Bacterial vaginosis, intrauterine infection, neonatal outcome – a review of current knowledge

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Abstract
There have been major advances in the care of preterm infants. Reduction in mortality among very low birth weight infants has lead to a rise in the number of survivors with severe handicaps. The understanding of preterm labour has evolved, leading to a significant change in the management of preterm labour. Despite this, infection still remains a major cause of preterm delivery. In our review we present the recent knowledge concerning intrauterine infection, preterm delivery and its implications for the very low birth weight infant. Amniotic cavity infection are most frequently related to microbial invasion, which leads to cytokine production and release of prostaglandins, followed by preterm delivery. Additionally bacteria present in the amnion may be swallowed by the foetus leading to a foetal inflammation syndrome (FIRS), characterized by bacteraemia and multi-organ failure. Intrauterine microbial invasion of the foetus has important prognostic implications for the preterm newborn. Based on our review we postulate that neonatologists should always request pathologic examination of the placenta after each preterm delivery at less than 32 weeks of gestation.

Key words: bacterial vaginosis, intrauterine infection, neonatal outcome

Introduction

Recent advances in perinatal care have led to an increase in the survival of very low birth weight infants in Poland and throughout the world. Due to the regionalisation of perinatal care, use of antenatal steroids and surfactant, as well as improvement of mechanical ventilation methods the number of survivors has significantly increased. Reduction of morality has been accompanied by a rise in the number of ex preterm infants with severe neurological handicaps. It is estimated that despite efforts to reduce the number of preterm deliveries, the rate of preterm births still comprises 11% of deliveries in Poland.

For many years it was believed that term and preterm labour are the same processes, except for the gestational age at which they occur. Both processes share a common terminal pathway which consists of myometrial contractility, cervical ripening and decidual/membrane activation. Fetal fibronectin detection is among many methods used to indentify women at risk of preterm labour. Positive fibronectin test usually leads to antibiotic administration, assuming that positive fibronectin finding is due to subclinical intrauterine infection. Despite multiple evidence that there is a firm causal link between intrauterine infection and preterm labour, this intervention has not been proven to be successful [1, 2].

Intra-amniotic infection has been associated with preterm delivery for many years. There is some evidence that states that at least 40% of all women with preterm birth have silent intrauterine infection [1]. As expected the lower the gestational age, the higher the risk of intrauterine infection.

It has been well established that microorganisms leading to an intra-amniotic inflammation processes gain access to the amniotic cavity through the following pathways: 1) ascending through the vagina and cervix, 2) haematogenous dissemination through the placenta, 3) retrograde seeding through the fallopian tubes, 4) iatrogenic introduction during invasive procedures. Evidence suggests that the ascending route is the most frequent pathway [3].

Data regarding microbial isolates from the amniotic cavities of women with preterm labour remains quiet elusive. Fusobacterium sp, Streptococcus agalactiae, Peptostreptococcus sp, Staphylococcus aureus, Gardnerella vaginalis, S. viridans and Bacteroids sp, are among the microorganisms indentified in the amniotic fluid of women with preterm delivery. Bacteria such as Acinetomyces sp; Prevotella Bivia; Corynebacterium sp; E.coli as well as Ureaplasma urealyticum and Mycoplasma hominis have a stronger link with chorionic plate inflammation. Although placental cultures are not preformed routinely, there is increasing data suggesting a close relation between microbial invasion of the amniotic cavity and chorioamnionitis [4, 5]. Interestingly there is mounting evidence suggesting that Ureaplasma urealyticum
and *Mycoplasma hominis* play a significant role in inducing placental inflammation [6], organisms which are not covered by standard treatment of congenital infections in preterm infants.

The role of *Candida* sp in intra-amniotic infection, should be highlight despite it’s rare occurrence. *Candida* related (especially *C. albicans*) infections are associated with very high mortality in preterm infants. Typically these infections manifest with pinpoint yellow – white nodules on the umbilical cord [7]. Early diagnosis, and adequate antifungal treatment may decrease the mortality due to *Candida* infection.

Microbial invasion leads to an interaction between the microbes and the decidual membrane interface. This results in a pathological activation of labour. What probably happens is that microbes or their byproducts trigger cytokine production and the release of prostaglandins. This is followed by cervical ripening and myometrial activation.

Presence of bacteria in the amniotic cavity may not always lead to intrauterine infection instantly. Data suggests that women with positive amniotic fluid cultures do not have to have clinical evidence of infection at presentation [1]. These women have a higher risk for developing clinical and histologic chorioamnionitis. Hillier et al. has reported a strong relationship between the presence of histologic chorioamnionitis and microbial presence in the amniotic cavity [8]. The rates of chorioamnionitis diagnosed during pathological examination are higher than the number of positive amniotic cultures, which indicates the role of other etiological factors.

It has been proven, that pathological findings in the preterm placenta show clinical relevance. There is consistent data, which indicates an association between particular findings and a increased risk of neonatal sepsis, poor neonatal outcome such as bronchopulmonary dysplasia, necrotizing enterocolitis and cerebral palsy. An inflammatory response in the placenta such as necrotizing chorioamnionitis is defined as neutrophil karyorrhexis, amniocyte necrosis, or basement membrane thickening/hypereosinophilia in greater than 30% of the membranes [9]. Foetal response to amniotic cavity infection is diagnosed based on the presence of the following findings: intense chorionic or umbilical vasculitis with vessel damage or concentric perivasculitis of the umbilical vessels-funisitis [6].

There are several possible pathways of foetal infection. Probably the foetus swallows bacteria, which are present in the amniotic cavity. This may lead to pneumonia or pneumonia followed by bacteraemia and multiple organ failure (Fetal Inflammation Syndrome – FIRS). Delivery can occur at any stage of infection. It is believed that affected foetuses have a higher rate of neonatal complications such as neonatal sepsis, long term handicap, including bronchopulmonary dysplasia and cerebral palsy (CP) [10-13]. Studies in preterm infants have shown a strong association of funisitis and CP. White-matter lesions are associated with elevated concentrations of cytokines in the amniotic fluid and a subsequent development of CP.

Pathological examination of the preterm placenta can reveal important information for the neonatologist especially when intrauterine infection is suspected. Inflammation of the chorionic plate or funisitis are crucial prognostic factors, which may have further implications for the preterm neonate. Thus, histologic evaluation of the placenta should be requested after each preterm delivery below 32 weeks of gestation.

References


