

KEY WORDS: malaria, diagnostics, treatment, prophylaxis

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PREVALENCE OF HUMAN PAPILLOMAVIRUS INFECTION OF THE UPPER RESPIRATORY TRACT AMONG HEALTHY CHILDREN

D. Velyvyte,¹ A. Laiskonis,¹ A. Gozdicka-Jozefiak²

Kaunas University of Medicine¹, A. Mickiewicz University of Poznan²

SUMMARY

Infection with high-risk human papillomaviruses (HPV) is a significant risk factor for malignancy. The identification of particular HPV types is important for identifying patients with premalignant lesions who are at risk of progression to malignancy and for epidemiological studies. We present data on the prevalence of HPV infection in the upper respiratory tract of healthy children.

KEY WORDS: papillomavirus, malignancy, identification, amplification

Human papillomaviruses (HPV) constitute a group of deoxyribonucleic acid (DNA) viruses related to the genesis of various benign and malignant human lesions in the upper respiratory tract, skin and the genital tract [5]. Over 100 HPV types have been identified, of which about 30 infect mucosal epithelia [17]. These can be divided into low-risk types (e.g., HPV-6 and -11) associated with papillomas (or warts) of mucosa of oral-nasal cavities, pharynx, larynx, or genital tract and generally remain benign, and high-risk types (e.g., HPV-16 and -18) associated with the lesions that can progress to cancer [1, 13]. High-risk HPV DNA is detectable in about 95% of cases of cervical cancer [2].

The role of HPV in airway papillomas has been well defined in recent literature [7]. Papillomatosis of upper respiratory tract is a benign virally (HPV-6 and -11) induced neoplastic disease that may obstruct the airway and tend to recur frequently. The chronicity and recurrence of papillomas has been postulated to be a result of residual viral genome in normal-appearing cell adjoining papilloma tissues. The development of malignancies from papillomas has been reported [14]. Papillomatosis of upper respiratory tract and particularly laryngeal papillomatosis is a disease of all ages, more often first diagnosed in the first decade. The transmission of HPV infection of the upper respiratory tract remains poorly understood. For some time it has been recognized that laryngeal papillomatosis in children is caused by HPVs are transmitted vertically from mother to infant, that was associated with a high viral load in the genital tract during pregnancy [3, 12]. Despite this opinion and observations, some researches are reluctant to accept the occurrence of vertical transmission [4].

Human papillomaviruses such as types 6 and 11 can cause lifelong infections in airway

epithelial cells in the patients. Our aim was to establish the prevalence of human papillomaviruses in the upper respiratory tract of healthy children, and to find possible facilitating factors of persistence and spreading HPV infection. Obtained information will be useful for making the preventive recommendations against HPV infection.

The group of 405 Kaunas pre-school and school healthy children (217 female (53.6%) and 188 male (46.4%)), mean age, 7 years, range, 2-11) was examined after getting a consent from their parents. Approval for the study was obtained from the Independent Ethics Committee of Kaunas University of Medicine. Epidemiologic characteristics were analyzed. Routine laryngological examination was performed. Pharyngeal swabs were taken and analyzed for the presence of HPV DNA. DNA from smears was isolated by proteinase K digestion (proteinase K 50µg/ml, SDS 0.5%, Tris HCl 50mM pH 7.5, EDTA 5mM pH 8.0, NaCl 50mM) for 24 h at 37°C and phenol-chloroform extraction as described by Fife et al. [6]. DNA was precipitated from supernatant in a sodium acetate ethanol solution, dissolved in 50µl of TE (Tris HCl 10 mM pH 8.0, EDTA 1mM pH8.0) and used for future study. Polymerase chain reaction (PCR) was performed as described by Tucker et al. [16]. In all PCRs stringent precautions were taken to avoid contamination. To confirm that the samples were of sufficient quantity and quality for PCR, all samples were tested for c-fos DNA by PCR. Four primer pairs from L1 region of HPV-16, E1 region of HPV-18, L1 region of 5 types HPV (6b, 11,16, 18, 33) and L1 region of 33 types of HPV (5,6,8,11,16,18,26,27,30, 31,33,35,39,40,41,42, 43,45,47,48,51,52,53,54,55,57,58,59) were used for amplification of DNA. The amplified DNA was separated by electrophoresis on a 2%

agarose gel in 0.04M Tris-acetate (pH 8.0) and 0.001M EDTA at 100V and 10mA for 1h. The gel was stained with ethidium bromide and visualized by UV transillumination. Viral typing using PCR was performed in the Department of Molecular Virology A. Mickiewicz University, Poznan.

All the specimens were positive for c-fos. There were found 93 infected children (23.0%) in the study group, the criterion being the presence of DNA sequence characteristic for HPV in pharyngeal swabs. There were no

significant differences in prevalence of HPV infection according to sex: 48 (51.6%) of infected children were girls and 45 (48.4%) - boys.

Examinations of children using PCR method with specific primers revealed mainly HPV type 6 and 11 (Table I). High risk HPVs were observed in 8.4% of cases. HPV-16 was identified in 33 of the analyzed cases. The DNA sequence characteristic for HPV-18 was found only in one child.

Table 1

Results Obtained with PCR

PCR result with specific primers			Number (%) of children with these results
HPV-6, 11	HPV-16	HPV-18	
+	-	-	59 (14.6%)
-	+	-	6 (1.5%)
+	+	-	27 (6.7%)
+	-	+	1 (0.2%)
-	-	-	312 (77.0%)
Total			405 (100.0%)

It was found out from epidemiological anamnesis that the parents of HPV positive children were active smokers in 67.7% of cases, while in the rest of the studied group the percentage was 56.1%. The fact worth consideration is the standard of living, which in the families of HPV positive children was estimated by 11.8% of parents as low, while in the other group - 2.2% of parents gave similarly bad estimation. It was ascertained that 23 (24.7%) of HPV positive children had various infections of upper respiratory tract earlier in the history of previous diseases, while in HPV negative children frequent episodes of such infections were found out only in 8 (2.6%) cases.

On physical examination enlargement of submandibular lymph nodes was found in 28% of HPV infected children and dental caries in 57% of HPV infected children, while in HPV negative children the percentage was 18.3 and 36.2 accordingly.

This study provides evidence for mucosal HPV infection in upper respiratory tract of healthy children. Using PCR, HPV DNA was detected in 23% pharyngeal swabs from 405 2-11-year-old children. Other studies detected HPV DNA in pharyngeal swabs from up to 36.4% healthy children [15]. These data suggest that respiratory tract infection due to HPV is a very common phenomenon. A similarly high level of HPV DNA (30%) was revealed in cervical brush-scrapes of healthy women [8]. Detected prevalence of "high risk" HPV in upper respiratory tract of children reached only 8.4%. Other study have reported up to 26% prevalence of HPV-16 DNA in children [11]. It should be noted that "high-risk" HPV DNA has been detected more often in the oral cavity of adults (22-44%) [1, 9].

It was shown in one study, that virus may persist for at least the first two years of life in children who acquired infection from their mothers [10]. Puranen et al. also identified HPV DNA in buccal brush-swabs from children aged 0.3-11 years, who were born to HPV negative mothers [12]. In our study there were some differences in HPV prevalence according to age among children aged 2 to 11 years, suggesting that infection may occur in early life and persists but becomes more often established in 7-10 years of life. These data suggest that the infection may spread horizontally through a direct contact with an infected tissue or through an indirect contact with contaminated objects. Alternatively repeated infections may occur, to sustain prevalence at a constant rate.

There were no significant differences in prevalence of HPV infection according to sex.

The study showed relationship between the prevalence of HPV infection and frequent episodes of various infections of upper respiratory tract earlier in the history. Besides HPV infection was more often detected in children with enlarged lymph nodes and dental caries. Significantly higher level of the carriers state in the families of active smokers and the families of a low living standard show a considerable contribution of environmental factors in the spread of HPV infection. The consequences of vertical or early childhood HPV infection are not quite clear yet, however it thought that early transmission of HPVs may induce premalignant lesions. Therefore it is recommended to observe and to examine prophylactic HPV positive children, especially who have "high risk" HPVs in their upper respiratory tract.

The prevalence of HPV type 6 and 11 in the

upper respiratory tract of healthy children is relatively high. The prevalence of "high risk" HPV among healthy children is rather low. HPV was more often detected in children with unfavourable epidemiological conditions and

chronic infectious foci. Children infected with "high risk" HPVs must be observed and examined prophylactic for early identification of premalignant lesions.

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ПРЕВАЛИРОВАНИЕ ИНФИЦИРОВАНИЯ ВЕРХНЕГО РЕСПИРАТОРНОГО ТРАКТА ЗДОРОВЫХ ДЕТЕЙ ЧЕЛОВЕЧЕСКИМ ПАПИЛЛОМАВИРУСОМ

Д. Веливите,¹ А. Лаисконис,¹ А. Гозджицка-Жозефяк²

Каунаський медичинський університет¹, Познанський університет А. Міцкевича²

РЕЗЮМЕ

Инфицирование с высоким риском человеческим папилломавирусом (ЧПВ) является важным фактором риска малигнизации. Идентификация определенных типов ЧПВ имеет значение для диагностики пациентов с предраковыми заболеваниями, с риском озлокачествления, и для эпидемиологических исследований. Мы представляем данные о преваливании ЧПВ инфекции верхнего респираторного тракта у здоровых детей.

КЛЮЧЕВЫЕ СЛОВА: папилломавирус, малигнизация, идентификация, амплификация

ПРЕВАЛЮВАННЯ ІНФІКУВАННЯ ВЕРХНЬОГО РЕСПІРАТОРНОГО ТРАКТУ ЗДОРОВИХ ДІТЕЙ ЛЮДСЬКИМ ПАПІЛОМАВІРУСОМ.

Д. Веливите,¹ А. Лаисконис,¹ А. Гозджицка-Жозефяк²

Каунаський медичний університет¹, Познанський університет А. Міцкевича²

РЕЗЮМЕ

Інфікування з високим ризиком людським папіломавірусом (ЛПВ) є важливим фактором ризику малигізації. Ідентифікація визначених типів ЛПВ має значення для діагностики пацієнтів із передраковими захворюваннями, з ризиком злоякісності, і для епідеміологічних досліджень. Подаються дані про превалювання ЛПВ інфекції верхнього респіраторного тракту у здорових дітей.

КЛЮЧОВІ СЛОВА: папіломавірус, малигізація, ідентифікація, ампліфікація

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СОВРЕМЕННЫЕ ПОДХОДЫ К ЛЕЧЕНИЮ ТЯЖЕЛЫХ ФОРМ МЕНИНГОКОККОВОЙ ИНФЕКЦИИ

М.А. Георгиянц, В.А. Корсунов

Харьковская медицинская академия последипломного образования

РЕЗЮМЕ

В статье отражены современные подходы к проведению интенсивной терапии у больных с тяжелыми формами менингококковой инфекции. Представлены основные направления антибактериальной терапии, интенсивной терапии шока, ДВС-синдрома, респираторной поддержки, энтерального и парентерального питания. Уделено внимание состоянию проблемы применения стероидов, экстракорпоральных методов детоксикации.