Population pharmacokinetics of antibiotics to prevent group B streptococcal disease: from mother to neonate

Muller, A.E.

Chapter 3

Morbidity related to maternal group B streptococcal infections.

Anouk E. Muller, Paul M. Oostvogel, Eric A.P. Steegers, P. Joep Dörr

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Abstract

Group B streptococcus is known to be a leading cause of neonatal infection, but less appreciated is the fact that it causes maternal infection also. Maternal group B streptococcal infections during pregnancy and delivery threaten not only the mother, but the child as well. Postpartum infection, such as mastitis, bacteremia, sepsis, meningitis, endometritis and wound infections are hazards to the mother. We describe the various maternal group B streptococcal infections, their characteristics, associated neonatal morbidity, and prevention and treatment strategies during pregnancy, delivery and in the postpartum period.

Introduction

Group B streptococcus (GBS, *Streptococcus agalactiae*) has been known as a human pathogen since 1938[1]. It emerged as leading infectious cause of neonatal morbidity and mortality in the 1970s[2]. Because of this, much attention has been given to the prevention of neonatal GBS disease. Guidelines to prevent neonatal GBS disease were developed in the 1990s. After the implementation of these preventive guidelines, the incidence of early onset disease decreased markedly from an estimated 1.8 cases per 1000 live births in 1990 to 0.32 cases per 1000 live births in 2003 in the Unites States[3,4]. Other countries showed a similar decrease. However, despite the decrease in the incidence, GBS remains the number one cause of infectious neonatal morbidity and mortality in the Western world. The majority of cases of early-onset GBS disease occur in infants whose mothers screened negative for GBS colonization[5].

GBS has also been recognized as an important maternal pathogen. A variety of maternal GBS infections may occur in the course of pregnancy and the postpartum period. Apart from cervicovaginal colonization, which is usually asymptomatic, GBS can cause urinary tract infections, vulvovaginitis, intra-amniotic infection, mastitis, bacteremia, sepsis, meningitis, endometritis and wound infections[6].

Because of the serious complications that may affect both mother and fetus, these maternal infections require special attention and proper treatment. In this paper the various maternal infections, their characteristics and the specific prevention and/or treatment strategies are reviewed. The infections are described in the chronological order in which they may be encountered during and after pregnancy.

The pathogen

GBS is a Gram-positive coccus, growing in chains or as diplococci. Because GBS causes complete destruction of red blood cells on sheep blood agar, colonies produce a characteristic appearance with narrow surrounding zones of β-hemolysis. Serologic identification of GBS suspected colonies is performed using latex agglutination.

GBS is serologically classified into nine serotypes based on antigenic capsular carbohydrates as Ia, Ib and II-VIII. Surface proteins are expressed nearly independent of those serotypes. Differences in the expression of carbohydrates and surface proteins account for differences in the pathogenesis of infections[7,8]. Factors playing a role in the development of an asymptomatic or invasive infection have not yet fully been elucidated[7]. As colonization can often occur without symptoms, it is possible that only certain virulent GBS serotypes or surface proteins may cause symptomatic infections. This is currently an area of research[7,8]. However, the present knowledge on the different GBS types is insufficient to be clinically relevant.

During pregnancy

Urinary tract infections

General

Urinary tract infections (UTI) are the most common bacterial infections during pregnancy. GBS causes asymptomatic bacteriuria, cystitis, and pyelonephritis acquired by an ascending route from the vagina. UTI due to GBS are clinically indistinguishable from UTI due to other bacteria in pregnant and in non-pregnant women. GBS bacteriuria, often with low bacterial count, complicates up to 7% of pregnancies[9-11], of which 70% are asymptomatic[12]. The frequency of symptomatic UTI in pregnancy could reflect asymptomatic bacteriuria acquired earlier in life. GBS causes about 10% of the cases of acute pyelonephritis, mainly in the second trimester[13]. Serotype III and non-typable strains are responsible for the majority of bacteriuria[14,15].

Sequelae

UTI due to GBS have been associated with adverse pregnancy outcomes such as (preterm) premature rupture of the membranes ((P)PROM), preterm labor, and neonatal GBS infections, even with low bacterial counts ($<10^2$ bacteria per ml of urine)[12]. Nevertheless, the causal relation between GBS bacteriuria and preterm delivery and PROM is controversial, as several studies report contradictory results [12,16-20].

It has been suggested that GBS bacteriuria may be associated with neonatal GBS disease as well and is therefore one of the commonly used risk factors for neonatal GBS disease[21]. However, there is little evidence for a causal relation. The association with increased neonatal GBS disease is based on two studies, with 10 and 14 patients respectively[9,14]. A third study reported several cases of neonatal GBS sepsis in patients with both GBS bacteriuria and premature delivery[12]. It has been assumed that asymptomatic GBS bacteriuria during pregnancy is associated with heavy genital colonization with GBS[9,10,14], based on an enhanced prevalence of adverse neonatal outcomes. However, no quantitative cultures have been performed in these studies to confirm this. Two studies investigating the relation between bacteriuria and genital colonization reported a positive predictive value of GBS bacteriuria in first trimester of pregnancy for positive GBS genital culture at the time of labor of 30.2%[11] and 61%[22] respectively. McKenna et al. reported that in women with GBS bacteriuria, in only 63% the same serotype was found in the urine and genital cultures[11].

Acute pyelonephritis is a serious threat to maternal and fetal well-being[23]. It can lead to perinatal complications including premature delivery, low birth weight and fetal mortality[15]. Maternal acute pyelonephritis is associated with

anemia, thrombocytopenia, septicemia, transient renal dysfunction, preeclampsia, pregnancy-induced hypertension, and pulmonary insufficiency[13,15].

Prevention

Strong evidence for a causal relation between GBS bacteriuria and adverse outcomes is absent, however screening for bacteriuria early in pregnancy may be considered. GBS bacteriuria should be treated, whether symptomatic or not[24]. Treatment in the first trimester has been shown to reduce the incidence of symptomatic cystitis and pyelonephritis[25]. Treatment of asymptomatic GBS bacteriuria at 28 weeks gestation has been shown to reduce the risk of preterm labor and PPROM in one randomized controlled trial[20].

Though there is evidence for the benefit of treatment of GBS bacteriuria in third trimester as mentioned before, there is no evidence that treatment of GBS bacteriuria in first trimester prevents adverse neonatal outcome. First trimester bacteriuria does not automatically equate to heavy genital tract colonization at 35-37 weeks gestation[11]. Nevertheless, current Centers for Disease Control and Prevention (CDC) guidelines call for intrapartum prophylaxis for early onset neonatal GBS disease if bacteriuria was diagnosed during the pregnancy[21], and thus there is no need for rectovaginal culture at 35-37 weeks in women in whom GBS bacteriuria was diagnosed.

Treatment

There are many antibiotics available for the treatment of urinary tract infections. However, there are insufficient data to recommend any specific regimen in general[26], but during pregnancy the use of nitrofurantoin covers most common microorganisms, such as *E. coli* and other Gram-negative bacteria[26,27].

First choice therapy of (a)symptomatic bacteriuria due to GBS is oral administration of penicillin for 4-7 days[20,28]. The effectiveness of shorter treatment has not yet been proven[28]. One week after completion of the antibiotic treatment the urine-culture should be repeated to confirm the effectiveness. Because of the high recurrence rate of bacteriuria during pregnancy[29], urine cultures should be repeated monthly. GBS pyelonephritis is treated with penicillin G for a total duration of 14 days, starting with intravenous administration. After clinical response to intravenous therapy, treatment should be continued orally. In some settings daily suppressive antibiotic therapy is continued until delivery.

Vaginitis and GBS

General

GBS is a commensal endogenous bacterium in the gastrointestinal tract, which is the likely source of subsequent vaginal colonization. Studies indicate that 10-30% of all pregnant women are colonized with GBS in the gastrointestinal or genital tract[30,31]. Colonization can be transient, chronic or intermittent. Most carriers are asymptomatic.

Bacterial vaginosis associated with various anaerobic bacteria, *Gardnerella vaginalis* and *Mycoplasma hominis*, is the most common cause of vaginitis. It is not clear whether there is an etiological role of GBS in pregnant women for excessive vaginal discharge and symptomatic vaginitis. In non-pregnant women there is some evidence that GBS could be capable of causing symptomatic vaginitis. GBS seems to be more prevalent in patients with purulent or excessive vaginal discharge[32,33]. Vaginitis seems to be related to colonization with GBS[33]. However, there is no consensus whether GBS is the actual causative microorganism in these cases or whether GBS is present only as a cofactor[34,35].

Sequelae

Whether vaginal GBS colonization is a risk factor for PROM, PPROM and preterm delivery is still controversial. Associations between the colonization with GBS and PROM or with preterm delivery have not been found consistently[36-38]. PROM and preterm delivery are risk factors of early-onset neonatal GBS infection.

Vaginal GBS colonization increases the risk on several maternal infections, such as urinary tract infection, endometritis and wound infection. Other additional risks are secondary to PROM, PPROM, and the use of corticosteroids, antibiotics or tocolytic agents.

Studies on GBS transmission in colonized mothers during delivery report incidences between 16-53%[39-42] and neonatal disease develops with a frequency of 1%[40] to 22%[39] in colonized neonates. Only 1-2% of infants of colonized women develop early-onset GBS disease in the first week of life.

Prevention

During labor there are different strategies to prevent neonatal GBS disease. Guidelines from CDC and Canadian guidelines[21,43] recommend universal screening for rectovaginal GBS colonization in pregnant women at 35-37 weeks of gestation and administration of prophylactic antibiotics during labor to all GBS positive women. Prior to these guidelines a risk-based strategy was common in the USA, indicating that only women with a risk factor should receive antibiotics during labor. Risk factors for neonatal GBS disease are prematurity, ruptured membranes for more than 18 hours, fever, GBS bacteriuria in current pregnancy, or a previous

neonate with GBS disease. A risk-based strategy is still being applied in the Netherlands. Another possibility is to combine the risk-based and the screening based strategy and treat only GBS positive women with a risk factor[44]. Schrag et al.[45] demonstrated that routine screening for group B streptococcus prevents more cases of early-onset disease than the risk-based approach.

Treatment
There is no evidence that screening and treatment of asymptomatic bacterial vaginosis reduces adverse neonatal outcome[46]. Symptomatic bacterial vaginosis should be treated with a regimen based on the culture results[46] or empiric with metronidazole[47]. It is advised not to treat GBS colonization before the onset of labor, because recolonization is likely to occur[34,35].

During delivery

Intra-amniotic infection

General
The term intra-amniotic infection (IAI) refers to the clinical syndrome of infection of the placenta and membranes accompanied by signs and symptoms in the mother and/or the fetus. Although the diagnosis is made using clinical symptoms, no universally accepted criteria have been described so far. Commonly used criteria include maternal temperature of >38˚ C, fetal tachycardia (>160 beats/minute), uterine tenderness and foul smelling amniotic fluid[48]. IAI due to GBS occurs after ascending spread from the vagina. The reported incidence varies with the duration of gestation and the criteria used to diagnose IAI. The incidence of IAI based on clinical diagnosis is approximately 1-2% of all term deliveries, but in preterm deliveries the incidence is increased[49]. Bacteria normally present in the vagina are the most common amniotic fluid isolates in women with IAI. GBS was found in 15.4% of the amniotic fluid of patients with IAI and one of the most frequently isolated species in infected newborns delivered of mothers with IAI[50-52]. Colonization with GBS increases the risk on IAI during labor[53]. The risk for IAI increases with the duration of rupture of the membranes. However GBS can sometimes be cultured in amniotic fluid samples from patients with intact membranes as well[54,55].

Sequelae
The risks for maternal and neonatal morbidity and mortality is increased in patients with IAI. Maternal consequences include infection (serious maternal pelvic infections as well as sepsis), prolonged duration of labor, the need for higher doses of oxytocin when uterine stimulation is required[56] and an increased risk for delivery

by caesarean section[57]. Postpartum hemorrhage is more common in these patients, due to impaired myometrial contraction. Bacteremia occurs in 2-6% of patients with IAI. However, when GBS is the cause of IAI much higher incidences of bacteremia are reported (up to in 18%)[58].

Fetal aspiration of infected amniotic fluid can lead to stillbirth, neonatal pneumonia, or sepsis[21]. Neurodevelopmental delay and cerebral palsy are potential long-term disabilities resulting from IAI[59,60].

Prevention

Most neonatal infections are acquired in utero, often without clinical signs of infection. The current CDC guidelines[21] recommend the administration of antibiotics to all GBS positive women during labor to prevent IAI due to GBS. The previously used risk-based strategy advised antibiotics only in situations with an enhanced risk for neonatal GBS disease[61].

The presence of GBS influences the choice of management in patients with PPROM, since subclinical GBS intrauterine infection has been implicated as a major factor in the pathogenesis and consequential maternal and neonatal morbidity. For patients with PPROM and a positive or unknown GBS culture antibiotic therapy is recommended to prevent or treat ascending intrauterine infection[21]. Due to the administration of antibiotics pregnancy will be prolonged and both maternal and neonatal infectious morbidity is decreased[62,63]. Unfortunately, the majority of cases of IAI in the setting of PPROM do not produce the signs and symptoms traditionally used as diagnostic criteria for clinical chorioamnionitis.

Treatment

When signs of infection are present antibiotic treatment is advised and delivery is expedited. Several studies have demonstrated the benefit of intrapartum therapy compared to maternal therapy starting postpartum for both the incidence of neonatal sepsis and maternal morbidity[50,64]. This was especially prominent with sepsis due to GBS. A Cochrane systematic review[65] concluded that the outcome after intrapartum and postpartum treatment was not significantly different probably because the number of patients included was too low[50]. However, it should be noted that the interim analysis of Gibbs' study[50] was in strong favor of intrapartum treatment. Therefore, this study had to be stopped due to clearly worse neonatal outcome in the postpartum treatment group.

It is still under debate what is the optimal treatment regimen should be[65]. Most IAI are caused by either *E. coli* or GBS. However, culture results are not available at the time treatment starts. Therefore, treatment is usually initiated on an empirical basis with a combination of a penicillin for GBS and gentamicin for *E. coli*[50], starting intrapartum. Some authors advise the addition of clindamycin to cover anaerobic bacteria[66,67].

Postpartum infections

Mastitis

General
Mastitis is a parenchymatous infection of the mammary glands, most commonly caused by *Staphylococcus aureus*. Puerperal mastitis due to GBS can be either symptomatic or asymptomatic. The incidence of acute puerperal mastitis varies from 2.9% to 24%. Only one study has examined the breast GBS carriage rate in humans, finding an incidence of 3.5% in 1132 milk samples from healthy lactating mothers[68].

Sequelae
Maternal milk (in cases of either clinical or sub-clinical mastitis) is a potential source of infection resulting in either late-onset (i.e. from one week of life to three months) or recurrent neonatal GBS disease[69-75]. However, the pathogenesis of mastitis is unclear. Most likely, infection of the maternal breast follows colonization of the neonate in the oropharynx acquired during delivery. Afterwards, neonatal infection is thought to occur as a result of aspiration of organisms in the mammary ducts when negative pressure is created by sucking[70]. But it is also possible that GBS has entered the mammary glands prior to labor and does not originate from the neonate itself.

Prevention
It is important to be aware of the possibility of GBS mastitis and GBS carriage in breast milk. Since the pathogenesis of GBS mastitis is unclear, prevention is difficult. In case of suspected or recurrent GBS neonatal disease, breast milk should be cultured and breast feeding stopped until the cultures are negative.

Treatment
Treatment of mild cases of mastitis is conservative, with the use of compresses, rest, and antipyretics. Antibiotics are used only in febrile patients[76]. Empiric therapy consists of cloxacillin, or erythromycin[77]. All cases of GBS mastitis should be treated with ampicillin, because of the possibility of serious neonatal morbidity.

Bacteremia and sepsis

General
Bacteremia in pregnancy and the puerperium may result from common medical illnesses (e.g. pneumonia, appendicitis) or conditions unique to pregnancy (e.g.

endometritis, chorioamnionitis). Among cases of GBS puerperal infection, bacteremia occurred in 31% to 35%[78]. In general, bacteremia progresses to sepsis in 5-25%, while septic shock is rare[79]. Bacteremia within 15 minutes after manual removal of the placenta prior to the administration of prophylactic antibiotics was found in 14% (13 out of 93 patients) of patients in labor who were delivered by caesarean section. GBS are among of the most commonly isolated microorganisms (38%)[80].

Sequelae
The maternal sequelae due to GBS sepsis do not differ from those related to other bacteria. Sepsis remains an important cause of maternal mortality. In developing countries puerperal sepsis is one of the main factors leading to maternal mortality[81]. Nevertheless, in obstetric patients the incidence of death from sepsis is low, as it is estimated at 0-3%, compared to 10-81% in non-pregnant adults[79]. Another maternal complication of bacteremia is meningitis.

Prevention
Several factors predispose for bacteremia and sepsis. In vaginal delivery, prevention of predisposing factors might reduce the risk for bacteremia. Predisposing factors of bacteremia are early gestational age, low birth weight, internal fetal monitoring, and a positive chorioamnionic membrane culture[80]. Predisposing factors of puerperal sepsis include anemia in pregnancy, prolonged labor (at least 12 hours), frequent vaginal examination during labor (more than 5 times) and premature rupture of membranes[82]. To reduce the risk of bacteremia after caesarean delivery, antibiotics should be administered[80].

Treatment
To prevent the sequelae of bacteremia or sepsis rapid intervention with broad-spectrum antibiotics (beta-lactam with aminoglycoside) is required on an empirical basis[83]. In case culture results show GBS bacteremia the narrow-spectrum antibiotic penicillin is sufficient. Microbiological evaluation should include specimens from blood, urine, wound and endometrium. Antibiotic treatment should continue for 5-7 days.

Meningitis

General
The overall incidence of GBS meningitis is 0.3 cases/ 100.000 population[84]. Postpartum maternal GBS meningitis is rare[85]. In the literature only 10 cases have been described. All cases but one followed a vaginal delivery[86,87]. Only one patient

presented meningitis before delivery whereas one patient was diagnosed 6 months postpartum. The other 8 cases manifested between 14 hours and 6 days postpartum. One patient died. None of the mothers had received antibiotic prophylaxis during delivery. One additional case of GBS meningitis has been reported as a likely complication of obstetric epidural anesthesia[88].

Bacterial meningitis usually develops after hematogenous spread. Bacteria then cross the blood-brain barrier into the subarachnoid space. In an experimental animal model, a high degree of bacteremia had been shown to be a primary determinant for meningeal invasion by GBS[89]. To cause meningitis via the bloodstream, bacteria have to escape the host defenses, multiply and reach the threshold level of bacteremia to invade the meninges. Another possible route of infection is after direct inoculation into the cerebrospinal fluid.

Sequelae

For young adults, outcome is related to the level of consciousness and the presence of seizures at the time treatment is initiated. Potential complications are dementia, seizures, hydrocephalus, cerebral infarction, cerebral venous thrombosis and brain abscesses. Ten percent of patients suffer from hearing deficits after bacterial meningitis. In general, about 30-50% of the survivors sustain neurological sequelae after bacterial meningitis[90].

Prevention

Since the degree of bacteremia in the patient seems to be the primary determinant in the pathogenesis of GBS meningitis[89], prevention of bacteremia should also prevent meningitis. The incidence of bacteremia after cesarean delivery is high, but GBS meningitis occurs predominantly after vaginal delivery. This can probably be explained by the fact that antibiotic prophylaxis in cesarean deliveries lowers the bacterial load.

Treatment

To prevent complications from GBS meningitis treatment should start as soon as the diagnosis is suspected. Lumbar puncture and isolation of GBS is diagnostic. Treatment will start empirically with a 3rd generation cephalosporin[91]. GBS meningitis should be treated with penicillin G or ampicillin for a total period of 2-3 weeks intravenously.

Endometritis

General

Endometritis is a more common complication of cesarean section than of vaginal deliveries (11.4 versus 0.4%)[92]. Endometritis following vaginal delivery develops more frequently in women who had pregnancies associated with adverse fetal outcomes including stillbirth, low birthweight, preterm delivery and serious neonatal morbidity[93,94]. Postpartum endometritis can occur up to 6 weeks following delivery.

Risk factors for the development of endometritis include delivery by caesarean section, instrumental delivery, long duration of labor, internal fetal monitoring, frequent vaginal examinations, preterm labor, premature rupture of membranes, manual removal of the placenta, low socioeconomic status, infection with *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, and colonization with GBS[94,95]. Patients with meconium have a higher risk for endometritis[96], probably because the growth of GBS and *E. coli* is enhanced in meconium stained amniotic fluid[97].

In early postpartum endometritis (i.e. within the first 48 hours), GBS is an important contributor as it is most frequently isolated[98]. High-spiking fever (at least 39˚ C) developing within the first 24 hours after delivery may be associated with very virulent pelvic infection caused by either group A or group B streptococcus[53]. In studies of endometritis, GBS has been identified as the sole pathogen in 2 to 14 percent of cases. It appeared the only pathogen more often after vaginal delivery as compared to caesarean section[99,100].

Sequelae

Maternal morbidity associated with endometritis depends on the type of sequelae. Infection can extend to the peritoneal cavity followed by peritonitis and pelvic abscesses and can even cause sepsis. Septic pelvic thrombophlebitis is a rare complication.

Prevention

Several strategies have been suggested for the prevention of endometritis in general. To reduce the incidence of endometritis antibiotic prophylaxis at the time of cesarean delivery has become a common practice[101]. Fernandez et al.[102] demonstrated that a single dose of amoxicillin and clavulanic acid is beneficial after vaginal deliveries. However, low incidence of endometritis after vaginal delivery and preference for the restrictive use of antibiotics make such practice undesired. There is also some evidence that the intravaginal administration of metronidazole gel reduces the incidence of post cesarean endometritis[103]. The efficacy of chlorhexidine before caesarean delivery and the use of methergine in the postpartum period is controversial[104-108].

Strategies specifically aiming at GBS may be helpful as well. The incidence of GBS endometritis declined after the introduction of the GBS prophylaxis[109]. In a longitudinal study Locksmith et al.[110] compared the infection rates following three consecutive protocols for the prevention of GBS disease. In the selective screening protocol, GBS cultures were obtained from women with PPROM or preterm labor and intrapartum antibiotics were administered to all women with positive culture and a risk factor for neonatal GBS disease. In the risk-based protocol, intrapartum antibiotics were given to all women with unknown colonization status and a risk factor for neonatal GBS disease[111]. Under the universal screening protocol, a culture was performed between the 35-37 week of gestation and intrapartum antibiotic prophylaxis given to all women with a positive GBS culture. Under all three protocols the postpartum endometritis rates were reduced[110]. The best success rate was achieved with universal screening[110].

Treatment

Commonly postpartum endometritis is treated with an empiric regimen against mixed aerobic and anaerobic organisms. The combination of clindamycin with once daily gentamicin is appropriate. Once uncomplicated endometritis has clinically improved with intravenous therapy, oral therapy is not needed[112]. In case GBS is detected the same regimen should be followed to cover the often mixed flora causing postpartum endometritis.

Wound infections

General

Infections in perineal and abdominal wounds after delivery can be caused by GBS. Infections with hemolytic streptococci progress rapidly. Cellulitis, lymphangitis, and bleb formations are typical. Watery exudate from the wound is common. Infection of perineal wounds is relatively uncommon, despite the high prevalence of bacteria present at the site of infection. Owen et al. described episiotomy infections to occur in only 0.05% of all cases[113]. Besides technical procedures, duration of cesarean section over one hour and induction of labor increase the risk of wound infection[114].

Early-onset wound infection is commonly caused by group A streptococcus, presenting with systemic illness. Group B streptococcus may present in a similar fashion[115]. It is not known to what extent GBS contributes to the incidence of wound infections. Abdominal wound infections after caesarean section may be caused by the same microorganisms that can be isolated from the amniotic fluid. At caesarean section after rupture of the membranes for at least 6 hours, GBS can be cultured from the amniotic fluid 8% of the time[116].

Sequelae

Episiotomy dehiscence is most commonly associated with infection. Maternal risks include the extension of the infection, fistula formation and sepsis. Failure to treat these infections exposes patients to the risk of necrotizing fasciitis and bacteremia.

Necrotizing fasciitis is a rare obstetric complication. It involves the superficial fascia, subcutaneous tissue, and, occasionally, deeper tissue layers. It can be fatal and is often rapidly progressive and associated with significant tissue necrosis. Initially it is often unrecognized and later it presents as a fulminating disease with marked high mortality. Prognosis depends on the delay of diagnosis, antimicrobial treatment and wide surgical excision of all necrotic tissue[117]. Necrotizing fasciitis arising from an infected episiotomy due to GBS has been described[118]. Necrotizing fasciitis of an episiotomy may extend to the thighs, buttocks and the abdominal wall. Usually symptoms appear from 3 to 5 days postpartum. Risk factors postpartum for necrotizing fasciitis are diabetes mellitus, obesity, hypertension and drug abuse[119].

Prevention

Puerperal endometritis increases the risk of wound infections[114]. Prevention of endometritis is therefore important for the prevention of wound infection. There is some evidence that GBS prophylaxis is also beneficial in the prevention of wound infections[92]. It is unclear whether this is a direct effect of the antibiotics, or indirectly through a reduction in the incidence of endometritis.

General strategies to prevent wound infection and its extension are straightforward and not specific for GBS. Most important is proper hygiene and proper surgical technique.

Treatment

If the wound infection is mild, antibiotics are not required. If the infection is severe, but does not involve deep tissues, a combination of ampicillin and metronidazole should be prescribed. In case deep tissues are involved or first signs of necrotizing fasciitis appear, a combination of broad spectrum antibiotics (penicillin, gentamicin and metronidazole) and surgical treatment are indicated[77]. Necrotizing fasciitis requires wide surgical debridement. GBS may be involved in most types of wound infections, but no specific approach is required.

Conclusion

GBS not only is an important cause of serious neonatal infection, but also causes a variety of maternal infections. These infections cause less morbidity than neonatal infections, but occur more commonly. Especially during the course of pregnancy and delivery GBS can endanger both the mother and fetus. Mastitis may be a cause of late-onset or recurrent neonatal GBS disease. With early recognition and proper treatment, maternal and neonatal severe morbidity and mortality due to GBS infections are rare.

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