

Antiviral Prophylaxis of Neonatal Herpes Infection

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Abstract: Herpes simplex virus (HSV) is considered to be one of the most frequent viral infectious agents in humans. Transmission of HSV from mother to foetus during pregnancy is uncommon with about 85% of transmission occurring perinatally, when neonates acquire HSV during vaginal birth from infected genital tract secretions. For women, who present with an episode of recurrent genital herpes several weeks before the expected delivery date, suppressive therapy with acyclovir or valacyclovir is recommended during the last 4 weeks of pregnancy. The study group consists of 21 women with recurrent genital tract herpes, who delivered between the years 2007–2009 at the Department of Obstetrics and Gynaecology, University Hospital Na Bulovce. Women in the last month of pregnancy were administered prophylactic viralstatic treatment with acyclovir 3 × 400 mg per day orally until delivery. In this study, no patient showed signs of acute lesions and viral DNA was not detectable on PCR in vaginal secretions. One woman delivered by acute caesarean section following signs of foetal hypoxia during the first stage of labour, two women were delivered by forceps. No newborns showed signs of HSV neonatal infection. Antiviral prophylaxis in the last month of pregnancy in women with recurrent genital herpes infection is considered to be safe and effective in the prevention of vulvar lesions and in decreasing the incidence of caesarean sections in this group of women.

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Introduction

Herpes simplex virus (HSV) is considered to be one of the most common viral infectious agents in humans. There are two genetically related viral types, the HSV type 1 (HSV-1) and HSV type 2 (HSV-2), which are slightly different. In Czech Republic, the prevalence of HSV-1 antibodies reaches high levels in more than 90% of adults whereas nearly 9% of the adult population possess antibodies to HSV-2 (Pebody et al., 2004). The greatest incidence of HSV infection occurs in women of reproductive age and the risk of maternal transmission of the virus to the foetus or neonate has become a major health concern (Baker, 2007; Kriebs, 2008). In the US, approximately 22% of pregnant women are infected with HSV-2, 10% are at risk of acquisition of genital HSV from their infected partners, and 2% of women acquire genital herpes during pregnancy (Brown et al., 2003, 2005; Baker, 2007). The acquisition of genital herpes during pregnancy has been associated with spontaneous abortion, intrauterine growth retardation, preterm labour, congenital and neonatal herpes infection (Brown et al., 1997). Maternal-foetal transmission of the virus can cause severe and permanent neurological damage to the neonate (Brown et al., 1991). Transmission of HSV from mother to foetus during pregnancy is uncommon (about 5%), about 85% of perinatal transmission occurs during the intrapartum period, neonates acquire HSV during vaginal birth, from infected genital tract secretions. The major sites of viral entry are the eyes, nasopharynx or a traumatized scalp (Boucher et al., 1990; Whitley and Roizman, 2001; Enright and Prober, 2002). If active genital HSV lesions are present or prodromal symptoms occur at the onset of delivery and consequently the risk of viral exposure to the infant is high, a caesarean section should be performed as quickly as possible within 4–6 hours after membranes rupture if foetal lungs are mature (Swiss Herpes Management Forum, 2004; Anzivino et al., 2009). Primary or recurrent herpes of the vulva in the case of obstetrics are indications for caesarean section according to professional societies in many countries (Braig and Chanzy, 2004; Swiss Herpes Management Forum, 2004; ACOG Committee on Practice Bulletins, 2007). The adverse effects on the newborn are so significant that a 3% risk of infections in recurrent lesions is very high. In an attempt to lower the percentage of necessary operative deliveries, many authors recommend prophylactic care in cases of infected deliveries.

For women, who present with an episode of recurrent genital herpes several weeks before the expected delivery date, a suppressive therapy with acyclovir or valacyclovir is recommended during the last 4 weeks of pregnancy (ACOG Committee on Practice Bulletins, 2007; Anzivino et al., 2009; Holub et al., 2009). Antenatal antiviral prophylaxis decreases viral shedding, recurrences at delivery, and reduces the need for caesarean delivery for genital herpes (Hollier and Wendel, 2008).

Material and Methods

At the Department of Obstetrics and Gynaecology of University Hospital Na Bulovce in the year 2007 was established a specialized outpatient department for

pregnant women with herpes genitalis. This outpatient department works in close cooperation between the department of infectious diseases and obstetrics, and pregnant women are referred from their private gynaecologists or from other clinics. Included in this study, where all women, who were seen in this outpatient clinic and delivered at the Department of Obstetrics and Gynaecology of University Hospital Na Bulovce in the time from January 2007 to December 2009, a group consisting of 21 women. All women since the 36th week of pregnancy took 3 × 400 mg of acyclovir daily, and before delivery a vaginal smear was taken to determine viral shedding with the aid of PCR. Exclusion criteria involved planned caesarean sections for another indication and foetus mortuus. No patient was excluded from the study.

The viral DNA was detected with the above method used. The use of viral DNA method real time PCR kit HSV 1,2 typing primer and probe set produced by Cepheid, USA, equipment Smart Cycle. Specific ready to use, (for one time use) for current detection of 2 types of herpes simplex virus – HSV 1,2 in the system of real time PCR (clinical modification of PCR) reagents-primer (glycoprotein D and G) and probes marked with fluorogenic colours are prepared with beads (HSV typing ASP lympholysed beads contain primers and probes for 2 DNA target sequences in the HSV genome glycoprotein D and G).

In the case of a negative smear and absence of herpetic genital ulceration at the time of delivery, a spontaneous delivery was conducted.

Results

All women in the study group suffer from recurrent genital herpes prior and during pregnancy. Table 1 shows some demographic characteristics in the study group. Median rate of recurrence in pregnancy was 3 (2–7). One woman also had chronic viral hepatitis C with normal levels of transaminases. Average age was 29.6 (25–33) years; all women gave birth at term.

We didn't observe any clinical recurrence at time of delivery, and no woman had positive vaginal specimens of viral nuclear acid on PCR. The average gestational age among the pregnant women was 39 weeks (38–41 weeks) the average duration of prophylaxis use was 18 days (10–29 days). No caesarean sections were performed for herpes genitalis, only one caesarean section in the study group was done because of foetal hypoxia in I. stage of labour. 20 women

Table 1 – Demographic and obstetrical data of study sample

Marital status		Education		Parity	
single	11	elementary	8	Primipara	16
married	9	college	12	Secundipara	4
divorced	1	graduate	1	Tercipara	0
				Quartipara	1

delivered vaginally, 18 spontaneously, 2 forceps delivery because of signs of foetal hypoxia in II. stage of labour. The average weight of the newborns was 3295 g (2580–4260 g), two neonates had an Apgar score at 1 minute of less than 7, and 5 and 10 minutes all neonates had a score of 7 or more. One neonate had pH from the umbilical artery of 7.15, and the other newborns had a pH of 7.20 or more. No newborn showed signs of neonatal herpes during hospitalization, 20 neonates were discharged home in healthy status 4 days following delivery. One newborn was discharged on the 6th day because of neonatal hyperbilirubinemia. No side effects from viral static therapy were observed in either the mother or the child.

Discussion

On the basis of the hospital discharge data, frequency of neonatal HSV infection in the US varies according to the patient population, with the rate of infection ranging from 1 case per 12,500 live births to 1 per 1700 live births. In a retrospective study in California, the rate was 12.2 cases per 100,000 live births from 1995 to 2003 (Morris et al., 2008). Analysis of data from 30 US health plans, which included 17 million enrollees, showed a rate of 60 cases per 100,000 live births (Whitley et al., 2007). Prospective, single-centre studies in the US have shown rates of neonatal HSV infection as high as 31.2 cases per 100,000 live births (Brown et al., 2003). The incidence data for neonatal HSV infection are similar to those for perinatal human immunodeficiency virus (HIV) infection before the advent of the routine use of antiretroviral agents in pregnancy, and the incidence is higher than that of congenital syphilis, toxoplasmosis and congenital rubella (Corey and Wald, 2009).

The percent of caesarean sections in the west has been increasing year by year. Due to antibiotic prophylaxis, low molecular weight heparin, and improved operative techniques, the risk of frequent caesarean section complication has decreased; remained the importance of attention to later complications, or complications in the following pregnancy (Zahumensky et al., 2008).

Current guidelines recommend caesarean deliveries in women with clinical evidence of recurrent genital herpes at term (ACOG Committee on Practice Bulletins, 2007). Several small studies have shown that the use of antiviral agents daily at the end of pregnancy can reduce recurrences of genital HSV infection and shedding at term, as well as the need for subsequent caesarean deliveries (OR 0.30), but these studies have not addressed the question of whether such treatment can reduce the risk of neonatal HSV infection (Sheffield et al., 2003). The levels of acyclovir in amniotic fluid can be similar to those seen in infants treated with systemic acyclovir, and neutropenia develops in up to 20% of such infants (Kimberlin et al., 2001). Thus, the routine use of antiviral agents in HSV-2 seropositive women in late pregnancy is recommended only in women with a history of clinical recurrent genital herpes.

Conclusion

In our study, the use of prophylactic virostatic therapy of acyclovir in the last month of pregnancy was well tolerated, no adverse effects were observed in either the mother or the child. No women at the time of delivery had any clinical manifestations of disease and we did not detect any viral shedding in vaginal secretion.

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