Prophylactic Antibiotics for Spontaneous Pre-labor Rupture of Membranes at Term

Theses

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و آخر دعوانا أن الحمد لله رب العالمين...

D.Doaa Ahmed Ahmed Radwan.

List of Contents

List of Abbreviations

AE	Adverse Drug Reaction
AF	Amniotic Fluid
AF Cells	Amniotic Fluid Cells
AFI	Amniotic Fluid Index
AFP	Alpha-fetoprotein
AFP	A-Feto Protein
AFS	Antenatal Fetal Surveillance
AFV	Amniotic Fluid Volume
AROM	Artificial Rupture of Membrane
BPP	Biophysical profile
BV	Bacterial Vaginosis
CA	Chorio Amnion
CAPs	Contraction Associated Proteins
CNS	Central Nervous System
CS	Caesarean Section
CSF	Cerebrospinal Fluid
ECM	Extracellular Matrix
fFN	Fetal Fibronectin
FHR	Fetal Heart Rate
FM	Fetal Membranes
GBS	Group B Streptococcus
GnRH	Gonadotrophin Releasing Hormone
IGFBP-١	Insulin-like growth factor binding protein-١
IL	Interleukin
LH	Luteinizing hormone

LPS	Lipopolysaccharide
MMPs	Matrix Metalloproteinases
MVP	Maximal Vertical Pocket
NICU	Neonatal Intensive Care Unit
NST	Non-Stress Test
PPROM	Preterm Premature Rupture of Membrane
PROM	Premature Rupture of Membrane
RDS	Respiratory Distress Syndrome
ROM	Rupture of membrane
SD	Standard Deviation
SROM	Spontaneous Rupture Of Membrane
TIMP	Tissue Inhibitors of Metalloproteinases
vAF	vaginal amniotic fluid
VD	Vaginal Delivery

List of Tables

List of Figures

Introduction

Spontaneous rupture of the fetal membranes (SROM) prior to the onset of labor occurs in ٨٪ of term pregnancies ***(Marowitz and Jordan, ٢٠٠٧).***

Traditionally, 'term' is defined as gestations of ٣٧ to ٤١ weeks inclusive ***(Flenady and King, ٢٠٠٢).***

Approximately ٦٠٪ to ٨٠٪ of women with prelabor rupture of membranes (PROM) at term will enter spontaneous labor within ٢٤hours ***(Marowitz and Jordan, ٢٠٠٧).***

The cascade of events culminating into term PROM is not clear. The point of spontaneous rupture of fetal membranes at term is thought to be a weak zone that is present over the cervix. This weak zone is characterized by changes in Matrix Metallomternase-٩ (MMP-٩), Tissue Inhibitor Metallomternase٣ (TIMP-٣) and Pregnancy Associated Reactive Proteins (PARP) cleavage suggestive of collagen remodeling and apoptosis ***(Moore et al., ٢٠٠٦).***

The two questions that are raised with this common daily practice issue are whether to induce labor and whether to administer prophylactic antibiotics. There is a possible risk of maternal and fetal morbidity in cases of PROM at term. Neonatal infections in the term population occur in ٢-٤٪ of

cases and have the potential for causing mortality or serious morbidity including the need for neonatal intensive care and mechanical ventilation ***(Flenady and King, ٢٠٠٦).*** The risks of chorioamnionitis and endomyometritis are significantly increased at ١٢ hours and ١٦ hours, respectively ***(Trans et al., ٢٠٠٨).***

Prelabor rupture of membranes at term is managed expectantly or by elective birth, but not clear if waiting for birth to occur spontaneously is better than intervening. A recent Cochrane systematic review has concluded that induction of labor reduces the risk of some maternal infectious morbidity without increasing caesarean sections and operative vaginal births. Fewer infants went to neonatal intensive care under planned management although no differences were seen in neonatal infection rates. Since planned and expectant management may not be very different, women need to have appropriate information to make informed choices ***(Dare et al., ٢٠٠٦).***

It is still unclear if the routine use of antibiotics for women at the time of term PROM may reduce the risk of maternal and neonatal infections ***(Flenady and King, ٢٠٠٦).*** Group B Streptococcus (GBS) is the most common cause of serious neonatal infection in the first seven days of life. However, if GBS culture result is unknown, antibiotic

prophylaxis should only be administered if the woman has ruptured membranes at term for greater than ١٨ hours **(*Money and Dobson,* ٢٠٠٤)**. It is not clear if antibiotics should be routinely administered to women with term PROM for prevention of perinatal infections caused by organisms other than GBS ***(Markowitz and Jordan,* ٢٠٠٧).**

The factor of safety must be considered in the absence of a clear benefit of routine prophylactic antibiotics in term PROM. A recent study has shown that newborns of mothers who received intrapartum antibiotics were significantly more likely to be treated for clinical sepsis than were newborns of mothers who had not received them ***(Glasgow et al.,* ٢٠٠٧).**

Another study has shown that infants with late-onset serious bacterial infections were more likely to have been exposed to intrapartum antibiotics than non infected infants. Pathogens that cause late-onset neonatal sepsis were more likely to be resistant to ampicillin when the infant had been exposed to intrapartum antibiotics ***(Young et al.,* ٢٠٠٥).**

The burden on health facilities particularly in low income or middle income countries is a critical issue. The average length of stay and the cost of caring for newborns whose mothers received intrapartum antibiotics were significantly more than newborns whose mothers did not receive antibiotics ***(Glasgow et al.,* ٢٠٠٧).**

Despite the clinical importance of this issue in our daily obstetric practice, there is paucity of studies addressing this issue. There is gap in our current knowledge and lack of evidence indicating overall benefit from prophylactic antibiotics for PROM at term ***(Flenady and King, ٢٠٠٦).***

The wise justified evidence based use of prophylactic antibiotics is warranted due to increasing problems with bacteria! resistance and the burden on health services particularly in developing countries. This was the justification of conducting this study to address the balance of risks and benefits to the mother and infant of antibiotic prophylaxis for prelabor rupture of the membranes at term.

Aim of the Work

Objectives & Specific Aims:

To assess the effects of prophylactic antibiotics administered to women with prelabor rupture of the membranes at ٣٦ weeks or beyond, on maternal and neonatal outcomes.

MEDICAL APPLICATION (Significance):

The importance and possible usefulness of the results of this study is to provide evidence and to fill the gap in our current knowledge regarding the use of prophylactic antibiotic in term PROM.

Chapter (*I*)
Prelabor Rupture of Membrane

Spontaneous rupture of the amniotic membranes before the Onset of labor occurs in about ٨٪ of term pregnancies ***(Cammu et al., ١٩٩٠).***

Approximately ٦٠٪ to ٨٠٪ of women with prelabor rupture of membranes at term will enter spontaneous labor within ٢٤ hours ***(Kappy et al., ١٩٧٩).***

The risk of maternal and neonatal infection increases following rupture of the membranes, but the etiology of infection following prelabor rupture of membranes can be difficult to ascertain because pre-existing infection can cause prelabor rupture ***(Naeye, ١٩٨٣).***

Premature rupture of membranes is a commonly used term, although prelabor rupture of membranes is more precise, and less likely to cause confusion regarding gestational age. Conveniently, either (prelabor rupture of membranes) or (premature Rupture of membranes) can be shortened to PROM. PROM can occur at any gestational age, and it is further specified as term PROM (٣٧ weeks estimated gestational age [EGA]) or preterm PROM (٣٧ weeks' EGA). The timing

between membrane rupture and onset of labor has also varied in the historical definitions of PROM. Traditionally, the rupture of membranes before the onset of term labor was defined as PROM only if there was a certain latency period between rupture and labor. However, there was no agreement on the length of the latency period, and clinical research that assessed the consequences of PROM used different latency intervals ***(Keirse et al., ١٩٩٦).***

Early and accurate diagnosis of ROM would allow for gestational age specific Obstetric interventions designed to optimize perinatal outcome and minimize serious complications such as cord prolapse and infectious morbidity (chorioamnionitis, neonatal sepsis). Conversely, a false positive diagnosis of ROM may lead to unnecessary obstetric interventions, including hospitalization, administration of antibiotics and corticosteroids, and even induction of labor ***(Shin Park et al., ٢٠٠٧).***

Fetal Membranes:

The membranous structure that surrounds the developing fetus and forms the amniotic cavity is derived from fetal tissue and is composed of two layers: the amnion (inner layer) and the chorion (outer layer).The amnion is translucent structure adjacent to the amniotic fluid, which provides necessary nutrients to the amnion cells. The chorion is more opaque

membrane that is attached to the decidua (i.e., maternal tissue that lines the uterus during pregnancy). The amnion and chorion are separated by the exocoelomic cavity until approximately three months gestation, when they become fused. Intact, healthy fetal membranes are required for an optimal pregnancy outcome ***(SethGuller, ٢٠١١).***

Inspection of the fetal membranes following delivery reveals amnion that is mildly adherent to the fetal side of the chorion. Small amounts of maternal decidual tissue can be observed attached to the outer, maternal side of the chorion ***(Cunningham et al., ٢٠٠٥).***

Amnion and chorion fuse at about ١٢ weeks gestation, via an Intermediate layer of tissue, the spongy layer. The resulting amniochorion fuses intimately to the maternal decidua parietals at ٢٠-٢٥ weeks gestation ***(McParland and Taylor ٢٠٠٥).***

The amnion and chorion laeve, although slightly adherent, are never intimately Connected and usually can be separated easily, even at term ***(Cunningham et al., ٢٠٠٥).***

Anatomy of the amnion & chorion:

The Amnion

It is the inner most fetal membrane and is contiguous with amniotic fluid. The amnion is the tissue that provides

almost all of the tensile strength of the fetal membranes. Therefore, the development of the components of the amnion that protect against its rupture or tearing is vitally important to successful pregnancy outcome ***(Cunningham et al., ٢٠٠٥).***

Anatomy of the amnion:

Amnion is a thin translucent membrane. The fetal surface of which is smooth and glistening. It is reflected from the root of the cord to the fetal surface of the placenta, and then at the margin of the placenta it is continuous to line the surface of the chorion leave. Through the amnion three umbilical vessels can be seen imbedded in Wharton jelly, these are two umbilical arteries and one umbilical vein. The amnion is loosely attached to Wharton jelly except at the site of insertion of the umbilical cord in the placenta where they are firmly attached ***(Mcparland et al., ٢٠٠٠).***

It is divided into ٣ parts ***(Sagol et al., ٢٠٠٢):***

A- Placental amnion: covers the inner aspect of the placenta.

B- Dependent amnion: ١-٢ cm overlying the internal os of the cervix.

C- Reflected amnion: the reminder part of the amnion.

Embryology of the amnion:

The amnion develops from an ectodermal cell nest in the dorsal aspect of the embryo ٨ days after conception ***(Calvin and Oyen, ٢٠٠٧).*** When first formed the amnion is in contact