ORIGINAL RESEARCH

A Study on the Effect of Antenatal Corticosteroids on Glycemic Response in Preterm Patients

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Abstract

Aim: Antenatal corticosteroids (ACS) are recommended for use in antenatal mothers at risk of preterm delivery before 34 weeks. One common side effect is the propensity to cause hyperglycemia. Our study aimed at characterizing glycemic response to betamethasone in preterm women and compared this response in patients with gestational diabetes mellitus (GDM) and those without GDM.

Materials and methods: After ethical clearance, 160 preterm antenatal patients who required ACS were included between 28- and 34-week periods of gestation. They were allotted into two groups: those with GDM and those without GDM. Fasting blood sugar (FBS) and postprandial blood sugar (PPBS) were followed for 4 days after betamethasone administration.

Results: A total of 54.65% showed an elevated FBS in the normal group on D2 and this reduced to 29.53% on D4 and 19.76% on D5. Similarly, PPBS was elevated in 54.65% on D2 and reduced to 26.7% on D4 and 13.95% on D5, whereas in the GDM group, FBS remained elevated on D2–D4 in 77.02, 81.08, and 71.62%, respectively, and started showing a downward trend with 45.94% on D5. Similarly, PPBS was elevated in 78.38, 77.03, and 67.57% on D2–D4, respectively, and reduced slightly to 56.76% on D5.

Conclusion: Our findings highlight the need for monitoring the glycemic levels even up to 5 days after ACS administration.

Clinical significance: With the increasing prevalence of GDM in antenatal mothers in India, this study highlights the need for more stringent glucose monitoring after steroid administration and also the need for protocols on the frequency of monitoring and dosage of insulin regimen.

Keywords: Antenatal corticosteroids, Gestational diabetes mellitus, Preterm.

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Introduction

Antenatal corticosteroids are an effective prenatal intervention for the reduction of perinatal morbidity and mortality related to preterm birth.

Antenatal corticosteroids were first recommended for use in the National Institutes of Health (NIH) Consensus Development Conference statement 1995.[1]

The need for ACS in preterm women likely to have a preterm birth, particularly those with gestational diabetes mellitus is more pronounced in modern-day obstetrics as they are at a higher risk of developing obstetric and neonatal complications. Use of glucocorticoids, either dexamethasone or betamethasone, in these antenatal women prevents respiratory distress in infants and lowers the risk of hyaline membrane disease in them.

Gestational diabetes is not considered a relative contraindication for corticosteroid administration. On the contrary, women with gestational diabetes, according to a study conducted in Canada[2] were more likely (odds ratio 1.21; 95% confidence interval 1.05–1.40) to receive ACS. Hyperglycemia which is a frequent side effect though is a cause for concern.

The increased risk of diabetes among those receiving long-term glucocorticoid therapy is documented,[3,4] but the effect of a few doses of corticosteroids on glucose metabolism is less documented, particularly in pregnant women who are already at a risk of glucose intolerance.

Glucocorticoids induce insulin resistance by inhibiting glucose uptake and reducing storage.[5] The glycemic effect of steroids has been documented to begin about 12 hours after the first dose and last up to 5 days.[6] Some studies have suggested that the effect of steroids on glucose level in nondiabetic women lasts 24 hours.[7]

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There is a 60% increase in the need for insulin in the third trimester owing to insulin resistance as compared to pre-pregnancy level. Almost all diabetics will experience a derangement in glycemic values despite care and will require initiation of insulin or an increase in dose.

National Institute for Health and Care Excellence (NICE) guidelines recommend that diabetic women receiving steroids should have additional insulin according to a preformed protocol.[8] Indian guidelines on inpatient management of diabetes recommend a 20% increase in the dose of insulin in diabetics who receive steroid therapy.[7]

An increase in insulin doses of at least 30–50% (average of 40%) is usually required.[9]

This study was thus aimed to characterize the maternal glycemic response to betamethasone in preterm patients and to compare

the maternal glycemic response in patients with GDM and those without GDM.

Materials and Methods

A prospective observational study was conducted on 160 patients admitted to the antenatal ward of Father Muller Medical College, Mangaluru, over a period of 20 months after obtaining ethical clearance.

Inclusion Criteria

All antenatal primigravid mothers between 28 and 35 weeks of gestation admitted to the antenatal ward of Father Muller Medical College and who required betamethasone in view of possibility of preterm birth are included in the study.

Exclusion Criteria

Patients with multiple gestation, those presenting with PPROM and those <28 weeks and >35 weeks POG are excluded from the study.

All antenatal women who received corticosteroids for the enhancement of fetal pulmonary maturity during an inpatient admission were selected. They were divided into two groups:

- Group I: Women with no GDM/pre gestational diabetes mellitus (PreGDM)
- Group II (a): Women with GDM on medical nutrition therapy (MNT)
- Group II (b): Women with GDM on oral hypoglycemic agents (OHA)
- Group II (c): Women with GDM on insulin
- Group II (d): Women with PreGDM.

Patients were considered as nondiabetics if the oral glucose challenge test (OGCT) value during routine antenatal visits was <140 mg%. Patient was considered as having GDM if they had two values of oral glucose tolerance test (OGTT) elevated. MNT was given in the form of split meals explained by the dietician in the hospital.

Data recorded included maternal age, gestational age, indication for steroids, and fasting and 2-hour postprandial serum glucose levels. Data collection began on the first day of steroid administration and continued for another 4 days. The day the first dose of corticosteroid was administered was designated day 1 (D1). Steroids were given on D1 and D2. Regular fetomaternal surveillance along with routine obstetric care was continued for all patients till discharge.

Statistical Analysis

Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) package.

Results

This study was conducted on 185 antenatal patients admitted to Father Muller Medical College to receive betamethasone injection.

However, as all the fasting blood sugar and postprandial blood sugar (PPBS) values for all 4 days were not available for 25 patients, they were excluded from the study.

So a total of 160 patients were included for analysis, of which 86 were in Group I and 74 in Group II (Table 1).

In Group I, elevated FBS was seen in 54.65% cases on D2, 59.3% on D3, reduced to 39.53% on D4, and 19.76% on D5.

In Group II (a), elevated FBS was seen 83.3% cases on D2, 75% on D3, 62.5% on D4, and reduced to 41.6% on D5.

In Group II (b), elevated FBS was seen 83.3% cases on D2 and D3, 75% on D4, and reduced to 33.3% on D5.

In Group II (c), elevated FBS was seen 66.6% cases on D2, 83.3% on D3, 75% on D4, and 54.2% on D5.

In Group II (d), elevated FBS was seen 78.57% cases on D2, 87.71% on D3, 78.57% on D4, and 50% on D5 (Table 2).

In Group I, elevated PPBS was seen in 54.65% cases on D2, 46.5% on D3, reduced to 26.7% on D4, and 13.95% on D5.

In Group II (a), elevated PPBS was seen 75% cases on D2, 66.6% on D3, 50% on D4, and reduced to 54.15% on D5.

In Group II (b), elevated PPBS was seen 66.6% cases on D2, 83.3% on D3, 75% on D4, and reduced to 50% on D5.

In Group II (c), elevated PPBS was seen 83.3% cases on D2, 75% on D3 and D4 and 58.3% on D5.

In Group II (d), elevated PPBS was seen 87.71% cases on D2, 92.86% on D3, 78.57% on D4, and 64.3% on D5 (Table 3).

Insulin was started in 14 out of 86 patients of Group I (16.27%), of which 2 had to continue insulin at discharge.

Three out of 24 (12.5%) patients with GDM on MNT, 8 out of 12 (66.66%) patients with GDM on OHA had to be started on insulin.

None on MNT needed insulin at discharge, however, 6 from the group on OHAs needed to continue insulin.

Out of the 24 patients already on insulin, the dose had to be increased for 16 patients (66.66%), and for 8, it remained the same (33.33%).

Table 1: Distribution of cases

	No. of subjects
No GDM/PreGDM	86 (53.75%)
GDM on MNT	24 (15%)
GDM on OHA	12 (7.5%)
GDM on insulin	24 (15%)
PreGDM	14 (8.75%)
Total	160

Table 2: Distribution of cases according to elevated FBS

	D2	*D3*	*D4*	*D5*	*Total*
Normal	47	51	34	17	86
GDM on MNT	20	18	15	10	24
GDM on OHA	10	10	9	4	12
GDM on insulin	16	20	18	13	24
PreGDM	11	12	11	7	14
Total					160

Table 3: Distribution of cases according to elevated PPBS

	D2	*D3*	*D4*	*D5*	*Total*
Normal	47	40	23	12	86
GDM on MNT	18	16	12	13	24
GDM on OHA	8	10	9	6	12
GDM on insulin	20	18	18	14	24
PreGDM	12	13	11	9	14
Total					160

Out of the 14 patients with PreGDM, the dose of insulin had to be increased for 9 patients (64.28%), while 5 (35.71%) continued with the same dose.

Discussion

Antenatal corticosteroids are recommended to women at risk of preterm births and should be administered between 24 and 34 weeks. Women with GDM are at an increased risk to deliver preterm either spontaneous or induced.[10]

In our study, 54.65% showed an elevated FBS in the normal group on D2 and this reduced to 29.53% on D4 and 19.76% on d5. Similarly, PPBS was elevated in 54.65% on D2 and reduced to 26.7% on D4 and 13.95% on D5, whereas in the GDM group, FBS remained elevated on D2–D4 in 77.02, 81.08, and 71.62%, respectively, and started showing a downward trend with 45.94% on D5. Similarly, PPBS was elevated in 78.38, 77.03, and 67.57% on D2–D4, respectively, and reduced slightly to 56.76% on D5.

Renuka et al.[11] in their study noted that postprandial sugar levels started rising from day 2 after betamethasone administration and became normal on day 3 and 4 in 46% and on day 6 in 80%. Fasting sugar levels started rising from day 2 with 56% reaching normalcy on day 3 and 4 and 74% on day 6.

They, however, did not differentiate between diabetics and nondiabetics.

In a study by Beena et al.,[12] 62 out of 105 (66%) patients had an elevated FBS and PPBS on D2. A total of 62.9% of patients without GDM required insulin after ACS. About 71.4% of patients of GDM on OHA and 82.5% of patients of GDM on MNT required insulin. Out of 35 patients who were in GDM on insulin group, 23 patients received a higher dose of insulin, and out of 12 in overt DM, 9 patients received a higher dose of insulin.

Of the 66 patients who started on insulin in the non-GDM group, 17 (16.2%) patients had to continue insulin and out of 33 in MNT subgroup 10 (25%) had to continue with insulin at the time of discharge.

Our study too showed similar results with 54.65% of patients without GDM showing elevated FBS and PPBS on D2. However, in our study only 16.27% of patients without GDM and 12.5% of patients with GDM on MNT required insulin to be started which was much lower than that according to Beena et al. For those on OHA, however, similar rates were noted, 66.66% in our study as against 71.4%.

In a retrospective study by Kreiner et al.,[13] the impact of ACS on FBS and PPBS was measured. Fasting blood sugar >95 mg% was elevated in over 90% of women on day 2 and day 3 after ACS administration. At least one PPBS value was elevated (>120 mg%) in 81–98% of women on days 1 to 3. Out of 55 patients with GDM who received ACS, insulin had to be started in 11 of 19 women who were controlled on MNT and in 3 of 6 patients on OHA.

Ramirez-Torres,[14] however, in their study did not show hyperglycemia in 10 healthy pregnant women volunteers, acting as a control group who received 12 mg betamethasone twice daily for one day. In their study, they noted that patients with GDM managed by MNT alone required insulin in 40% cases, those already on insulin needed an increase of 39–112% in the daily insulin dose and women with PreGDM needed a 26–64% increment in insulin dose.

Beena et al.[12] in their study noted a continued rise in FBS and PPBS in 13.5 and 15.2%, respectively, of normal patients and 23.76 and 25.74%, respectively, in the GDM group. Compared to our study, we demonstrated a higher increase in PPBS levels at discharge. About 19.76 and 45.94% rise in FBS in normal and GDM group, respectively, and 13.96 and 56.75% rise in PPBS in normal and GDM group, respectively. In another study, 34% had suboptimal FSG and 30% had suboptimal PPSG at the time of discharge or delivery.[15]

Conclusion

It has been proven that ACS improves neonatal survival in antenatal women at risk of preterm birth, many of whom may have coexisting GDM. Our findings highlight the need for regular glycemic monitoring in addition to regular fetomaternal surveillance for at least 5 days after ACS administration. Frequency and nature of monitoring required may vary depending on the nature of diabetes.

Although there is no recommendation to check blood glucose prior to administration of ACS, we recommend random blood glucose check prior to ACS administration.

Medical nutrition therapy should be reinforced in all patients receiving ACS, irrespective of prior glycemic status.

Insulin therapy may be required for a short period, after ACS therapy, even in women who were previously well controlled on MNT. It may also be prudent to increase the dose of insulin even before hyperglycemia is documented. The dose may need to be individualized.

Limitations

We did not calculate the increase in insulin dose required after ACS administration. A longer period of follow-up would have indicated when the glucose levels got back to normal levels, but was not feasible as patients were not willing for prolonged inpatient stay.

Clinical Significance

An increasing number of patients with GDM present these days to the obstetrician, more so those requiring ACS. In the absence of specific guidelines and protocols on frequency of monitoring glucose levels and dosage increase in insulin and mode of administration, management of these patients becomes difficult. Our study attempts at identifying a pattern in glycemic response to steroids to enable protocols to be formed in this respect.

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