REVIEW ARTICLE

DEXAMETHASONE IN PREGNANT WOMEN WITH HEMOLYSIS, ELEVATED LIVER ENZYMES, AND LOW PLATELET COUNT (HELLP) SYNDROME- A CASE REPORT

Author

[1]Mariana Szpakowski, Pharm.D.

[2]Antonia Carbone Pharm D, BCPS, BCACP

[3]Anna Dushenkov BS Pharm, PharmD, BCPS

[4]Julie Kalabalik PharmD, BCPS, BCCCP

Affiliations

[1] Pharmacist
Overlook Medical Center
99 Beauvoir Avenue, Summit, NJ 07901

[2] Clinical Assistant Professor of Pharmacy Practice and Ambulatory Care Clinical Pharmacist
Fairleigh Dickinson University School of Pharmacy, 230 Park Avenue, Florham Park, NJ 07932
Overlook Medical Center, 99 Beauvoir Avenue, Summit, NJ 07901

[3] Assistant Professor of Pharmacy Practice
Fairleigh Dickinson University School of Pharmacy
230 Park Avenue, Florham Park, NJ 07932

[4] Assistant Professor of Pharmacy Practice
Fairleigh Dickinson University School of Pharmacy
230 Park Avenue, Florham Park, NJ 07932

Correspondence author:

[1]Antonia Carbone Pharm D, BCPS, BCACP

Clinical Assistant Professor of Pharmacy Practice and Ambulatory Care Clinical Pharmacist
Fairleigh Dickinson University School of Pharmacy, 230 Park Avenue, Florham Park, NJ 07932
Overlook Medical Center, 99 Beauvoir Avenue, Summit, NJ 07901

Email: acarbone@fdu.edu

Abstract

Introduction: HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome is a hypertensive disorder in pregnancy with severe pre-eclampsia, resulting in increased maternal and neonatal morbidity and mortality. The management of HELLP syndrome is controversial because the pathophysiology of the disease is not well understood. The current standard of care is supportive therapy and immediate delivery of the fetus. However, the use of corticotherapy may have potential benefit on improving maternal recovery, but various studies reported inadequate and inconsistent findings.

Case presentation: A 25-year-old pregnant patient presented to the emergency room with vaginal bleeding and hypertension. She was diagnosed with severe pre-eclampsia and underwent delivery via a cesarean section and was then transferred to the intensive care unit (ICU) due to exacerbation of HELLP syndrome. Prompt initiation of supportive care was provided and dexamethasone 10 mg IV Q 12 hours was administered. The patient recovered and was discharged from the hospital four days after corticotherapy was initiated, on day eight.

Conclusion: Various studies evaluated the use of corticosteroids, specifically dexamethasone, in the improvement of HELLP syndrome and maternal outcomes. Evidence on the management of the syndrome remains controversial due to limits in the strength of the conclusions of various clinical trials. As a result, the evidence is insufficient to justify the use of corticotherapy in the management of HELLP syndrome to improve maternal outcomes.

Key words: Corticosteroids, dexamethasone, hemolysis, elevated liver enzymes, and low platelet count syndrome, pregnant women

Introduction:

HELLP syndrome is a severe phenomenon of pre-eclampsia in pregnancy, categorized by hemolysis, elevated liver enzymes, and low platelets (HELLP) and is often associated with complications leading to increased morbidity and mortality for women and their offspring.[1] HELLP syndrome occurs in approximately 2 out of 1,000 pregnancies. This complication develops prior to full term (less than 37 weeks gestation) or postpartum. Seventy percent of pregnancies complicated by HELLP syndrome require preterm delivery, with 15% occurring before 27 weeks gestational age, leading to an increased risk of neonatal complications.1

Maternal complications may include acute liver failure, pulmonary edema, adult respiratory distress syndrome, and perinatal complications such as prematurity and growth restriction.

The management of HELLP syndrome is difficult since no specific treatment is available. This is in part due to the fact that the exact cause of the disease has not been conclusively determined. However, various hypotheses propose vascular endothelial dysfunction, generation of vasoconstrictors, and activation of the clotting cascade.1-3 As a result, treatment has been limited to supportive care interventions such as controlling blood pressure, seizure prophylaxis, and immediate delivery. Supportive care is suggested to result in rapid resolution of the syndrome in many patients. However, some patients have a delayed recovery, which is associated with a higher risk of maternal morbidity and mortality. 2

Administration of corticosteroids antepartum, particularly dexamethasone, may lead to improvement and stabilization of the complications associated with HELLP syndrome, thereby allowing pregnancy to be maintained until the appropriate conditions for delivery have been achieved. Additionally, laboratory abnormalities tend to worsen approximately 24-48 hours after delivery and platelet counts may be predictive of hemorrhagic complications.2,4 Therefore, the role of corticosteroids in expediting maternal postpartum recovery has been explored.3 Despite a suggested benefit in observational studies, the evidence is insufficient to demonstrate improvement in maternal and fetal outcomes in those receiving steroids for the management of HELLP syndrome, regardless of the timing of development of HELLP syndrome. However, corticosteroid use may be justified in situations where the rate of platelet count recovery is clinically valuable.1,3,5,6 More conclusive evidence supporting the use of cortisteroids in treating HELLP syndrome to alleviate the burden of maternal and neonatal complications is needed..

Patient case:

A 25-year-old female G1P0 presents to the emergency department at 31 weeks and 3 days gestational age with suspected vaginal bleeding and hypertension. The patient had no significant past medical history, unknown family history, and no known drug

allergies. She denied any tobacco, drug or alcohol use. She underwent a cesarean section due to severe preeclampsia and was provided supportive care. Prior to delivery, the patient was given beclomethasone 12 mg IM for two days for fetal lung maturity, magnesium sulfate 4 g IV over 30 minutes for seizure prophylaxis, cefazolin 2 g IV once for infection prophylaxis, oxytocin 20 units IV for 16 hours, and acetaminophen 650 mg PO every 4 hours as needed for headache. The patient was recovering well postoperatively until the following day when she began experiencing shortness of breath and became hypoxic. Postpartum lab findings revealed large increases in white blood cell count (WBC), aspartate and alanine aminotransferase (AST/ALT), lactate dehydrogenase (LDH), and blood pressure, as well as a drastic decrease in hemoglobin, hematocrit, and platelet count (Table 1: Patient Hematology and Chemistry Lab Findings). Elevated liver enzymes and LDH, hypertension, and thrombocytopenia are indicative of HELLP syndrome. The patient was transferred to the intensive care unit (ICU) due to worsening of HELLP syndrome, hypoxia, and shortness of breath, for closer monitoring and further management. The patient received the following medications postpartum: magnesium sulfate 40g/1000mL at 25ml/hr by continuous intravenous (IV) infusion to prevent seizures and convulsions, dexamethasone 10mg IV push followed by dexamethasone 10 mg intramuscularly (IM) every 12 hours x 8 doses to expedite the recovery rate and prevent severe thrombocytopenia, labetalol 200mg by mouth every 12 hours, nifedipine 10 mg PO every 6 hours as needed, and hydralazine 5 mg IV bolus over 5-6 minutes every 20 minutes as needed for blood pressure control, and oxycodone/acetaminophen 5mg/325mg by mouth every 4 hours as needed for pain management. Within 24-48 hours, lab parameters improved (Table 1: Patient Hematology and Chemistry Lab Findings). Specifically, platelets began to increase and AST/ALT and LDH decreased. The patient was discharged four days after initiation of corticotherapy, on day eight after admission.

Discussion:

The course of HELLP syndrome in pregnancy may be characterized by a sudden decline in maternal condition. Once the diagnosis is confirmed, medical judgment must be used in regards to appropriate timing of delivery, which is often based on gestational age and the condition of both mother and fetus. Prompt delivery is recommended if the patient is experiencing multiorgan dysfunction, liver hemorrhage, renal failure, or alarming fetal status.[8]

To stabilize the conditions of HELLP syndrome, available therapeutic and prophylactic options include magnesium sulfate and anti-hypertensive medications.[8] Aside from supportive care, there is much disagreement on the treatment of HELLP syndrome due to the complexity of the disease and unclear pathophysiology.[2,8]

The use of corticosteroids, specifically dexamethasone, have been explored in the treatment of HELLP syndrome. Corticosteroids are known to decrease prenatal morbidity and mortality by preventing

respiratory complications.[1] However, due to the pathophysiological uncertainty of HELLP syndrome, the beneficial effects of corticosteroids on the syndrome are unclear. A possible mechanism of action of corticosteroids in HELLP syndrome involves preventing the release of platelet activating substances from the damaged endothelial cells, thereby stabilizing the cell membrane.[9] Conflicting evidence on the correlation between corticosteroid use and recovery time has been noted in the literature.[1,3,10,11] Studies have explored whether postpartum dexamethasone has an effect on duration of hospital stay and maternal morbidity.[3] A randomized controlled study of 30 cases analyzed the effect of dexamethasone treatment during early postpartum (36 hours following childbirth) and concluded that the recovery rate was accelerated (mean arterial blood pressure improved by 28 hours and AST by 40 hours, while urinary output and platelet count increased at 20 and 36 hours postpartum respectively).[9] The length of postpartum hospital stay was 4-15 days (mean 6.0±4.1 days) for the 15 patients treated with corticotherapy, and 6-21 days (mean 10.5±3.2 days) for the 15 control patients ($p<0.01$). Similar results were also reported in a prospective, randomized controlled trial, which assessed 40 patients with the use of high dose dexamethasone, and analyzed for the recovery of HELLP syndrome by measuring mean arterial pressure, urinary output, platelet count, LDH, and AST/ALT.[4] Those receiving dexamethasone had a significant decrease in mean arterial pressure at 22 hours, an increase in urinary output and platelet count by 16 and 24 hours respectively, while LDH and AST/ALT decreased by 36 hours. Patients who were treated with corticotherapy recovered more rapidly than the control subjects, but the length of hospital stay in steroid-treated patients was not reported. Hence, the authors postulated that overall maternal morbidity, mortality, and the length of stay within the hospital could be decreased with the use of dexamethasone.

A prospective randomized clinical trial conducted among 132 patients with HELLP syndrome did not find a statistically significant difference in mean duration of hospital stay in patients who received dexamethasone compared to placebo.[11] A subsequent randomized, double-blinded, placebo controlled trial was conducted in 105 women hospitalized with HELLP syndrome, who were randomly assigned dexamethasone post-delivery. The outcomes measured included clinical parameters, maternal morbidity, recovery time, and duration of hospital stay. The results did not support the use of dexamethasone for recovery in patients with HELLP syndrome due to the fact that there were no significant differences between both groups in outcomes measured.[3] There was no difference in the percentage of patients requiring blood transfusions (28.6% in dexamethasone group and 38.8% in placebo group, $p=0.27$). The duration of hospitalization was ten days in both groups ($p=0.72$). Recovery of lab parameters were also similar between both groups. A Cochrane review evaluated randomized controlled trials comparing corticotherapy with placebo or no treatment in pregnant and postpartum women with HELLP syndrome[1]. Of the eleven trials analyzed, with a total of 550 women, it was concluded that the use of

corticosteroids made no difference in the risk of maternal death, morbidity, or infant death, but did improve platelet count, especially when administered antenatally. The American College of Obstetrics and Gynecolog(ACOG) guidelines for Hypertension in Pregnancy suggest 24-48 hours of corticosteroid use prior to delivery for potential fetal benefit in women <34 weeks gestation with HELLP syndrome whose condition remains stable, noting that the use of steroids in a clinical setting in which an increase in platelet count is needed may be useful. [6] ACOG suggests delivery for women >34 weeks gestation with HELLP syndrome once stable.

A multicenter, triple blind, randomized controlled study of approximately 360 patients with HELLP syndrome is currently underway to determine the effectiveness of dexamethasone compared to placebo in accelerating postpartum recovery.[10] One recent case report recommended the use of dexamethasone for patients presenting with HELLP syndrome based on clinical experience and prompt recovery following administration of corticosteroids.[12]

Although some studies reported benefit of corticosteroid use in patients with HELLP syndrome, there were concerns with study limitations including lack of blinding, inclusion of women with mild forms of the disease, and small sample size.[4,5,8]

Conclusion:

HELLP syndrome is a severe form of preeclampsia that worsens the prognosis of maternal outcomes. Our case discussed a 25-year-old pregnant patient, who presented to the emergency room and underwent a cesarean section due to severe pre-eclampsia. The patient was transferred to the ICU due to worsening symptoms of HELLP syndrome. She was administered supportive therapy including a 10 mg IV bolus of dexa-methasone followed by dexamethasone 10 mg IV Q 12 hours. The patient recovered from HELLP syndrome and was discharged home on day eight. The role of corticosteroids in improving patient outcomes is unclear in this case due to the concomitant prompt initiation of supportive care. The use of postpartum corticosteroids in the improvement of maternal outcomes has been investigated previously in the literature. The current published evidence is insufficient to justify the use of corticosteroids in the management of HELLP syndrome to improve clinical outcomes.

Competing Interests:

There are no competing interests involved in the conduct of this case report.

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Table 1

	Antepartum	Date of Delivery	Postpartum Day 1*	Postpartum Day 2	Postpartum Day 3	Reference Range
WBC	15.8	14.6	20.76	24.48	29.95	4.50-11.00 /nL
HGB	10.7	12	12	10.7	9.2	12.5-16.0 g/dL
HCT	31.4	35.1	35.1	31.3	27.6	37.0-45.0 %
Platelets	221	178	75	86	133	150-450 /nL
Albumin	1.6	1.7	1.7	1.5	1.5	3.4-5.0 g/dL
AST	42	109/388**	389	156	54	15-37 U/L
ALT	39	95/314**	343	219	121	12-78 U/L
LDH	269	387/750**	940	n/a	419	85-240 U/L

*Dexamethasone 10 mg IV administered

**Represent morning and evening laboratory findings

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