Case III (2)	82	73	101	138	20.04	13.68	1.26	1.06	4	2	27.49	56.05	238.68	423.44	0.1	0.3	Expired
Case IV (5)	66	70	63	96	71.74	35.35	1.41	1.5	9	1	83.18	10.35	689.52	221	1	1.5	Expired
Case V (2)	74	82	209	58	22.26	15.88	1.2	1.1	4	2	29.27	22.13	309.40	185.64	0.5	1	Alive

PE=Plasma exchange

Table 3: Clinical profile of patients suspected of HELLP

Features	Case I	Case II	Case III	Case IV
Age (years)	20	25	30	28
Gravida	Primi	Multi G3P2002	Primi	Multi
Mode of delivery	NVD for IUFD	NVD breech at home	LSCS	NVD
Status of baby	Stillbirth	Alive	Alive	Stillbirth
Antenatal period	hypertension	uneventful	hypertension in the last trimester	hypertension
Onset of clinical signs and symptoms (postpartum/ postabortion)	Day 1	Day 5	Day 5	Day 1
Time between illness onset and PE	6 days	0 day	2 days	7 days
Presenting clinical features	Oliguria, facial and pedal edema	Oliguria, facial and pedal edema	Ascites, anuria, pedal edema	Increased bilirubin, swelling over the face and pedal edema
Hemodialysis (number of procedures)	5	3	Nil	10
Length of hospital stay (days)	21	6	12	31

NVD=Normal vaginal delivery, LSCS=Lower segment caesarean section, IUFD=Intra uterine fetal death, PE=Plasma exchange

Response to plasma exchange therapy and outcome of suspected HELLP patients

PE was initiated in all of these patients within 7 days of the onset of illness. Three patients were on alternate-day hemodialysis. Of four patients, three had oliguria and one had normal urine output. After PE therapy, urine output and other renal function parameters [Table 4] improved in the oliguric patients, however, one patient (Case IV) expired due to pulmonary aspiration.

Discussion

Pregnancy is a state of increased prothrombotic activity because of increased concentration of procoagulants, decreased fibrinolytic activity, loss of thrombomodulin, and decreased activity of ADAMTS13 level.[4] Activation of alternate pathway by systemic infection, hemorrhage, and inflammation along with predisposition due to various mutations in complement pathway regulators results in complement dysregulation.[5] This dysregulation

Table 4: Pre- and post-plasma exchange pattern of laboratory (hematological and renal) profile of suspected HELLP patients

Case/PE procedures	Laboratory profile of suspected HELLP syndrome patients																Outcome (4 months)
	Hematological profile										Renal profile						
	Hemoglobin (g/l)		Platelet count (10^9/L)		Lactate dehydrogenase (µkat/L)		Bilirubin (mg/dl)		Peripheral blood film (% schistocytes)		Serum urea (mmol/L)		Serum creatinine (µmol/L)		Urine output (ml/kg/h)		
	Pre-PE	Post-PE	Pre-PE	Post-PE	Pre-PE	Post-PE	Pre-PE	Post-PE	Pre-PE	Post-PE	Pre-PE	Post-PE	Pre-PE	Post-PE	Pre-PE	Post-PE	
Case I (3)	84	81	117	220	66.62	23.13	0.7	0.3	4	2	31.06	29.06	406.64	495.04	0	1.2	Alive with 88.40 creatinine
Case II (2)	78	129	36	63	20.79	23.28	14	8.0	6	Nil	44.98	41.77	426.60	397.80	0.15	0.19	Expired
Case III (5)	96	63	65	173	33.97	10.25	8.4	2.0	4	2	64.97	21.42	362.44	134.37	1.2	1.2	Alive with creatinine 97.24
Case IV (3)	112	76	59	279	40.10	23.85	4.0	2.4	9	1	67.83	14.64	545.43	265.20	0	0.6	Alive with creatinine 265.20

PE=Plasma exchange

or loss of this effective control of complement activation results in signs and symptoms of HUS in pregnancy.[6]

Literature supports that pregnancy is a precipitating event for TTP/HUS in women with congenital TTP-HUS who present with the first episode during their first pregnancy associated with the early appearance of signs and symptoms such as severe pallor, oliguria, and renal failure. Four of five patients in our study were primigravida, and all of them presented with low urine output within 1 week of delivery. There was no family history as well as past history of similar illness in these patients. One of them was a multigravida, who developed signs/symptoms of HUS after abortion at 28 weeks most probably due to sepsis following a severe postpartum hemorrhage. The early onset of postpartum HUS has been reported in the age group of 27 ± 6 years,[5] and our patients were in the range of 23–30 years with the early onset of HUS in postpartum period which is comparable to the study by Shrivastava *et al*. and Wessel *et al*.[7,8] Since these patients were referred from community health-care centers to our tertiary care center, due to renal insufficiency in postpartum period, hence HUS was considered as provisional diagnosis. PE therapy was started without delay in these patients without waiting for ADAMTS13 inhibitor and complement-level estimation as these tests are not routinely done in our center, and samples are to be sent to the reference laboratories. The early initiation of PE therapy is also supported by the current ASFA guidelines[1] for TTP-HUS on empirical basis.

Since patients went into sepsis due to poor postpartum care so, only 2 of 5 (40%) patients could survive even after extensive PE therapy and alternate hemodialysis despite an early referral. Whereas, in a study by Shrivastava *et al*.,[7] 2 patients of 3 were doing well in their follow-up. Due to high mortality reported with postpartum HUS, it is important for the obstetricians to be aware and consider urgent initiation of PEs in addition to hemodialysis in cases of postpartum/abortion females presenting with acute renal failure and anemia with thrombocytopenia by timely referral or bedside initiation of PE to decrease the mortality associated with the disease.

Another complication of pregnancy is HELLP syndrome that presents mostly in the last trimester of pregnancy or in postpartum period in some cases. The exact pathogenesis is not clear, but endothelial dysfunction and inflammatory response may contribute to thrombotic microangiopathy in HELLP. The condition is characterized by signs and symptoms of preeclampsia such as hypertension and proteinuria. All our patients suspected of HELLP had evidence of antenatal hypertension in the last trimester of pregnancy. The coagulation profile and liver functions

tests were highly deranged in patients of HELLP syndrome.[9] The definite treatment for HELLP is to terminate the pregnancy by LSCS, but if the condition is not improving even after delivery, PE is considered in these patients as PE removes circulatory protein-bound platelet aggregates and procoagulant factors released from platelets and endothelial cells. Studies have shown increased maternal mortality and very poor neonatal outcome born to a mother with HELLP syndrome[10] as observed in our study with stillbirth in 2 of 4 HELLP patients; however, after PE, three of four patients of HELLP survived in our study which further emphasizes the need of urgent initiation of PE procedures on a daily basis.

Conclusion

Thus, increased morbidity and mortality burden of pregnancy-induced microangiopathies can be decreased through the early detection of clinical signs and symptoms in pregnancy/postpartum and timely initiation of PE therapy along with improvement of maternal and child health-care facilities in peripheral health settings in India.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1. Schwartz J, Padmanabhan A, Aqui N, Balogun RA, Connelly-Smith L, Delaney M, *et al*. Guidelines on the use of therapeutic apheresis in clinical practice-evidence-based approach from the writing committee of the American society for apheresis: The seventh special issue. J Clin Apher 2016;31:149-62.
2. Rao S, Jim B. Acute kidney injury in pregnancy: The changing landscape for the 21st century. Kidney Int Rep 2018;3:247-57.
3. Liu Y, Ma X, Zheng J, Liu X, Yan T. Pregnancy outcomes in patients with acute kidney injury during pregnancy: A systematic review and meta-analysis. BMC Pregnancy Childbirth 2017;17:235.
4. Motto D. Endothelial cells and thrombotic microangiopathy. Semin Nephrol 2012;32:208-14.
5. Fakhouri F, Roumenina L, Provot F, Sallée M, Caillard S, Couzi L, *et al*. Pregnancy-associated hemolytic uremic syndrome revisited in the era of complement gene mutations. J Am Soc Nephrol 2010;21:859-67.
6. Delmas Y, Helou S, Chabanier P, Ryman A, Pelluard F, Carles D. Incidence of obstetrical thrombotic thrombocytopenic purpura in a retrospective study within thrombocytopenic pregnant women. A difficult diagnosis and a treatable disease. BMC Pregnancy Childbirth 2015;15:137.
7. Shrivastava M, Modi G, Singh RK, Navaid S. Early diagnosis and management of postpartum hemolytic uremic syndrome with plasma exchange. Transfus Apher Sci 2011;44:257-62.
8. Wessel CH, Andreescu CE, Rombout-De Weerd S, Levin MD. Postpartum microangiopathic disorders: A case report and review of the literature. Case Rep Womens Health 2014;3-4:3-6.
9. Narayana L, Garikapati K, Kodey PD, Gayathri KB. Study on HELLP syndrome – Maternal and perinatal outcome. Int J Reprod Contracept Obstet Gynecol 2017;6:714-19.
10. Dekker RR, Schutte JM, Stekelenburg J, Zwart JJ, van Roosmalen J. Maternal mortality and severe maternal morbidity from acute fatty liver of pregnancy in the Netherlands. Eur J Obstet Gynecol Reprod Biol 2011;157:27-31.