Misoprostol before Elective Caesarean Section for Decreasing the Neonatal Respiratory Morbidity In diabetic patients

Master Degree in Obstetrics and Gynecology

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بسم الله الرحمن الرحيم

وقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ
ورَسُولُهُ والْمُؤْمِنُونَ

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List of Content

List of Abbreviations

Abbr.	Full-term
AA	Arachidonic Acid
ABCA 3	ATP Binding cassette gne
ABG	Arterial Blood Gases
AQP5	Aquaporin 5 water channel
ASUMH	Ain Shams University Maternity Hospital
ATP	Adenosine Triphosphate
BNP	Brain Natriuretic Peptide
BPD	Bronchopulmonary Dysplasia
CRF	Case Record Form
C.S	Caesarean Section
C.T	Computed Tomography
CDMR	Caesarean Delivery on Maternal Request
cGMP	Cyclic Guanosine Mono Phosphate
CI	Confidence Interval
CNS	Central Nervous System
CONSORT	Consolidated Standards of Reporting Trials
COX	Cyclooxygenase
C-PAP	Continuous Positive Airway Pressure

ECD	Elective Caesarean Delivery
ECMO	Extra Corporial Membrane Oxygenation
EDA	Epidural Anaesthesia
ENaC	Epithelial Na Channels
eNO	Endothelial Nitric Oxide
EP	E Prostanoid receptor
ET	Endothelin
GA	General Anaesthesia
HFOV	High Frequency Oscillatory Ventillation
HMD	Hyaline Membrane Disease
IM	Intra muscular
iNO	Inhaled Nitric Oxide
IP3	Inositol Triphosphate
IV	Intra venous
IVH	Intra Ventricular Haemorrhage
LDA	Lactate Dehydrogenase
MRI	Magnetic Resonance Imaging
mRNA	Messanger Ribonucleic Acid
NEC	Necrotizing Enterocolitis
NG	Nasogastric
NICHD	National Institute Of Child Health and Human Development
NICU	Neonatal Intensive Care Unit

N-SAIDS	Non Steroidal Anti Inflamatory Drugs
NTproBNP	Plasma N terminal pro-B-type Natriuretic Peptide.
$PaCO_2$	Partial Pressure of Carbon Dioxide in Arterial Gas
PaO_2	Partial Pressure of Oxygen in Arterial Gas
PDA	Patent Ductus Arteriosis
PGI2	Prostaglandin I2 (Prostacyclin)
PLA	Phospholipase A
PMT	Pulmonary Mechanics Testing
PPHN	Persistant Pulmonary Hypertension
PVR	Pulmonary Vascular Resistance
RCT	Randomized Controlled Trial
RD	Respiratory Distress
RDS	Respiratory Distress Syndrome
ROP	Retinopathy of Prematurity
RR	Risk Ratio
RR	Respiratory Rate
SR	Sarcoplasmic Reticulum
SVR	Systemic Vascular Resistance
Tmax	Time of maximum plasma concentration
TTN	Transient Tachypnea of The Newborn
TXA2	Thromboxane A2

US	Ultrasound
UK	United Kingdom
VLBW	Very Low Birth Weight
SD	Standard Deviation
SPSS	Statistical Package for Social Science

List of Tables

List of Figures

Introduction

The increased incidence of the idiopathic respiratory distress syndrome (IRDS) in infants of diabetic mothers may be explained by preterm delivery and asphyxia but the metabolic derangement per se may also be responsible for the inadequate production of lung surfactant. In addition, the activities of key enzymes responsible for the production of these phospholipids are decreased in the fetal lung tissue. ***(Tydénet al.,2017).***

Neonatal respiratory distress may occur in either term or preterm newborns with a higher relative risk in preterm, and whether born vaginally or through caesarean section, but in a higher percentage after elective caesarean section whose rate is rising either due to maternal request ***(Minkoffet al., 2003)***, obesity ***(Poobalanet al., 2009)***, and older maternal age ***(Callawayet al., 2005)*** than after normal vaginal delivery **(*Zanardo et al., 2004)*** or emergency caesarean section ***(Hansen et al.,2007)***.

It is responsible for 30% of neonatal deaths ***(Harrison, et al., 2008)***. It has several subdivisions:

One is the respiratory distress syndrome (RDS) which is called hyaline membrane disease, it can occur in about 1% of pregnancies as a result of a pathology in lung surfactant either qualitative or quantitative ***(Whitsett et al., 2005)***, and usually in preterm neonates ***(Blandet al.,2008)***.

Another is transient tachypnea of the newborn (TTN) in which there is respiratory distress and increased

respiratory rate due to delayed resorption of pulmonary fluid, as a result of defective catecholamine surge ***(Faxeliuset al., 1983),*** its incidence is 5.7/1000 deliveries (95% CI;1.7-2.7)***(Morrison et al., 1995).***

And also includes persistent pulmonary hypertension in which the fetal pulmonary vascular resistance remains high and the pulmonary blood flow still low after delivery ***(Whitsettet al., 2005)***.

Catecholamines can stimulate pulmonary fluid reabsorption through acting upon beta-adrenergic receptors in fetal lung which present more late in gestation ***(Bland,et al., 2008)***, and thus enable the secretion of surfactant ***(Whitsettet al., 2005)***.

This surge of catecholamines can be provoked through prostaglandins given before caesarean section to pregnant diabetic females ***(Singhet al., 2004)*** as those who are born vaginally are found to be adapted metabolically through a higher catecholamine level at birth ***(Hagneviket al., 1984)***.

So, prostaglandins may be given about one hour before an elective caesarean section after excluding the presence of contraindication to their use to decrease the neonatal respiratory diseases and thus, the number of children who suffered from bronchopulmonary dysplasia that occurs frequently in children who had previously TTN will diminish ***(Whitsett et al., 2005)***.

The prostaglandins in common use are misoprostol (prostaglandin E_1) and dinoprostone (prostaglandin E_2). Prostaglandin E_1 (Misoprostol) is available as a cervical ripening agent in the form of 100 or 200 mcg tablets which can be taken orally, vaginally, or sublingually, their Tmax is 12 +/- 3 minutes with terminal half life ranging from 20 to 40 minutes ***(Woodet al.,2001)***.

Prostaglandins E_2 which are available as oral tablets, pessaries, or vaginal gels are uteroselective agents ***(O'Brienet al., 1995)*** widely used for induction of labour, start action within 10 minutes and become in full action after about 12 hours ***(Rayburnet al., 1989)***.

In a previous prospective study of 36 women scheduled for an elective caesarean section beyond 38weeks ***(Motaze et al., 2013),***18 women received intravaginal prostaglanadin E_2 gel and 18 received placebo, there was one neonatal respiratory distress case in the control group which was reported as transient tachypnea of the newborn (risk ratio (RR) 0.33, 95% confidence interval (CI) 0.01 to 7.68) with similar Apgar score at one and five minutes and no need to mechanical ventilation nor side effects related to treatment in either group, so no difference in respiratory outcome reported although there was a significantly higher catecholamine level in the intervention group.

Aim of the work

The aim of this study is to assess the efficacy of Prostaglandin E_1 on the reduction of the neonatal respiratory morbidity in diabetic women scheduled for elective caesarean section.

Research hypothesis: In diabetic pregnant women undergoing elective C.S, Prostaglandin E_1 may reduce neonatal respiratory morbidity.

Research question: In diabetic pregnant women undergoing elective C.S, Does prostaglandin E1 decrease the rate of neonatal respiratory morbidity ?