ORIGINAL ARTICLE

Comparison of DexamethasoneversusBetamethasone for the management of females with HELLP syndrome

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ABSTRACT

Background:HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome is a severe manifestation of preeclampsia with significant morbidity and mortality for pregnant women and their neonates.HELLP syndrome occurs in 0.1%-0.6% of all pregnancies and in 4%-12% of patients with preeclampsia. HELLP syndrome typically occurs between 27 weeks of gestation and delivery or immediately postpartum in 15%-30% of cases.

Aim: To compare the mean decrease in mean arterial pressurewith dexamethasone versusbetamethasonefor management of females presenting with postpartum HELLP syndrome at term

Methods: This Randomized Controlled Trial was conducted at Department of Obstetrics & GynecologyUnit III, Lady Willingdon Hospital/KEMU, Lahore for one year from 1.1.2016 to 31.12.2016. After approval from ethical committee of the hospital, 100femalesfulfilling selection criteria were enrolled through post-delivery wards. Informed consent was obtained. Demographic profile was also noted. Females were randomly divided in two groups by using lottery method. Baseline MAP was recorded. In group A, 10mg dexamethasone sodium phosphate IV every 12 hours was given while in group B, 12mg combination of betamethasone acetate and betamethasone sodium phosphate IM every 24 hrs. **Results:**Mean age of women in Group-A and in Group-B was 29.38±5.24 and 31.68±6.30 years. Mean gestational age of women in Group-A and in Group-B was 39.66±1.133 and 39.66±1.11weeks. From baseline till 48 hours mean decreases in Group-A and in Group-B was 48.08%±7.78 and 30.36%±8.24 respectively. As per p-value statistically significant difference was seen for arterial pressure in both treatment groups. Percentage reduction in mean arterial pressure was significantly higher in Group-A as compared to that of Group-B.

Conclusions: Decrease in mean arterial pressure with dexamethasone was significantly higher than that of betamethasone for management of females presenting with postpartum HELLP syndrome.

Key words:HELLP syndrome, Postpartum, Term, Arterial pressure, Betamethasone, Dexamethasone

INTRODUCTION

HELLP syndrome is a serious complication in pregnancy characterized by hemolysis, elevated liver enzymes and low platelet count usually develops before birth, only one-third occurring postpartum[1].The exact cause of HELLP syndrome is unknown. Some theorize that it is a variant of preeclampsia, the pathophysiology stems from a common source[2]. In general, activation of the coagulation cascade is considered the main underlying problem. Fibrin forms crosslinked networks in the small blood vessels[3]. It leads to a microangiopathic hemolytic anemia: the mesh causes destruction of red blood cells as if they were being forced through a strainer. Additionally, platelets are consumed. As the liver appears to be the main site of this process, downstream liver cells suffer ischemia, leading to periportal necrosis[4]. Other organs can be similarly affected. HELLP syndrome leads to a variant form of disseminated intravascular coagulation, leading to paradoxical bleeding[5]. Clinical course of women with true HELLP syndrome is usually characterized by progressive and sometimes sudden deterioration in the maternal condition[6]. Some of the measures used are bed rest, antihypertensive agents, parenteral magnesium sulfate, antithrombotic agents (low-dose aspirin, dipyridamole), plasma volume expanders (crystalloids, albumin, fresh frozen plasma), and steroids (prednisone, dexamethasone, or betamethasone)[7]. Corticosteroids are commonly used in the treatment of HELLP syndrome in the belief that they improve outcome[8].Steroids may alter the degree of intravascular endothelial injury and prevent further hepatocyte death and platelet activation. While evidence of maternal improvement is limited, studies have demonstrated improved laboratory findings, including improved platelet

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counts, liver function, blood pressure, and urine output with the use of high-dose dexamethasone[9]. Intravenous glucocorticoids appear superior to intramuscular steroids and are dose-dependent. Therefore, aggressive therapy with high-dose dexamethasone has been recommended over the standard regimens used for enhancing fetal lung maturity[10]. A meta-analysis concluded that the cases of HELLP syndrome receiving steroids particularly dexamethasone showed significantly greater improvement in platelet counts and lowering of MAP than those receiving betamethasone[11].A randomized trial conducted on 40 cases showed that with betamethasone (n=21), the mean decrease in MAP was 8.1±1.4mmHg which was significantly less than mean decrease in MAP (15.6±1.4mmHg) with dexamethasone (n=19)[12]. One more randomized trial conducted on 36 cases showed that with betamethasone (n=18), the mean decrease in MAP was 7.5±1.4mmHg which was significantly less than mean decrease in MAP (15.3±1.4mmHg) with dexamethasone (n=18)[13].

Rationale of our study was to compare the mean decrease in mean arterial pressure with dexamethasone verses betamethasone for managing females presenting with postpartum HELLP syndrome at term by keeping the fact in mind that HELLP syndrome after delivery is also hazardous for females.

In routine, corticosteroids like dexamethasone, betamethasone e.g. are available to control blood pressure in females with HELLP syndrome. But no local data is available which can help in implementation of better drug,moreover, the previous studies were done on very small sample size. We conducted this study on large sample size to get more reliable and precise results, so that we may be able to plan better management protocols for HELLP syndrome. Which will help to update local guidelines for management of such critical cases.

MATERIAL AND METHODS

ThisRandomized Controlled Trial was conducted at Department of Obstetrics & Gynecology Unit III, Lady Willingdon Hospital/KEMU Lahore, for a duration of one year from 1.1.2016 to 31.12.2016.Total of 100 cases were recruited by non-probability, consecutive sampling technique; 50 cases in each group were calculated with 95% confidence level, 80% power of test and taking magnitude i.e. mean±SD of mean decrease in MAP i.e.15.3±1.4mmHg with dexamethasone and 7.5±1.4mmHg with betamethasone for management of females presenting with postpartum HELLP syndrome at term.

Inclusion Criteria: Females of age 20-40years, parity<6, at gestational age >37 weeks (on LMP) with postpartum HELLP syndrome (hemolysis on peripheral blood smear with serum lactate dehydrogenase >600 IU/L; serum AST>70 IU/L; and platelet count <100,000/µ L)

Exclusion Criteria

1. Multiple pregnancy (on USG)
2. Allergy to any content of trial drug
3. Females with eclampsia (convulsions with PIH), and with RFTs (serum creatinine>1.2mg/dl),having anemia (Hb<10mg/dl).

After approval from ethical committee of the hospital, 100femalesfulfilling selection criteria wereenrolled through post-delivery wards of Department of Obstetrics & Gynecology, Lady Willingdon Hospital, Lahore. Informed consent was obtained. Demographic profile (name, age, parity, gestational age at delivery) were also noted. Females were randomly divided in two groups by using lottery method. Baseline MAP was recorded. In group A, 10mg dexamethasone sodium phosphate IV every 12 hrs.was given while in group B, 12mg combination of betamethasone acetate and betamethasone sodiumphosphate IM every 24 hrs. Then patients were followed-up for48 hours for assessment decrease in MAP (as per operational definition). All this information was recorded on research proforma.

The collected data was entered and analyzed statistically by using SPSS version 20. Quantitative variables like age, gestational age at delivery, MAP baseline and after 48 hours, decrease in MAP and parity was presented in form of mean ± S.D. Qualitative variables like parity, was presented in form of frequency and percentage. Both groups were compared for mean decrease in MAP by using independent sample t-test. Data was stratified for age, gestational age and parity. Stratified groupwas compared by using independent sample t-test taking p-value<0.05 as significant.

RESULTS

Mean age of women in Group-A and in Group-B was 29.38±5.24 and 31.68±6.30 years respectively. Minimum and maximum age of women in both treatment groups was 21 and 40 years respectively can be seen in Tabel-1.

Mean gestational age of women in Group-A and in Group-B was 39.66±1.133 and 39.66±1.11weeks. Minimum and maximum gestational age of women in both treatment groups was 38 and 41weeks respectively (Table2)

Regarding parity, in Group-A there were 12(24%) females were primiparas, 17(34%) had parity 1, 15(30%) had parity 2, 4(8%) had parity 3

and only 2(4%) women had parity 4. In Group-B there were 10(20%) females were primiparas, 14(28%) had parity 1, 12(24%) had parity 2, 8(16%) had parity 3 and only 6(12%) had parity 4 (Table-3).

Baseline mean arterial pressure in Group-A and in Group-B was 120.60±6.36 and 120.30±5.66. After 48 hours mean arterial pressure in Group-A and in Group-B was 72.52±4.52 and 89.94±5.69. From baseline till 48 hours mean decreases in Group-A and in Group-B was 48.08%±7.78 and 30.36%±8.24 respectively. As per p-value statistically significant difference was seen for arterial pressure in both treatment groups. Percentage reduction in mean arterial pressure was significantly higher in Group-A as compared to that of Group-B(Table4).

Women in the age group 21-30 and 31-40 years in both these group reductions in mean arterial pressure was significantly higher with dexamethasone as compared to that of betamethasone. i.e., 21-30 years; Group-A: 48.83% vs. Group-B: 31.40%, p-value=0.000& 31-40 years; Group-A: 47.05% vs. Group-B: 29.32%, p-value=0.000 respectively (Table5).

Women with gestational age 38-39 weeks and 40-41weeks, among them reduction in mean arterial pressure was significantly higher with dexamethasone as compared to that of betamethasone. i.e., 38-39weeks; Group-A: 49.26% vs. Group-B: 30.85%, p-value=0.000 &40-41weeks; Group-A: 47.07% vs. Group-B: 30.03%, p-value=0.000 respectively (Table-6).

Among primiparas, reduction in MAP was significantly higher with dexamethasone as compared to that of betamethasone i.e., Group-A: 50.08±8.43% vs. Group-B: 29.30±8.45%, p-value=0.000. Similarly, among multiparous, reduction in MAP was significantly higher with dexamethasone as compared to that of betamethasone i.e. Group-A: 47.45±7.58% vs. Group-B: 30.63±8.29%, p-value=0.000. (Table-7)

Table 1: Age distribution of women

	Group-A	Group-B	Total
N	50	50	100
Mean	29.38	31.68	30.53
SD	5.245	6.307	5.89
Minimum	21	21	21
Maximum	40	40	40

Group-A= Dexamethasone Group-B= Betamethasone

Table2: Gestational age of women

	Group-A	Group-B	Total
N	50	50	100
Mean		39.66	39.66
SD	1.136	1.118	1.12
Minimum	38	38	38
Maximum	41	41	41

Group-A= Dexamethasone Group-B= Betamethasone

Table3: Parity Status of women

Parity	Group-A	Group-B	Total
0	12(24%)	10(20%)	22 (22%)
1	17(34%)	14(28%)	31 (31%)
2	15(30%)	12(24%)	27 (27%)
3	4(8%)	8(16%)	12 (12%)
4	2(4%)	6(12%)	8 (8%)
Mean±SD	1.34±1.06	1.72±1.29	1.53±1.19

Group-A= Dexamethasone Group-B= Betamethasone

Table4:Mean Arterial Pressure at Base Line &at 48 Hours

	Base Line		48 Hours		% Decrease	
	Group-A	Group-B	Group-A	Group-B	Group-A	Group-B
N	50	50	50	50	50	50
Mean	120.60	120.30	72.52	89.94	48.08%	30.36%
SD	6.36	5.66	4.52	5.69	7.78%	8.24%
Minimum	110	110	65	80	34%	11%
Maximum	130	130	80	100	64%	49%
p-value	0.804		0.000		0.000	

Group-A= Dexamethasone Group-B= Betamethasone

Table-5: Mean Arterial Pressure at Base Line &At 48 Hours in relation to age groups of women

AgeGroup	MAP	Groups	n	Mean±SD		p-value
21-30 Years	Baseline	Dexamethasone	29	121.00	6.024	0.959
		Betamethasone	25	121.08	5.314	
	48hours	Dexamethasone	29	72.17	4.972	0.000
		Betamethasone	25	89.68	5.970	
	% Decrease	Dexamethasone	29	48.83%	8.242	0.000
		Betamethasone	25	31.40%	7.303	
31-40 Years	Baseline	Dexamethasone	21	120.05	6.917	0.783
		Betamethasone	25	119.52	5.994	
	48hours	Dexamethasone	21	73.00	3.899	0.000
		Betamethasone	25	90.20	5.508	
	% Decrease	Dexamethasone	21	47.05%	7.166	0.000
		Betamethasone	25	29.32%	9.127	

Table6: Mean arterial pressure at base line & at 48 hours in relation to gestational age of women

Gestational age	MAP	Groups	n	Mean± SD		p-value
38-39 Weeks	Baseline	Dexamethasone	23	121.26	7.14	0.578
		Betamethasone	20	120.15	5.61	
	48hours	Dexamethasone	23	72.00	4.96	0.000
		Betamethasone	20	89.30	5.49	
	% Decrease	Dexamethasone	23	49.26	9.09	0.000
		Betamethasone	20	30.85	8.08	
40-41 Weeks	Baseline	Dexamethasone	23	120.04	5.69	0.813
		Betamethasone	20	120.40	5.78	
	48hours	Dexamethasone	23	72.96	4.16	0.000
		Betamethasone	20	90.37	5.86	
	% Decrease	Dexamethasone	23	47.07	6.47	0.000
		Betamethasone	20	30.03	8.47	

Table-7: Mean arterial pressure at base line & at 48 hours in relation to parity of women

Parity	MAP	Groups	n	Mean± SD		p-value
Primiparas	Baseline	Dexamethasone	12	122.25	6.02	0.505
		Betamethasone	10	120.60	5.23	
	48hours	Dexamethasone	12	72.17	5.18	0.000
		Betamethasone	10	91.30	6.68	
	% Decrease	Dexamethasone	12	50.08	8.43	0.000
		Betamethasone	10	29.30	8.45	
Multiparous	Baseline	Dexamethasone	38	120.08	6.46	.917
		Betamethasone	40	120.23	5.82	
	48hours	Dexamethasone	38	72.63	4.37	0.000
		Betamethasone	40	89.60	5.46	
	% Decrease	Dexamethasone	38	47.45	7.58	0.000
		Betamethasone	40	30.63	8.29	

DISCUSSION

Although a growing body of published studies and many years of clinical experience is leading toward confirmation of benefits of corticosteroid use for the treatment of patients with HELLP syndrome, an optimal corticosteroid agent and an optimal treatment regimen have not been conclusively demonstrated[14].

Dexamethasone has been the potent glucocorticoid used in the Mississippi trials investigating the stabilization of HELLP syndrome. Both betamethasone and dexamethasone are used for induction of fetal lung maturity, with betamethasone being used more commonly. Neither agent has significant mineralocorticoid activity and, therefore, should not promote sodium retention that could exacerbate hypertension or edema. Because most obstetricians appear to preferentially utilize betamethasone for fetal lung maturation which could be modified or extended to treat a maternal disease as HELLP syndrome[15].

In ourstudy, it was observed that mean reduction in arterial pressure was significantly higher in Group-A (Dexamethasone) women as compared to Group-B (Betamethasone) women. i.e.% reduction in MAP Group-A: 48.08% vs. Group-B: 30.36% respectively at 48th hours. (p-value=0.000). Same results were seen in different age groups of women that in age group 21-30 and 31-40 years Dexamethasone causes more reduction in mean arterial pressure at 48th hour as compared to that of Betamethasone % decreases in MAP (21-30 years) Group-A: 48.83% vs. Group-B: 31.40% & % decreases in MAP (31-40 years) Group-A: 47.05% vs. Group-B: 29.32% respectively. Similar trend was seen for women with different gestational age. % decreases in MAP (38-39 weeks) Group-A: 49.26% vs. Group-B: 30.85% & % decreases in MAP (40-41 weeks) Group-A: 47.07% vs. Group-B: 30.03% respectively. Ayla SARGIN ORUÇ recently in his study reported that relative to the control group, the mean arterial pressure became significantly decreased at 42 hours in the steroid-treated group (Dexamethasone). In the treatment group (Dexamethasone), MAP was found to be at or below 160/100 mmHg by 36 hours postpartum and after that moment MAP taken every 6 hours of the treatment group was significantly lower than the control group (p=0.0035 and p= 0.009 for postpartum 42nd and 48th hours respectively[16]. Results of their study confirm and support the that Dexamethasone more effectively decreases the MAP for maternal disease in women with HELLP.

Magann et al. who reported a significant improvement in MAP by 24 hours with corticosteroid therapy[17]. However, VigilDeGracia and Gracia Caceres failed to show a significant difference for

these parameters between the two groups[18].However,Magann advocated the use of Dexamethasone and Gracia Caceres did not for lowering of MAP in women suffering form HELP syndrome.

C.M. Isler compared the efficacy of dexamethasone and betamethasone to ameliorate the course of HELP syndrome. Reduction in mean arterial blood pressure was more pronounced in the dexamethasone group as compared with the betamethasone group(-15.3±1.4 mmHg vs.-7.5±1.4 mmHg, respectively, p-value<0.01). Patients in the dexamethasone group required less antihypertensive treatment than the betamethasone group(6% vs. 50%,p-value<0.01)[13].

C.M. Isler in his earlier study determined whether dexamethasone or betamethasone is superior for the antepartum treatment of HELLP. As per his findings the improvement noted in MAP was significantly more pronounced (P< .001) among patients who received dexamethasone intravenously (–15.6±1.4mmHg) than among those in the intramuscularly administered betamethasone group (–8.1±1.4 mm Hg)[12].

Results of both studies by CM Isler showed dexamethasone to be more effective for controlling MAP as compared to that of betamethasone. Results of our study are also in line and findings of CM Isler.

Better and effective management of MAP in women with HELP syndrome not only accelerates the recovery, however it is also very effective and important to avoid the potentially increased maternal mortality and morbidity in clinical setting. Additionally, it shortens the intensive care period which may help reduce overall health costs so keeping in minds these benefits it can be recommend that the use of dexamethasone give better results.

CONCLUSION

Based on the findings of this study it can be concluded that the decrease in mean arterial pressure with dexamethasone is significantly higher than that of betamethasone for management of females presenting with postpartum HELLP syndrome at term.

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