The Effect of Intrapartum Versus Antepartum Penicillin On Vaginal Group B Streptococcus Colony Counts

Thesis

Submitted for partial fulfillment of master degree in

Obstetrics and Gynecology

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Cairo - 2014

بسم الله الرحمن الرحيم

وقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ
ورَسُولُهُ والْمُؤْمِنُونَ

صدق الله العظيم

سورة التوبة آية (105)

*First, thanks are all due to **Allah** for Blessing this work until it has reached its end, as a part of his generous help throughout our life.*

*My profound thanks and deep appreciation to **Prof. Dr. Ahmad Mohamed Nour El-Din Hashad**, Professor of Obstetrics and Gynaecology, Faculty of Medicine, Ain Shams University for his great support and advice, his valuable remarks that gave me the confidence and encouragement to fulfill this work.*

*I am deeply grateful to **Dr. Ahmad Adel Tharwat,** Lecturer in Obstetrics and Gynaecology, Faculty of Medicine, Ain Shams university for his great kindness, constant assistance and guidance.*

Last but not least, I dedicate this work to my family, whom without their sincere emotional support, pushing me forward this work would not have ever been completed.

Heba Tallah Mohamed Reda

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List of Abbreviations

CDC	:	Centers for Disease Control and Prevention
CNS	:	The central nervous system
DPPC	:	Dipalmotyl phosphatidylcholine
ELISA	:	Enzyme linked immunosorbent
GBS	:	Group B Streptococcal
HRT	:	Hormone replacement therapy
IL	:	Interleukin
iNOS	:	Inducible nitric oxide synthase
MIC	:	Minimum inhibitor concentrations
NO	:	Nitric oxide
PCN-G	:	Penicillin-G
PROM	:	Premature rupture of membranes
SodA	:	Superoxide dismutase
TNFa	:	Tumour necrosis factor-alpha
UTM	:	Universal transport media

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Introduction

Worldwide, colonization by Group B streptococcus (GBS) is highly prevalent among pregnant women, varying between 4% and 30% ***(Edwards et al., 2006).***

Although GBS infections tend to occur more commonly among adults than in neonates, but the overall mortality is higher in neonates. Approximately 60% of infants born to colonized mother become colonized with their mother's organisms. The likelihood of neonatal colonization at birth is higher if the mother is heavily colonized ***(Patrick et al., 2002).***

Early-onset group B streptococcus (GBS) disease in the neonate is an important preventable cause of neonatal morbidity and mortality with a 4% mortality rate and a 10% risk of neurologic sequelae, therefore prevention strategies are of great importance ***(Edwards et al., 2001).***

With the objective of reducing neonatal morbidity and mortality due to GBS, different countries have implemented strategies of intrapartum prophylactic antibiotic therapy, resulting in a significant decrease in the incidence of neonatal infection from 2.7 to 0.4 per 1,000 live births ***(Smaill et al., 2002).***

With respect to antimicrobial susceptibility, studies has shown that most cases present no resistance of GBS to penicillin ***(Lin et al., 2000).***

Although we know that antibiotic prophylaxis against GBS is effective, we do not know the mechanism by which administration of antibiotic to GBS culture-positive women in labor works. Is it by antibiotic loading of the fetus and amniotic fluid, by eradication of the vaginal GBS or by a combination of both? Penicillin's are known to enter both the fetus and amniotic fluid readily and also to decrease vaginal colony counts over periods of weeks to months when measured prenatally and again postpartum ***(Colombo et al., 2006).***

The effect of penicillin-G (PCN-G) on vaginal GBS colony counts in the hours after antibiotic administration has not been studied. It's known that severity of GBS disease correlates with degree of maternal colonization and that penicillin and its analogues reach bactericidal concentrations in fetal serum and amniotic fluid within minutes of maternal administration ***(MacAulay et al., 2007).***

Aim of The Work

The aim of this work is to compare the efficacy of maternal therapy with intrapartum intravenous Penicillin G versus antepartum combination of Amoxicillin and Clavulanic acid in the reduction of vaginal GBS count.

Chapter One

The Vaginal Ecology

Vaginal ecology is the concept that the vagina is a complex integrated environment. The vaginal vault is colonized within 24 hours of a female child's birth and remains colonized until death, comprising an ever-changing yet fine-tuned ecosystem with numerous factors (both internal and external) that have the potential to disrupt the ecosystem's fragile balance ***(Zhou et al., 2004)***.

The bacterial composition of the vagina, along with the presence of a range of innate and acquired immune system components, combine to prevent microbial pathogens from invading and/or proliferating at this, that is exposed to the external environment ***(Steven et al., 2007).***

A review of the current literature can be broken into the following phases of a woman's lifetime: birth and early childhood, puberty, reproductive years (which include menses and pregnancy), and menopause.

Birth and Early Childhood:

During the birth process and shortly after, the vaginal epithelium is high in glycogen content as the result of residual maternal estrogens, providing an environment in which lactic acid-producing microbes can thrive. Vaginal pH during early childhood is neutral or slightly alkaline. Due to the absence of

adrenal or gonadal action, as maternal estrogen depletes, the prevalence of lactic-acid producing microbes present in neonates also decreases ***(Farage et al., 2006).***

Analyses of the resident microbiota in children have been few. **Hammerschlag** in an ambitious study, looked at organisms present in the vaginal ecosystems of 100 girls, aged 2-15, by traditional methods and found high rates of colonization of diphtheroids (78%), *Staphylococcus epidermidis* (73%), α-hemolytic streptococci (39%), *Escherichia coli* (34%), and the mycoplasma *Ureaplasma urealyticum* (*UU*). Lower rates of prevalence were found with *Corynebacterium vaginale* (13.5%), *Candida* species (28%), *Klebsiella* (15%), Group D streptococci (8.5%), *S. aureus* (7%), *Haemophilus influenza* (5%), *Pseudomonas aeruginosa* (5%), *Proteus* (5%), and *Acinetobacter* species (3%) ***(Hammerschlag et al., 1978).***

Lactobacilli were isolated most frequently from older girls (a 45% prevalence in those under 2 years had increased to 88% by age 11); while enteric organisms were isolated most frequently from younger girls (*E. coli* was found in 90% of infants). *Corynebacterium* was more prevalent in children under 2 or over 10 years of age (18% and 63% respectively) ***(Hammerschlag et al., 1978).***

Mycoplasmas tended to be found together; all six children colonized with *M. hominis* were also colonized with *U. urealyticum*. *M. hominis* was more prevalent in those over

10 years of age (none was found in children under 2 years), while the prevalence of *U. urealyticum* was similar in all age groups. *C. albicans* and *C. tropicalis* were the most common yeast species identified and were more prevalent in infants and teenagers (post pubertal) than in older children (3 to 10 years). *C. tropicalis* was isolated only from infants. *Neisseria gonorrhoeae, Chlamydia trachomatis*, and *Trichomonas vaginalis* were only rarely identified. Although the presence of *N. gonorrhoeae* and *Chlamydia* are considered conclusive evidence of abuse in children, this study did not address the issue of sexual transmission of any organisms. In addition, the analysis of the data is difficult since both premenarchal and postmenarchal girls were included, and the described lack of sexual activity in some girls was not specified as virginal ***(Hammerschlag et al., 1978).***

A second study and similarly using traditional methods, looked specifically at anaerobic bacteria in the vagina of 25 girls (aged 2 months to 15 years). The most prevalent organism was *S. epidermidis* (84%). Diphtheroids, α-hemolytic streptococci, *E. coli, Klebsiella, P. aeruginosa, C. vaginale, H. influenzae*, and *S. aureus* were also identified. All but one of the subjects were colonized by anaerobic streptococci ***(Hammerschlag et al., 1978)***.

Another study by **Jaquiery** and his colleagues evaluated the microbiota in girls across income groups (**Hammerschlag** had looked only at low-income children) who underwent

surgery at a children's hospital. **Jaquiery** (looking only at premenarchal girls) found, like **Hammerschlag** that anaerobes, diphtheroids, coagulase-negative staphylococci, and *E. coli* were very common. **Jaquiery** who solicited information about prior sexual abuse and excluded those subjects, did not find *Gardnerella vaginalis*, *T. hominis*, genital *Mycoplasmas*, or *N. gonorrhoeae* in any culture. *C. trachomatis* was also negative for all specimens ***(Jaquiery et al., 1999)***.

Puberty period:

Both the morphology and physiology of the vulva and vagina change at puberty. With adrenal and gonadal maturation, cyclic hormonal patterns are established and menstruation begins. Mid-cycle estrogen levels produce peaks in the glycogen content of the vaginal epithelium, which increases the prevalence of lactic acid producing microbes in the microbiota ***(Farage et al., 2006).***

The vaginal microbiota was assessed in 171 girls (aged 13 to 21) by **Shafer** also by traditional methods. *Lactobacillus* species were isolated from nearly 70% of all subjects, with sexually active girls almost twice as likely to carry lactobacilli than non-sexually active girls. *C. trachomatis*, *N. gonorrhoeae*, and *T. vaginalis* were isolated only from sexually active adolescents. Active subjects had higher rates of *G. vaginalis*, lactobacilli, *Mycoplasma* species, and *U. urealyticum* than non-active participants ***(Shafer et al., 1985).***

Findings for teens who were not sexually active were similar to that reported by **Hammerschlag** for female children, while those for the sexually active group were more similar to results reported for adult women. *Gardnerella* was recovered from non-sexually active adolescents, but the prevalence nearly doubled with sexually activity. Yeast was also recovered from a significant percentage (10%) of non-sexually active girls. In this study, *Mycoplasmas* were not found in adolescents who were not sexually active, confirming an early study which found a linear relationship between the presence of *Mycoplasma* in the vaginal microbiota and sexual activity ***(Miranda et al., 2010).***

Menopausal and postmenopausal years:

Menopause is marked by a dramatic reduction in estrogen production, resulting in drying and atrophy of the vaginal epithelium. When estrogen levels drop, glycogen content in the vaginal epithelium drops as well, leading to depletion of lactobacilli. Falling numbers of lactobacilli result in a subsequent rise in vaginal pH, since glucose is not converted to lactic acid. High pH promotes growth of pathogenic bacteria, particularly colonization by enteric bacteria. Overall, the makeup of the vaginal microbiota will depend upon duration, rate, and severity of estrogen deficiency ***(Galhardo et al., 2006)***.

In an assessment of vaginal health by Gram-stained smears 76 healthy postmenopausal women without any