Does cesarean section protect against perinatal HPV infection?

Czy cięcie cesarskie zabezpiecza przed wertykalną infekcją wirusem HPV?

Mariusz Skoczyński [1/], Anna Goździcka-Józefiak [2/], Anna Kwaśniewska [1/]

[1/] Department of Obstetrics and Pathology of Pregnancy, Medical University of Lublin
[2/] Adam Mickiewicz University, Institute of Experimental Biology, Department of Molecular Virology, Poznan

Wstęp i cel pracy. W jaki sposób dochodzi do transmisji wirusa brodawczaka ludzkiego (HPV) w ciąży nadal nie jest w pełni wyjaśnione. Przytacza się wiele danych o istniejącej możliwości infekcji wewnątrzmacicznej. Nie brak również opinii dotyczących wpływu sposobu ukończenia ciąży na ryzyko przeniesienia infekcji w okresie okołoporodowym. Zakażenie noworodka niesie za sobą ryzyko rozwoju HPV-zależnych chorób wieku dziecięcego, a u potomstwa płci żeńskiej dodatkowo zwiększa ryzyko rozwoju raka szyjki macicy. W prowadzonych badaniach podjęliśmy próbę oceny częstości występowania infekcji HPV u noworodków w zależności od sposobu ukończenia ciąży.

Materiał i metoda. Do badań zakwalifikowano 135 zdrowych ciężarnych bez klinicznych objawów infekcji z prawidłowym rozmazem cytologicznym i bez obciążonego wywiadu przebytą infekcją wirusem brodawczaka. Obecność infekcji HPV sprawdzano metodą łańcuchowej reakcji polimerazy (PCR).

Wyniki. W badanej grupie rodzących stwierdzono 22 przypadki zakażenia HPV (16,3%). Wśród potomstwa badanych wykazano obecność materiału DNA HPV u 16 noworodków (11,85%). W badanym materiale nie stwierdzono wpływu sposobu porodu na częstość występowania infekcji u noworodków.

Wniosek. Ryzyko matczyno-noworodkowej transmisji wirusa HPV nie jest uwarunkowane drogą porodu.

Słowa kluczowe: *występowanie infekcji HPV, ciąża, sposób ukończenia ciąży*

Introduction & aim. The exact route of Human Papilloma Virus (HPV) transmission from a pregnant woman to her fetus has not been clearly established thus far. The data of many studies raise the possibility of intrauterine infection. In contrast, little is known about the probability of perinatal infection in the offspring of HPV-positive mothers, especially the association between the mode of delivery and the risk of HPV transmission. Persistent infection can lead to HPV-dependent childhood disorders such as Recurrent Respiratory Papillomatosis (RRP), and the risk of cervical cancer development in female offspring. Taking into account these discrepancies and threats, this study analyzed the relationship between the frequency of HPV infections in pregnant women and their offspring. The risk of maternal-neonatal infection was assessed depending on the mode of delivery.

Material & method. For the study we recruited healthy pregnant women with normal cervical cytology and without clinical signs of HPV infection. The prevalence of HPV was investigated by polymerase chain reaction method (PCR) which is a highly sensitive and specific technique.

Results. In our study 22 cases (16.3%) of HPV infection were found of all 135 pregnant women and 16 (11.85%) cases of neonatal HPV infections were detected. We did not confirm an association between the mode of delivery and the frequency of HPV DNA isolation from the studied neonates.

Conclusion. This finding would constitute another argument against the protective role of cesarean section in the prevention of perinatal infections with HPV.

Key words: *HPV prevalence, pregnancy, mode of delivery*

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Adres do korespondencji / Address for correspondence
Dr n. med. Mariusz Skoczyński
Lublin Staszica 16
tel/fax +81 53 266 12, e-mail: mskoczynski@wp.pl

Introduction

The exact route of Human Papilloma Virus (HPV) transmission from a pregnant woman to her fetus has not been clearly established thus far. The results of many studies raise the possibility of intrauterine infection [1-3]. In contrast, little is known on the probability of perinatal infection in the offspring of HPV-positive mothers, and particularly on association between the mode of delivery and the risk of HPV transmission. Moreover, sparse reports dealing with the problem in question are inconclusive, perhaps due to various selection criteria of studied groups, their different sizes, and variety of analytical methods applied [1, 3, 4].

A confirmed neonatal contamination with HPV is associated with the risk of persistent infection, leading to such HPV-dependent childhood disorders as Recurrent Respiratory Papillomatosis (RRP), and

carrying the risk of cervical cancer development in female offspring [3, 5, 6].

Aim

This study analyzed the relationship between the frequency of HPV infections in pregnant women and their offspring. The risk of maternal-neonatal infection was assessed depending on the mode of delivery.

Material and methods

This study was conducted between March 2009 and June 2011, and included pregnant women who delivered at the Clinic of Obstetrics and Pathology of Pregnancy, Medical University of Lublin (Poland). The studied group consisted of 135 randomly selected women. The exclusion criteria included: 1. history of HPV infection (n=7), 2. abnormal cervical smear (n=4), and 3. multiple pregnancy (n=6). The protocol of this study was approved by the Local Bioethical Committee of the Medical University of Lublin. The subjects gave their written informed consent before the start of any procedure. Our patients did not manifest any clinical signs of virus infection. The material for DNA HPV presence was taken prior to delivery from vaginal fornix and buccal mucosa of each pregnant woman. Immediately after birth, the discharge was aspirated from newborns' upper airways, and neonatal buccal smears were obtained. All samples were collected by the same properly trained person. The material was placed in sterile tubes for HPV DNA testing (Eurotubo®; Deltalab, Spain), frozen and stored at -70°C until further analyses. The material was tested for the presence of DNA by means of the PCR method. In the research statistical report a percentage was calculated. An association between the presence of neonatal HPV infection depending on the mode of delivery was analyzed using multivariate regression model, and odds ratios (ORs) were determined. All calculations were carried out using Statistica 10 (StatSoft®, Tulsa OK, USA) package, with the level of significance set at p=0.05.

Results

The study included 135 pregnant women. 80 (59.3%) patients' pregnancies were terminated by means of cesarean section, and 55 (40.7%) patients' pregnancies – by vaginal way. Twenty two cases of HPV infection (16.3%) were detected amongst pregnant women participating in this study. In 8 cases, HPV DNA was detected solely in vaginal smears, and in another 5 cases solely in the buccal smears; nine women had positive result of both samples tested. The offspring of studied women included 74 female and 61 male newborns. The presence of HPV DNA was revealed in 16 newborns (11.85%) (Table I). In five cases the infection was confirmed solely based on buccal smear testing, and in another two in the examination of the upper respiratory airway discharge; nine newborns had positive results of both samples tested.

Table I. Maternal and neonatal characteristics and obstetrical variables in HPV-positive and HPV-negative newborns

Parameter	HPV (+) (n=16)	HPV (-) (n=119)	OR (95% CI)	p value
Obstetrical characteristics				
Cesarean section	7 (43.8%)	73 (61.3%)	0.5 (0.2-1.4)	0.185
Vaginal delivery	9 (56.3%)	46 (38.7%)	2.0 (0.7-5.9)	0.185
Neonatal characteristics				
Female gender	10 (62.5%)	64 (53.8%)	1.4 (0.5-4.2)	0.512
Male gender	6 (37.5%)	55 (46.2%)	0.7 (0.2-2.1)	0.512

Discussion

In this study, the presence of HPV DNA was confirmed in 16.3% of asymptomatic pregnant women. Similar prevalence rate of asymptomatic HPV infection in pregnant women was previously reported by Rintala et al. [7]. However, the results of meta-analysis of nine large studies including a total number of 2111 pregnant women suggest that the prevalence rate of HPV infections in this group can vary between 5.5% and 65% [1]. Such marked discrepancies in infection rates can result from inhomogeneous selection criteria of the studied samples, their relatively small sizes, and use of various methods of HPV DNA detection. Furthermore, false positive results can occur due to secondary contamination of examined material with HPV DNA, and too small number of viral copies in the examined samples can be reflected by false negative results [8, 9]. Our study revealed 11.85% of prevalence of neonatal HPV infections. Specialists agree that the offspring of HPV-positive mothers has an increased risk of human papilloma virus infection [6, 7, 10]. However, as in the case of pregnant women, the literature data on the frequency of inherited neonatal infections is highly inconclusive. According to various reports, HPV DNA can be isolated from 1% to 20% of newborns who were delivered by asymptomatic HPV-positive mothers [9, 11]. We did not confirm an association between the mode of delivery and the frequency of HPV DNA isolation from the studied neonates. This finding would constitute another argument against the protective role of cesarean section in the prevention of perinatal infections with HPV. The number of scientists supporting this latter theory has decreased gradually in recent years [3, 6]. Nonetheless, many authors reported a frequent prevalence of HPV DNA in vaginally delivered newborns [1, 8]. This

phenomenon can result from contamination of the birth canal with genetic material of the virus and cause neonate transient infection. Nevertheless, one should consider the probability of perinatal vaginal infection during differential diagnosis and therapy of RRP [12], as well as in planning vaccination against HPV in younger, sexually-inactive girls [3].

Conclusion

The risk of maternal-neonatal transmission of HPV is not determined by the mode of delivery and other obstetrical characteristics.

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