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Comparison of Hyperglycemic Effects of Antenatal Administration of Dexamethasone in Gestational Diabetes: A Study of Recommended Versus Predicted Split Doses Regimens

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ABSTRACT

Objective: To compare three consecutive days of hyperglycemic response following antenatal Dexamethasone regimens of 12mg or 6mg in diet-controlled gestational diabetes, administered for fetal lung maturity.

Study Design: Quasi-experimental study

Place and Duration of Study: Department of Obstetrics and Gynaecology, Combined Military Hospital, Kharian Pakistan, from Oct 2020 to Mar 2021.

Methodology: Forty women who met inclusion criteria were selected and assigned to two Groups. Group-A was administered quartered 24 mg steroids 6 hours daily, and Group-B was administered halved 24mg 12 hours daily. Blood sugar levels (BSL) were recorded before and after meals, thrice a day for three consecutive days, and on proforma.

Results: Among the selected patients, the mean age was 25.5±2.9 years, and the mean gestational age (duration of pregnancy) was 30.3±2.0 weeks. Out of six blood sugar levels recorded daily for three consecutive days, the episodes of hyperglycemia in the (Group-B) 12-hourly steroid dose were found to be less significant than those in the (Group-A) split 6-hourly dose.

Conclusion: The recommended 12 mg, twice-a-day regimen of antenatal corticosteroids was better than the proposed 6mg, four times a day regimen as it caused fewer hyperglycemic episodes in gestational diabetics.

Keywords: Dexamethasone, Gestational Diabetes Mellitus, Preterm Labour, Respiratory distress.

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INTRODUCTION

Prematurity is one of the leading causes of neonatal deaths, accounting for about 24-28% of neonatal deaths.[1] Antenatal synthetic corticosteroids were first administered by Liggins and Howie in 1972.[2] They demonstrated that steroid treatment has beneficial effects on reducing the incidence of respiratory distress syndrome (RDS), necrotizing enterocolitis, and retinopathy of prematurity in preterm neonates.[3]

The International Association of Diabetes and Pregnancy Study Groups Consensus Panel (IADPSG) has defined the fasting blood sugar levels of >94mg/dl, 01 hours post-prandial 180 mg/dl and 02 hours post-prandial 153 mg/dl as maternal hyperglycemia.[4] 24+0 to 34 weeks of gestation is the period at which NICE and UK guidelines recommend maternal corticosteroids, and should be offered between 34 to 35+ six weeks of pregnancy if there is an expected, diagnosed or established preterm labour.[5,6]

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Maternal hyperglycemia is associated with increased morbidity and mortality among newborns,[7] namely delayed surfactant synthesis at any gestational age and reduced fluid clearance from the neonatal lungs, thus leading to respiratory distress syndrome and transient tachypnea of newborns, respectively.[8,9]

Our study aimed to compare antenatal steroid-induced hyperglycemic effects of the two regimens given in gestational diabetic women at risk of having preterm delivery to prevent neonatal respiratory distress. One of these is a 4-dose regimen of 6 mg Dexamethasone, 6 hours apart, also called a predicted split-dose regimen, recommended by the American College of Obstetrics and Gynaecology.[10] The other one is a 2-dose regimen of 12mg Dexamethasone, 12 hours apart, the dose recommended by NIH.

METHODOLOGY

The quasi-experimental study was conducted at the Department of Obstetrics and Gynaecology, Combined Military Hospital, Kharian Pakistan, from October 2020 to March 2021 after the approval of the Ethical Review Board (Ref no 13). The sample size was

estimated using WHO sample size calculator by taking the previous gestational diabetes prevalence of 1 in 6.[11]

Inclusion Criteria: Women with gestational diabetes and having impending risk of preterm delivery after 28 weeks of gestation who completed a dose of Dexamethasone, were included.

Exclusion Criteria: Patients with gestational diabetes before 28 weeks of pregnancy and patients with gestational diabetes who received Dexamethasone complete dose or partial dose and had delivery within 24 hours were excluded.

Selected patients were explained about the aim and procedure of the study, both verbally and in writing, and randomly divided women into two Groups with 20 patients each (Figure).

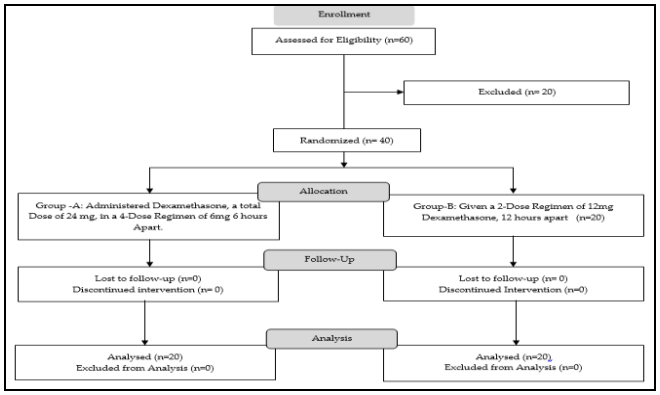

Figure: Patient Flow Diagram (n=40)

Group-A was administered Dexamethasone, a total dose of 24 mg, in a 4-dose regimen of 6mg 6 hours apart. Group-B was given a 2-dose regimen of 12mg Dexamethasone, 12 hours apart. The patient monitored six glucose levels using their glucometers, including fasting glucose, two pre-meal glucose, and three one-hour post-meal levels for three consecutive days. The average of three levels (fasting and two pre-meals) glucose levels were calculated daily and recorded. Similarly, an average of 3 one-hour post-meal glucose levels were calculated and recorded. The percentage of women with fasting blood glucose of >94.5 mg/dl and the percentage of women with one-hour post-meal blood glucose >140mg/dl were calculated. The correction of episodes of hyperglycemia was carried out by using regular insulin according to a sliding scale in order to maintain the target glucose levels of less than 94.5 to 140 mg/dl (fasting and one-hour post-prandial, respectively).[12,13]

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Kolmogorov–Smirnov test and the Shapiro–Wilk test were applied to check the normality of the data. Mean±SD was calculated for continuous variables of normal data, and median (IQR) was calculated for non-normal data. Frequency and percentage were calculated for categorical variables. The Mann-Whitney U test was used to determine the difference between Groups as the data deviated from the normal distribution. The *p*-value lower than or up to 0.05 was considered significant.

RESULTS

Selected forty patients were divided into Groups: Group A (4x6-mg) and Group B (2x12-mg). The mean age within the two Groups was 25.5±2.9 years, and the mean gestational age (duration of pregnancy) was 30.3±2.0 weeks, (Table-I).

Table-I: Descriptive Statistics of the Patients (n=40)

Characteristics	Dexamethasone Regimens	
	Group-A 4x6-mg (n=20)	Group-B 2x12-mg (n=20)
Gestational Age in weeks	28.3±2.8	30.5±2.9
Maternal Age in Years	25.5±2.9	27.5±3.0
Parity		
Nulliparous	3(15%)	2 (10%)
Parous>2	17(85%)	18(90%)
Body mass index kg/m²)		
<30	14(70%)	10(50%)
≥30	6(30%)	10(50%)
Patients-with raise Blood sugar Levels		
Normal	2(10%)	3(15%)
D1	6(30%)	7(35%)
D2	8(40%)	5(25%)
D3	4(20%)	5(25%)
Indications for Dexamethasone		
Preterm Labor	6(30%)	1(5%)
Reduced Fetal Movement	1(5%)	3(15%)
PPROM	1(5%)	1(5%)
Oligohydramnios	2(10%)	1(5%)
Others	10(50%)	12(60%)
Fetal Growth failure	0	2(10%)
Single or twin		
Single	19(95%)	20(100%)
Multiple	1(5%)	0

There was no significant difference in demography within the two Groups other than the Dexamethasone dosage regimen. Patients had complete three-day recordings of six blood glucose levels after antenatal Dexamethasone shots. Moreover, Table-II shows the recorded number of hyperglycemic episodes over three consecutive days. In the first 24 hours, out of six Blood Sugar Levels, there were

hyperglycemic episodes of 4 versus 4 for Group-A and Group-B, respectively.

Table-II: Episodes of Hyperglycemia in Study Groups in Three Days (n=40)

Number of Hyperglycemic Episodes	Dexamethasone Regimens		*p*-value
	Group-A 4x6-mg (n=20)	Group-B 2x12-mg (n=20)	
Primary Outcome			
First 24 hours	4(2.5-5)	4(3-5)	0.62
Second 24 hour	3(2–4)	1(0–3)	0.001
Third 24 hour	1(0–3)	0(0–1)	0.62
Secondary Outcomes			
Day 1-3	8(6–10)	6(4–8)	0.16

**Hyperglycemia at six blood sugar level (BSL) per day for Group A (4x6-mg) vs. Group B (2x12-mg) Dexamethasone regimen.*

The second day's blood sugar level showed hyperglycemia 3 episodes vs 1, a significant difference between the two regimens favouring fewer hyperglycemic episodes with Group-B than Group-A (*p*-value=0.001). One hyperglycemic episode was recorded in the Group-B on the third day. The total hyperglycemic episodes over the entire three days (18 points BSL) were eight versus 5 for Group-A (6 mg) and Group-B (12 mg), respectively. The point estimate favoured a 12-mg arm but was insignificant (*p*-value>0.05).

DISCUSSION

The use of antenatal corticosteroids for fetal maturation is a rare example of a technology that yields substantial cost savings and improves health.[14,15] The diabetogenic effect of corticosteroids is well acknowledged by the majority, if combined with placental insulin resistance in pregnancy, leads to a momentary increase in the blood glucose levels of pregnant women.[16] So, its cautious use is recommended in diabetic pregnant women.[17]

Our study followed a clear criterion in selecting the women with GDM who were at risk of preterm delivery. The index study identified the hyperglycemic effects of 2 different dose regimens of antenatal steroids given to women with gestational diabetes. The most noteworthy finding is that the 4x6-mg Dexamethasone regimen caused a marginally higher hyperglycemia response on the second day after therapy, followed by recovery to baseline by the third day of therapy. One study found similar results 23-38 hours after administration of the first dose of Dexamethasone.[18] This finding was also reported by Sukarna *et al*. in a randomized control trial in which they compared the two regimens.[19] The 4x6-mg regimen, on the other hand, showed a slightly lower hyperglycemia on the first day, followed by a prolonged hyperglycemia on the second day and a return to baseline on the third day. Few other studies have reported this finding as well.[20,21]

There was no significant difference in other maternal parameters between the two regimens of antenatal steroids. Our study is the first in Pakistan to compare the two antenatal Dexamethasone regimens. As discussed above in the NICE guidelines, ACOG recommends a 2x12 mg schedule as a better antenatal steroids regimen in preterm birth; similarly, our study confirms a lower hyperglycemic effect than the 4x6 mg regimen. Moreover, the patient's compliance could be improved as the number of injections was reduced.

LIMITATION OF STUDY

Our study had a limited number of patients and was done at a single centre, so it reduces its generalizability. Further studies may be done to differentiate the efficacy of the two regimens, and the differences in neonatal outcomes among the two Groups could also be evaluated.

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CONCLUSION

We conclude that the 12 mg, twice-a-day regimen of antenatal Dexamethasone is better than the 6mg, four times-a-day regimen as it causes fewer hyperglycemic episodes in gestational diabetic women.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SP & SB: Data acquisition, data analysis, critical review, approval of the final version to be published.

SR & NI: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

RR & IR: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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