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The Effect of Antenatal Corticosteroid on Fetal Lung Volume in Preterm Fetuses

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Abstract

Background: Prenatal corticosteroids help the fetus's lungs develop properly so that it can breathe air. Induction of proteins and enzymes, such as enhanced tissue and alveolar surfactant production, is the best-known method by which corticosteroids exert their effects. Preterm infants who get a single course of corticosteroids during respiratory distress syndrome (RDS), intraventricular hemorrhage, necrotizing enterocolitis, and death are reduced in pregnant females.

Aims and objectives: To look into the effects of antenatal corticosteroids on preterm fetal lung volume.

Patients and methods: According to the results of this research, case–control research with a prospective observational design at Al Hussein, Bab Al-Sharia, and Al-Azher University Hospitals during the period from March 2022 to May 2023.

Results: Distribution of the study sample by cases with preterm premature rupture of membranes (PPROM), previous history of preterm labor, gestational age (G.A.) at delivery, preterm birth, neonatal outcome, and comparison of total fetal lung volume before and two weeks later contrasted substantially among the studied groups. The average maternal age did not differ significantly across the groups, BMI (kg/m²).

Conclusion: Antenatal corticosteroids have a significant effect on fetal lung volume when given prophylactically to pregnant women known to have increased risk of preterm labor. The three dimensional assessment of fetal lung volume measured using virtual organ computer-aided analysis (VOCAL) technique although it is a noninvasive test to detect increased lung volume after antenatal corticosteroid administration.

Keywords: Antenatal corticosteroid, Fetal lung volume, Preterm fetuses

1. Introduction

The greatest concern in the management of elective birth is fetal lung immaturity, which predicts the occurrence of neonatal respiratory distress syndrome after delivery. To prevent respiratory distress syndrome, it is optimal to predict the lung maturity of the prenatal fetus before birth and to ascertain the effect of steroid medication in preterm fetuses using a noninvasive method.¹ Increasing fetal lung surfactant synthesis and speeding up embryonic lung maturation are two goals of the prolonged administration of synthetic corticosteroids (betamethasone or dexamethasone) to women at risk of preterm birth.² Premature infants who are given corticosteroids have a lower risk

of developing respiratory distress syndrome, intraventricular hemorrhage, necrotic enterocolitis, and death.³

Respiratory distress syndrome (RDS) is the greatest cause of early newborn morbidity and mortality and a major contributor to the high expenses of intensive care for newborns because of poor lung development.⁴

Three-dimensional sonographic measures have been shown to be helpful for estimating lung volume in developing embryos. Recent three dimensional ultrasonography-based estimates of fetal lung volumes show promise as an alternative to MRI.⁵

This prospective observational analysis aimed to investigate the association between prenatal

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corticosteroids and neonatal respiratory distress and fetal lung capacity in preterm infants.

2. Patients and methods

This was a prospective observational investigation (case–control study) performed between March 2022 and May 2023 at Al Hussein, Bab Al-Sharia, and Al-Azher University Hospitals.

In total, 100 expectant women were divided into two groups: the research group and the control group. Within the research team, 50 pregnant females were selected with risk factors of preterm labor included (previous history of miscarriage, history of PROM, cerclage, and previous history of preterm labor), they received four intramuscular doses of 6 mg of dexamethasone 12 h apart at 30 gestational weeks, started on the day after initial assessment of fetal lung volume (FLV), while in the control group, 50 pregnant females were with risk factors of preterm labor but did not receive any antenatal steroid injections or placebo.

In total, 100 pregnant women were followed up by using 4D ultrasonography at thirty wks., measuring lung volume, and administration of corticosteroid; the cases followed every 2 weeks by 2d ultrasound and then the new 4D ultrasonography at 37 wks By measuring the lung volume.

2.1. Inclusion criteria of the cases

Age: 18–35 yrs, previous delivery by cs, gestational age: 24–37 wks, and risk of preterm birth such as previous history of miscarriage, history of PROM, cerclage, twins, polyhydraminous, and previous history of preterm labor and BMI 18–30.

2.2. Exclusion criteria of the cases

Age below 18 or above 35, patients below 24 or above 37 weeks, primigravida, and BMI below 18 or above 30.

2.3. Confidentiality

Females were identified by their names in the data collection sheet, which was kept in privacy by the investigator.

2.4. Methods

Cases were subjected to a comprehensive case history, examination (general, abdominal, and local clinical examination), and investigations. Ethical consideration: Institution Research Board (IRB) of Al

Azhar University's Faculty of Medicine had been submitted a research protocol for approval. Each participant who participated in the report provided verbal consent and confidentiality and personal privacy was maintained at all stages of the report.

2.5. Sample size

The study is based on research conducted by Schmid et al. Epi-Info STATCALC was used to determine the sample size for the study. The calculations considered a 95 % two-sided confidence level, a power of 80 %, and an α error of 5 %. The resulting sample size from the Epi-Info output was 46 patients in each group. However, to account for potential dropouts during follow-up, the sample size was increased to 50 subjects in each group.⁶

Ethical approval code was 00000430.

2.6. Statistical analysis

The collected data will be tabulated and statistically evaluated using SPSS (Statistical Package for the Social Sciences) version 20.0.

Table 1. Comparison of the mean ages and BMIs (in years and kilograms per square meter) of the two categories.

	Study group	Control group	P value (t-test)
Maternal age (y)	29.8 ± 7.2	29.7 ± 6.1	0.94 (NS)
BMI (kg/m ²)	24.7 ± 3.4	25 ± 4.1	0.6913 (NS)

There was no significant difference between the average ages of mothers in the experimental and control groups ($P > 0.05$). The body mass index of neither the experimental group nor the control group differed significantly ($P > 0.05$).

Table 2. PPRM cases were distributed throughout the entire study sample.

	Study group	Control group	P value (Chi square)
PPROM			
Yes	17 (34 %)	10 (20 %)	= 0.1167 ^a
No	33 (66 %)	40 (80 %)	

Data are expressed as (%) and P-value. PPRM, preterm premature rupture of membranes.

^a = statistically significant.

Table 3. Distribution of the research sample by cases with a history of premature birth.

	Study group	Control group	P value (Chi square)
Previous preterm labor			
Yes	33 (66 %)	5 (10 %)	<0.0001**
No	17 (34 %)	45 (95 %)	

Data are expressed as (%) and P-value.

* = statistically significant.

Table 4. Comparison among both groups as regards gestational age at delivery.

	Minimum	Maximum	Mean \pm SD	P value (t-test)
Study group	30 WK	37WK	33.8 \pm 3.9	=0.047* S
Control group	30 WK	37 WK	35.1 \pm 2.4	

Table 5. Comparison among both groups as regards preterm birth.

	Study group	Control group	P value (Chi square)
Preterm birth			
Yes	12 (24 %)	10 (20 %)	<0.0910
No	38 (76 %)	40 (80 %)	

Data are expressed as (%) and P-value.

* = statistically insignificant.

Table 6. Statistical comparison of neonatal outcomes among both of the studied groups.

Item	Study group	Control group	P value (Chi square)
APGAR score			
>7	48 (96 %)	30 (60 %)	<0.0001**
\leq 7	2 (4 %)	20 (40 %)	
R.D.S.			
Not present	48 (96 %)	30 (60 %)	=0.0002**
Grade I	0	10 (20 %)	
Grade II	2 (4 %)	8 (16 %)	
Grade III	0	2 (4 %)	
Admission to the NICU			
Not admitted	48 (96 %)	30 (60 %)	<0.0001**
Admitted	2 (4 %)	20 (40 %)	

Data are expressed as (%) and P value.

* = statistically significant.

Descriptive statistics were calculated for numerical parametric data as the mean, standard deviation (SD), and minimum and maximum of the range; for numerical nonparametric data as the median and first and third interquartile ranges; and for categorical data as the number and percentage.

Inferential studies for quantitative variables were performed using the independent t-test for two

independent groups with parametric data and the Mann–Whitney U test for two separate groups with nonparametric data. The χ^2 test for independent groups was used to draw inferences from qualitative data. P less than 0.050 was established as the level of significance, otherwise, the result was declared inconsequential. The P-value is a statistical estimate of a possibility that an experiment's observed results are coincidental (Tables 1 and 2).

3. Results

This table reveals a highly significant statistical difference between the preterm premature rupture of membranes (PPROM) rates of the study group (34 %) and the control group (0 %), with PPROM being a preterm labor risk factor for 17 (34 %) of the expectant women in the research group ($P > 0.05$) (Table 3).

This table demonstrates that expectant women in the study group had a history of previous preterm labor as a risk factor for preterm labor, with a notable increase in the prevalence of previous preterm labor in the study group. There was a statistically significant difference between the research group and the control group ($P < 0.0001$) (Table 4).

This table shows that there was a significant statistical decline in gestational age at delivery in study group compared with the control group ($P < 0.05$) (Table 5).

This table shows 12 (24 %) preterm births in the research group and 10 (20 %) in the control group. There was a high statistically insignificant difference in preterm birth in the research group compared with control ($P < 0.0001$) (Table 6).

This table demonstrates that the APGAR score in the research group increased markedly compared with the control group ($P < 0.0001$). In the group that was studied, there was a considerable decline in RDS and neonatal intensive care unit (NICU)

Table 7. Comparison of total fetal lung volume before and 2 weeks later.

Sample type	Study group	Control group	P value (t-test)
Fetal lung volume			
Initial total lung volume (cm ³) at 30 weeks	72.8 \pm 15.4	73.5 \pm 15.3	0.8201 (NS)
Total lung volume after two weeks (cm ³) at 32 weeks	82.5 \pm 14.8	75.3 \pm 15.4	0.019 ^a (S)
Total lung volume after two weeks (cm ³) at 34 weeks	84.7 \pm 14.2	77.6 \pm 15.8	0.017 ^a (S)
Total lung volume after two weeks (cm ³) at 36 weeks	86.7 \pm 16.8	79.6 \pm 19.6	0.019 ^a (S)

Data are expressed as mean \pm SD and P value.

^a = statistically significant.

admission rates compared with the control group ($P < 0.0001$) (Table 7).

This table shows that two groups did not differ significantly, the mean initial total lung volume in the research group 72.8 ± 15.4 and that in the control group 73.5 ± 15.3 . And clarified a significant difference across the mean total lung volume in the research group after 2 weeks at 32 weeks 82.5 ± 14.8 and that in the control group 75.3 ± 15.4 , with P value = 0.019. At 34 weeks, there was a significant increase in FLV 84.7 ± 14.2 and that in the control group 77.3 ± 15.8 , with P value = 0.017. At 36 weeks, there was rapid growth in FLV 86.7 ± 16.8 and that in the control group 79.6 ± 19.6 , with P value = 0.019. This denotes that antenatal steroid injection caused a significant increase in FLV, which was not seen in the control group.

4. Discussion

This study compared the control group's mean total FLV (range: 72.8 ± 15.4) to the report group's mean total FLV (range: 73.5 ± 15.3) at the same gestational age (30–37 wks) twice: once a week 24 (control: 72.8 ± 15.4) and again at week 26 (control: 75.3 ± 15.4). Evidenced by a substantial increase in the mean total FLV 2 weeks after dexamethasone administration that was not detected in the control group (75.3 ± 15.8) ($P < 0.001$), the report revealed a favorable effect of dexamethasone therapy on fetal lung volume in the report group.

According to the authors Schmid and colleagues this is the first prospective MR imaging study to examine the impact of prenatal corticosteroid medication on lung development in a group of 21 singleton infants at risk for preterm birth. Following antenatal corticosteroid treatment, researchers found an increase in lung–liver signal-intensity ratios but not in embryonic lung volume ($46.6 \pm 20.7 \text{ cm}^3$ vs. $48.8 \pm 16.0 \text{ cm}^3$, $P = 0.292$). They thought that assessing the lung volumes of neonates with MR imaging could only be an approximation at best. Furthermore, they found that a significantly larger sample size is required to detect a significant lung volume change due to the inaccuracy of planimetric assessment of total lung volumes. Before starting prenatal corticosteroid medication, we assessed the infants with a measurement of FLV and baseline imaging.⁶

4.1. The effect of antenatal corticosteroids on lung volume in premature neonates

The majority of studies examining the effect of dexamethasone on fetal lung maturity have

employed invasive techniques involving amniotic fluid, which reveals biochemical or histological alterations in the maturing lung.

Using a randomized trial, Shanks and colleagues said that pregnancies with confirmed fetal lung immaturity benefit greatly from prenatal corticosteroids given across weeks 34 and 37 (increase in TDx-FLM-II: 28.4 vs. 9.8 without therapy).⁷

Another report by Mulder and colleagues examined the effect of glucocorticoid medication. Lamellar body count, planimetric and stoichiometric lecithin–sphingomyelin ratio (L/S), and phosphatidylglycerol were the metrics used to examine the AF samples. Steroids were observed to improve lung maturity indicators across the board between 24 and 33 weeks of gestation, with the exception of phosphatidylglycerol.⁸

Maged and colleagues discovered that giving mothers prenatal steroids does not change the association between FLVs and neonatal respiratory distress. This may be because they measured the FLV only one time and compared it with pregnant females who did not take dexamethasone, depending on historical information of pregnant females in regard to receiving antenatal steroids during pregnancy, in addition, they included term of 37–40 weeks and late preterm of 34–36 fetuses, while in this research, FLV was measured twice, before taking dexamethasone injection, and a week later, in cases of preterm fetus 28–35 weeks.⁹

Premature newborns have a higher risk of having RDS because their brains have not fully developed.⁹ Our research denoted a significant decrease in the incidence of RDS and NICU admission at birth in the study group ($P = 0.019$). About 96 % of neonates in the study group had not developed RDS and needed NICU admission, while 40 % of neonates in the control group had developed RDS and needed NICU admission. This can be explained by the presence of risk factors for preterm labor in the control group that caused increased risk of preterm birth less than 36 weeks (the minimum GA was 30 wks) compared with the control group who had no risk of preterm labor, who continued to full-term, and only 15 % had delivered preterm birth with GA 36 wks.

According to Koivisto and colleagues it is also estimated that the incidence rate in newborns at 28 weeks of gestation is 80%, 60 % at 29 weeks, and 15–30 % at 32–34 weeks, although it reduces with age to 5 % at 35–36 weeks and virtually 0 % by 39 weeks of gestation.¹⁰

Our findings suggest that measuring 3D fetal lung capacity using the virtual organ computer-aided analysis (VOCAL) methodology is noninvasive but

cannot be an accurate method of diagnosing neonatal respiratory distress syndrome.

Maged and colleagues on the other hand, proposed that 3D FLV assessment using VOCAL software could be an accurate noninvasive predictor of the occurrence of newborn RDS. FLV had sensitivity and specificity of 46 and 94, respectively, and an area under the curve (AUC) was 0.701. They relied on 2 examiners to perform all ultrasound examinations, whereas our ultrasound examinations were performed by multiple examiners and, as previously mentioned, the timeline of measuring the FLV among 2 studies was different.⁹

However, VOCALTM tends to overestimate genuine values. According to Raine-Fenning et al.,¹¹ in addition, while the volume dataset is rotating, it may be difficult to discern the limits of certain structures, which could lead to inaccurate estimates from the edges of these buildings and incorrect volume estimates.^{1,12}

4.2. Conclusion

Antenatal corticosteroids have a significant effect on fetal lung volume when given prophylactically to pregnant women known to have increased risk of preterm labor. 3D assessment of fetal lung volume measured using VOCAL technique although it is a noninvasive test to detect increased lung volume after antenatal corticosteroid administration, it can be used as a method for predicting neonatal RDS among preterm fetuses.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

Conflicts of interest

The authors declared that there were NO conflicts of interest.

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