Effect of Maternal Dxamethasone Administration on Fetal Doppler Indices

Thesis

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بِسْمِ اللّهِ الرّحمَنِ الرّحيمِ

[...رَبِّ أَوزِعنِي أَن أَشكُرَ نِعمَتَكَ
الَّتِي أَنْعَمْتَ عَلَيَّ و عَلى والِدَيَّ
و أَنْ أَعْمَلَ صَالِحاً تَرْضَاهُ و أَدْخِلْنِي
بِرَحْمَتِكَ فِي عِبَادِكَ الصَّالِحِينَ]

صدق الله العظيم

النمل.. اية رقم ١٩

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Hyam Abd El- Latif Abd El Aziz

List of Contents

List of Tables

List of Figures

List of Figures *(Cont...)*

Introduction

Corticosteroids reduce the occurrence of respiratory distress syndrome (RDS) and other complications following preterm birth, such as intraventricular hemorrhage, necrotizing enterocolitis and neonatal death. The benefits of betamethasone treatment have been questioned in severely growth-restricted fetuses ***(van Stralen et al., 2009)***.

Evaluation of fetal wellbeing with Doppler waveform studies after maternal corticosteroid administration is therefore important. Knowledge of fetal haemodynamic effects of exogenous corticosteroids is limited. Little is known about the impact of antenatal corticosteroid therapy on Doppler waveforms in fetal arteries ***(Wallace & Baker, 1999)***.

Aim of the Work

The aim of this study was to investigate the possible effects of antenatal dexamethasone administration on umbilical artery, middle cerebral artery, aortic artery and ductus arteriosus flow velocity waveforms indices in suspected preterm labour.

Chapter (1):
Preterm labor

Preterm labor is defined as labor occurring prior to 37 weeks gestation and is the leading cause of death in children under 5 years of age, second only to pneumonia ***(Blencowe et al., 2012)***.

Preterm labor is defined as the presence of uterine contractions of sufficient frequency and intensity to effect progressive effacement and dilation of the cervix prior to term gestation (between 20 and 37 wk) ***(Lowes, 2013)***.

Successful reduction of perinatal morbidity and mortality associated with prematurity may require the implementation of effective risk identification and behavioral modification programs for the prevention of preterm labor; these in turn require both an improved understanding of the psychosocial risk factors, etiology, and mechanisms of preterm labor and programs for accurate identification of pregnant women at risk for premature labor and delivery.

Evidence suggests that early identification of at-risk gravidas with timely referral for subspecialized obstetrical care may help identify women at risk for preterm labor and delivery and decrease the extreme prematurity (< 32 wk) rate, thereby reducing the morbidity, mortality, and expense associated with prematurity ***(Eden et al., 2005)***.

Epidemiology:

Premature labor is a common and costly health care condition, the magnitude of which is staggering. Every minute approximately 1,400 babies are born prematurely throughout the world and over 100 of these infants die ***(Beck et al., 2010)***. Preterm delivery is the leading cause of neonatal deaths worldwide, 99% of which occur in low and middle income countries ***(WHO, 2010)***.

Preterm birth is the largest cause of perinatal morbidity and mortality; with rates of preterm birth rising. In the USA, the preterm delivery rate is 12–13% and in Europe and other developed countries, reported rates are generally 5–9%. The UK now has the highest rate of premature birth in Europe with 7.8% of overall births in Scotland occurring before 37 weeks gestation ***(Gray, 2008)***.

Significant progress has been made in the care of premature infants, but not in reducing the prevalence of preterm birth. In the United States, there has been a 21% rise in the rate of preterm births since 1990, which peaked in 2006 with 12.8% of all 4 million annual live births born at less than 37 weeks of gestation ***(Russell et al., 2007)***.

The incidence in Europe and other developed countries lies between 5-9%. East Asian and Hispanic women typically have a low pre-term birth rate. However, the incidence of preterm birth continues to rise. Part of this escalation is due to the increased

indicated preterm delivery of artificially conceived multiple pregnancies, which account for 15-20% of all pre-term births ***(Goldenburg et al., 2008)***.

Approximately 30–35% of preterm births are indicated or iatrogenic due to medical or obstetric complications, 40–45% are related to spontaneous preterm labour, and 25–30% to preterm pre-labor rupture of membranes (PPROM). Spontaneous pre-term birth is most commonly caused by pre-term labour in Caucasians, and PPROM in black women indicating the existence of potentially different causative mechanisms ***(Goldenburg et al., 2008)***.

Preterm Labor Biology:

Pathogenesis:

The exact mechanism(s) of preterm labor is largely unknown but is believed to include decidual hemorrhage, (eg, abruption, mechanical factors such as uterine overdistension from multiple gestation or polyhydramnios), cervical incompetence (eg, trauma, cone biopsy), uterine distortion (eg, müllerian duct abnormalities, fibroid uterus), cervical inflammation (eg, resulting from bacterial vaginosis [BV], trichomonas), maternal inflammation/fever (eg, urinary tract infection), hormonal changes (eg, mediated by maternal or fetal stress), and uteroplacental insufficiency (eg, hypertension, insulin-dependent diabetes, drug abuse, smoking, alcohol consumption) ***(ACOG practice bulletin, 2003)***.

Nearly 40% of premature births have an unknown cause, studies suggest that there are four main causes of spontaneous preterm labor, namely: a) maternal and/or fetal stress, b) bleeding, c) stretching and d) infections/inflammation ***(Beck et al., 2010)***.

Chronic psychosocial stress of the mother or physical stress in the fetus induce production of corticotropin-releasing hormone (CRH), which in turn may trigger other hormones, such as prostaglandins, which trigger uterine contractions and eventually preterm birth ***(Goldenberg et al., 2008)***.

Uterine bleeding as a result of complications such as placental abruption (placenta peels away from the uterine wall before delivery), which may trigger release of proteins involved in clotting, such as thrombin, which in turn stimulates uterine contractions. Uterine distension by multi-fetal pregnancies may lead to increased gravitational weight exerted on the cervix and a positive feed-forward release of the hormone oxytocin, which stimulates uterine contractions ***(Goldenberg et al. 2008)***.

The bulk of preterm labor is induced by bacterial infections that lead to inflammation and preterm labor and account for the preterm premature rupture of membranes (PROM) (25-40%), and obstetrically indicated preterm delivery (20-25%) ***(Wen et al., 2004)***.

Iatrogenic preterm delivery

Iatrogenic preterm delivery accounts for more than 30% of all preterm deliveries. The preterm birth rate continues to escalate in many countries worldwide because of an increase in the indicated preterm births rate ***(Goldenberg et al., 2008)***.

Pre-eclampsia and placental abruption affects approximately 7% and 1% of all pregnancies, respectively. Along with intrauterine growth restriction and premature rupture of the membranes, they represent the most common reasons for indicated preterm delivery ***(Plunkett, 2008)***.

Multiple gestations make up 10% of all preterm births, the majority of which, (50%), are delivered preterm due to medical indications ***(Moutquin, 2003)***. The Obstetrician has to weigh up the benefits of allowing the pregnancy to continue in order to achieve improved perinatal outcome for the preterm infant, against delivering the fetus early for the health of the mother and infant. In 1995, The American College of Obstetricians and Gynecologists reported a survival rate for newborns at 34 weeks gestation as being within 1% of those born at or beyond 37 weeks ***(Hauth, 2006)***.

Risk factors:

A. Maternal factors:

Several lifestyles and factors have been identified to put a woman at risk for preterm birth, including: a) a history of preterm birth; b) size or multi-fetal pregnancies; c) certain

uterine or cervical abnormalities (such as shortened cervix); d) ethnicity, with the highest rate in black women; e) age, with teenage or older mothers at the greatest risk; f) education and socio-economic status highest in women with low education and socio-economic status; g) habits, such as cigarette smoking increase the risk; h) marital status: unmarried women or those not living with a partner are at a higher risk; i) occupation: women with stressful occupations are at a higher risk; j) body weight: low maternal pre-pregnancy body mass index, and poor or excessive weight gain increase the likelihood of a preterm birth ***(Wen et al. 2004)***.

Table (1): Risk Factors for Spontaneous Preterm labor

Risk Factors for Spontaneous Preterm Birth	
Non-modifiable Risk Factors	
Prior preterm birth African-American race Age <18 years or > 40 years Poor nutrition Low pre-pregnancy weight Low socioeconomic status Absent prenatal care	Cervical injury or anomaly Uterine anomaly Excessive uterine activity (?) Premature cervical dilatation (>2 cm) or effacement (>80%) Overdistended uterus (twins, polyhydramnios) Vaginal bleeding
Potentially Modifiable Risk Factors	
Cigarette smoking Illicit drug use Anemia Bacteriuria/urinary tract infection Gingival disease Strenuous work/work environment	Lower genital tract infections (including bacterial vaginosis, *Neisseria gonorrhoea, Chlamydia trachomatis*, Group B *Streptococcus*, *Ureaplasma urealyticum*, and *Trichomonas vaginalis)* High personal stress

(Errol et al., 2011)

- **<u>Previous preterm birth</u>**

The risk of preterm birth is increased among women who have had a previous preterm birth. Previous preterm birth is the