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ORIGINAL ARTICLE

Misoprostol Before Elective Cesarean Section to Reduce Transient Tachypnea of Newborn

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Abstract

Background: **The danger of respiratory diseases in the newborn, such as respiratory distress syndrome, is increased when the mother chooses to have the baby before 39 weeks of gestation through an elective cesarean section (ECS). Prostaglandins are helpful for the developing lungs because they stimulate the release of the stress hormone catecholamines, which in turn increases the production of the protective molecule surfactant. Nonetheless, the efficacy of antenatal preventive injections of prostaglandin is still debatable in clinical practice.**

Aim: **To assess the effectiveness of vaginal misoprostol in preventing transitory tachypnea in newborns before ECS.**

Patients and methods: **As a whole, 140 pregnant females who were listed to have an ECS at Al-Hussien University Hospital were recruited during antenatal care visits for this prospective randomized clinical research. They were split into two teams: the cases were separated into two groups: group I (misoprostol group; $n = 70$) contained females who were given a misoprostol vaginal tablet of 50 μg immediately before their ECS, and cases were divided into group II (no misoprostol group; $n = 70$), which consisted of women who were not given misoprostol.**

Result: **In comparison to the control groups, the vaginal misoprostol group saw a significantly lower incidence of tachypnea in newborns.**

Conclusion: **Ultimately, prophylactic vaginal misoprostol before ECS at 37–39 weeks of gestation decreases the rate of neonatal respiratory morbidity and may be an effective method to inhibit neonatal tachypnea in newborns.**

Keywords: Cesarean section, Misoprostol, Newborn, Tachypnea

1. Introduction

Worldwide, cesarean section (CSs) are performed more frequently than any other major surgical procedure on women.[1] In recent years, CS rates have skyrocketed all across the world, especially in high-income countries, leading some to worry about its excessive use.[2]

There is a double whammy for many nations because of CS.[3] Around 18.5 million CSs are performed annually around the world, with 21–33 % of all CS excess occurring in middle-income and high-income countries.[4]

Almost half of all deliveries are now performed via CS in middle-income nations, including Egypt, Turkey, Brazil, and Mexico. In a very recent analysis of medical records for all births that happened in April 2016 across 13 public hospitals in four governorates in Egypt (finding an overall CD rate of 54.2 %, ranging from 22.9 to 94.3 % among the different centers), researchers found that the CD rate varied greatly. Repeat CD was the most frequently reported medical condition (50 %), whereas 10 % had no underlying medical cause.[5,6]

Most frequently, a surgical site infection develops after CS, which raises the probability of maternal sickness or death. When compared with natural

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childbirth, CS increase the likelihood that the baby may experience trauma from being separated from his or her mother and from enduring invasive procedures like mechanical respiration.[7]

Approximately 27 % of newborns experience respiratory distress (RD), with the rate being higher for babies born via elective cesarean section ((ECS) than for those born via emergency CS or vaginally.[8] Newborns whose mothers undergo a CS before labor begins are in far greater danger of developing respiratory morbidity than those whose mothers undergo a CS during labor. A greater rate of respiratory morbidity was seen in kids born via ECS between 37 and 38 weeks of gestation. A higher hazard of pulmonary morbidity is associated with giving birth via ECS at 39 weeks of gestation compared with a planned vaginal delivery at 40 weeks.[9]

Tachypnea of more than 60 breaths per minute and other symptoms of RD characterize transient tachypnea of the newborn (TTN) (grunting, flaring of nostrils, and retraction of skin underneath or between the ribs when breathing). In late preterm newborns and term infants delivered by planned CS, the incidence of TTN might reach up to 13 %.[10]

Insufficient or delayed fetal lung fluid resorption into the pulmonary lymphatic system is regarded as the root cause of TTN. Neither the cause nor the development of TTN are well understood. The fetus's lungs transform from a fluid-secreting organ into an organ that absorbs fluid before and after birth. Hence, TTN may result from a lag in this physiological process.[11]

The absence of a physiological catecholamine rush and fluid retention in the lungs are possible causes of respiratory morbidity in cases of term elective cesarean deliveries, which differ from the pathophysiology of preterm deliveries. Intriguingly, recent research suggests that molecular processes (mostly lung epithelial sodium channels) promote alveolar fluid drainage and might be underactive in fetuses not exposed to the process of labor, in contrast to the conventional mechanical concept of a 'vaginal squeeze'.[12]

2. Patients and methods

A total of 140 pregnant females with planned ECSs were recruited during antenatal care visits at Al-Hussein University Hospital from the start of the study until its conclusion for a prospective randomized controlled clinical trial.

2.1. Inclusion criteria

One hundred and forty pregnant women who met the following criteria were involved in the research: maternal age between 18 and 40 years, singleton pregnancy, and a low-risk pregnancy between 37 and 39 weeks' gestation. The 140 women were divided into two groups. The misoprostol group included 70 pregnant females between the ages of 19 and 36 years with a median age of 25 years, and the control group included 70 pregnant females between the ages of 18 and 39 years with a median age of 26 years. No serious defects were present, and gestational age was affirmed using an early ultrasound measurement and the date of the last menstrual cycle in females with and without a history of CS.

2.2. Exclusion criteria

Causes for concern include: many pregnancies; fetal chromosomal abnormalities; a history of or current symptoms of chorioamnionitis; people with diabetes, placenta accreta, placenta previa, pregnancy complications, emergency CS, and sensitivity to or contraindication to prostaglandins in females all qualify as situations where these drugs should not be used.

All potential participants signed an informed consent form, had a thorough medical history obtained (including details about any complaints, pregnancies, menstrual cycles, previous surgeries, and family medical history), and underwent an abdominal examination before being considered for participation (inspection, palpation, and auscultation).

2.3. Cesarean section

It all started with a transverse incision made above the pubic area.

The next layer to be dissected was the subcutaneous one, and extreme caution was taken to prevent unnecessary blood loss by keeping incisions as close to the midline as possible until reaching the fascia and then proceeding with blunt dissections on the sides.

Midline incisions were made in the fascia, and these were subsequently extended laterally and dissected away from the rectus muscles. A clamp was used to progressively grab the fascia at its superior and inferior ends, and then dissection was performed using a combination of blunt and sharp techniques, such as scissors or cautery. It was taken into account that the rectus muscles lying beneath the skin could be harmed.

By cutting the midline rectus muscles, the peritoneum can be opened, allowing access to the abdominal cavity. The uterine incision was widened laterally to facilitate insertion into the uterus. By

placing a hand into the uterine cavity and lifting the fetus' head, we were able to bring the baby into the world with a vertex presentation. Using a vacuum cup or a single forceps blade, the fetus' head was lifted if this was not possible. The bladder blade was removed, and fundal pressure was used to force the fetus out of the uterus once the fetus' head had been lifted into the incision.

Feticide was performed by holding the fetus by the feet or hips if he was in breech presentation. In certain cases, a surgical towel was wrapped around the fetus to aid in the delivery, and gentle traction was used to bring the fetus to the level of the shoulders. A series of downward strokes were used to bring both arms together and complete the delivery. Following this, fundal pressure was applied to facilitate fetal head flexion and delivery. Umbilical cords are double-clamped and severed once a fetus is born. Two layers of the hysterotomy were sutured back together.

2.4. Ethical considerations

We made sure that the privacy of the patients was protected, and a written consent form was given to patients that granted us permission to proceed with the study.

2.5. Statistical analysis

SPSS (IBM SPSS statistics (Statistical Package for Social Sciences) software version 23.0, IBM Corp., Chicago, USA), version 23 was used for data entry, validation, and analysis. The consequences of this study were analyzed using the following statistical procedures:

Quantitative data were offered as mean ± SD, whereas qualitative data were presented as number and percentage.

3. Results

There is no statistically significant difference among vaginal misoprostol and control groups regarding maternal age, parity, or BMI (Table 1).

Infant heart rates and respiratory rates were statistically significantly lower in the vaginal misoprostol group than the control group (Table 2).

The vaginal misoprostol group has a statistically significant lower NICU admission rate than the control group (Table 3).

There is no statistically significant difference between vaginal misoprostol and control groups regarding APGAR scores (Table 4).

Table 1. Comparison between vaginal misoprostol and control groups regarding maternal data.

	Misoprostol group	Control group	t/χ^2	*P* value
	N = 70	*N* = 70		
Age (years)				
Mean ± SD	26.24 ± 4.75	26.63 ± 5.09		
Range	19–36	18–39	−0.463	0.644
Median (IQR)	25 (6.25)	26 (7.25)		
Parity [*n* (%)]				
Primigravida	20 (28.6)	25 (35.7)	0.819	0.366
Multipara	50 (71.4)	45 (64.3)		
BMI				
Mean ± SD	25.97 ± 3.19	25.93 ± 3.36		
Range	22–34	22–37	0.077	0.939
Median (IQR)	25.5 (6)	25 (4)		

IQR, interquartile range.

Table 2. Comparison between vaginal misoprostol and control groups regarding infant heart rate and respiratory rate.

	Misoprostol group	Control group	*t*	*P* value
	N = 70	*N* = 70		
HR (beat/min)				
Mean ± SD	125.97 ± 3.19	130.93 ± 3.38		
Range	122–134	127–142	−8.923	<0.0001
Median (IQR)	125.5 (6)	130 (4)		
RR (cycle/min)				
Mean ± SD	48.68 ± 6.76	54.26 ± 8.14		
Range	42–65	45–73	−4.404	<0.0001
Median (IQR)	46.5 (6.25)	50.5 (15)		

HR, heart rate; IQR, interquartile range; RR, respiratory rate.

Table 3. Comparison among vaginal misoprostol and control groups regarding neonatal ICU admission.

	Misoprostol group [*n* (%)]	Control group [*n* (%)]	t/χ^2	*P* value
	N = 70	*N* = 70		
NICU admission				
No	60 (85.7)	47 (67.1)	6.701	0.010
Yes	10 (14.3)	23 (32.9)		
NICU stay				
Mean ± SD	1.91 ± 0.85	2.00 ± 0.82	0.278	0.784
Range	1–3	1–3		
CPAP need				
No	67 (95.7)	65 (92.9)	0.530	0.466
Yes	3 (4.3)	5 (7.1)		

NICU, neonatal ICU.

The vaginal misoprostol group has a statistically significant lower frequency of TTN than the control groups (Table 5).

Table 4. Comparison among vaginal misoprostol and control groups regarding APGAR scores at first and fifth minutes.

	Misoprostol group	Control group	*t*	*P* value
	N = 70	*N* = 70		
APGAR 1st minute				
Mean ± SD	6.71 ± 0.45	6.64 ± 0.48	0.901	0.369
Range	6–7	6–7		
Median (IQR)	7 (1)	7 (1)		
APGAR 5th minute				
Mean ± SD	8.72 ± 0.46	8.64 ± 0.47	−0.899	0.368
Range	8–9	8–9		
Median (IQR)	9 (1)	9 (1)		

IQR, interquartile range.

Table 5. Comparison between vaginal misoprostol and control groups regarding infant outcome.

	Misoprostol group [*n* (%)]	Control group [*n* (%)]	χ^2	*P* value
	N = 70	*N* = 70		
TTN				
No	60 (85.7)	47 (67.1)	6.701	0.010
Yes	10 (14.3)	23 (32.9)		

TTN, transient tachypnea of the newborn.

Table 6. Correlation between the neonatal ICU stay and clinical data of the studied groups.

Variables	NICU stay	
	r	*P* value
GA (week)	−0.077	0.671
APGAR 1st min	0.342	0.051
APGAR 5 min	0.342	0.051
Birth weight (g)	−0.114	0.526
HR (beat/min)	0.389	0.025
RR (cycle/min)	0.508	0.003

GA, gestational age; HR, heart rate; NICU, neonatal ICU; RR, respiratory rate.

There is a statistically significant positive correlation among infant heart rate, respiratory rate, and the duration of the NICU stay (Table 6).

4. Discussion

When performed at a gestational age less than 39 weeks, ECS increases the danger of respiratory morbidity, respiratory distress syndrome (RDS), TTN, and persistent pulmonary hypertension of the newborn by a factor of 2–7.[4]

Anti-inflammatory effects and a notable involvement in lung maturation throughout pregnancy via the production of surfactant and sodium channel improvement are two of prenatal corticosteroids' actions important to RDS. Women who are between 34 and 37 weeks pregnant and are given prenatal corticosteroids see a significant decrease in the prevalence of RDS.[13]

Relative to mother age, parity, and BMI, there is no statistically significant difference among the vaginal misoprostol and control groups.

Considering that Abbas et al.[14] recruited 304 women for their investigation, our findings are consistent with theirs. Ten women were not accepted because they did not fulfill the requirements. Two ladies also opted out of taking part in the trial. A total of 292 female participants (146 in each group) were randomly assigned to the two study arms (misoprostol and control). There were no significant differences among the two groups when comparing their baseline data (maternal age, parity, and BMI). In the study in our hands, infant heart rates and respiratory rates were statistically significantly lower in the vaginal misoprostol group than the control group. Respiratory effort in the form of tachypnea, nasal flaring, and retraction is statistically significantly lower in the vaginal misoprostol group than in the control group. The vaginal misoprostol group has a statistically significant lower frequency of TTN than the control groups.

Our research results are consistent with those of Khairy et al.,[15] who found a statistically significant difference among groups with respect to the kind of respiratory morbidity.

In addition, a prior study by Pevzner et al.[16] found that 17.3 % of cases given misoprostol 100 μg and 6.8 % of cases given misoprostol 50 μg had aberrant CTG and uterine contractile abnormalities, such as hyperstimulation, hypertonus, and/or tachysystole, during labor induction.

When used in patients with an unripe cervix, misoprostol vaginal inserts of 200 g that release prostaglandins at a steady rate for 24 h were also associated with an increased risk of aberrant newborn intrapartum CTG tracing, according to a separate study by Mlodawski et al.[17]

In this study, researchers found no significant difference in APGAR scores between women who gave birth while using vaginal misoprostol and those who did not.

The findings of Abbas et al.[14] corroborated ours by showing that there was no difference in APGAR scores at 1 and 5 min among the research and control groups.

Contrary to our findings, Khairy et al.[15] found a statistically significant difference in APGAR score at 1.5 min between the intervention group and the placebo group.

Significantly fewer infants in the vaginal misoprostol group were admitted to the neonatal ICU than infants in the control group, according to the present research.

Consistent with our findings, Hassan et al.[18] showed an increase in NICU admissions for infant respiratory morbidity and the need for mechanical ventilation among the nonintervention group but no statistically significant differences in NICU mortality from respiratory morbidity.

Similarly, the χ^2 test performed by Khairy et al.[15] showed a highly significant difference among groups with respect to NICU days of admission, nasal ventilation, and mechanical ventilation, with a P value of 0.001.

We found a statistically significant positive relationship between infant heart rate, respiratory rate, and time spent in the NICU. High gestational age and misoprostol use were found to be protective against TTN in a logistic regression analysis of factors.

In line with the findings of Abbas et al.,[14] we found that maternal age, parity, and the reason for CS were not predictors of neonatal RD when subjected to multivariate logistic regression analysis. Only maternal age at delivery ($P = 0.001$) and prenatal misoprostol use ($P = 0.026$) independently influenced the incidence of neonatal RD.

4.1. Conclusion

The use of prophylactic vaginal misoprostol before ECS between 37 and 39 weeks of gestation has been shown to minimize the incidence of neonatal pulmonary TTN and may be an effective method of preventing this condition. Therefore, more large-scale studies with more participants and longer timeframes are recommended to confirm, expand on, and add to our results. On this basis, future studies should try to determine the most appropriate gestational age at which misoprostol administration is most beneficial.

Conflicts of interest

Authors declare that there is no conflict of interest and no financial interest to declare in relation to the content of this article.

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