Bulletin of the *Transilvania* University of Braşov
Series VI: Medical Sciences • Vol. 8 (57) No. 1 - 2015

KNOWLEDGE OF HUMAN PAPILLOMAVIRUS (HPV) INFECTION IN NON-MUSCLE INVASIVE BLADDER CANCER PATIENTS

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Abstract: *The etiological role of HPV infection in the pathogenesis of bladder tumors remains uncertain.*
Case-control study, NMIBC patients answered a 37 items questionnaire regarding knowledge of HPV, were compare with a healthy control group.
Group A started earlier the sexual life than the group B (18 vs. 19 years), but the first cohabitation took place later (37 vs. 24 years, p = 0. 03).Group A had more sexual partners than group B (>10, 32% respectively 17.6%). 56% of patients with NMIBC heard about HPV infection and only 47% of controls and 32% of group A respectively 41% of group B didn't know if HPV infection represents a risk for their health. From this study results a lack of knowledge about HPV infection in NMIBC patients.

Key words: *HPV, bladder cancer, risk factors, knowledge of HPV.*

1. Introduction

More and more studies on a possible involvement of HPV in the etiology of bladder cancer have been published in recent years [1], [3], [18], [22], the detection rate of HPV prevalence in frozen or fixed sections by using PCR were ranged between 0% and 45%. In terms of case-control studies results were at least controversial, with a detection rate of HPV ranging from 17.1% to 52.4% [4], [5], [10]. A recently published review revealed that the prevalence of HPV varies by population, geographic region and detection method used, emphasizing the need to develop new case-control studies, large-scale population to elucidate the possible involvement of HPV in the

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etiology of bladder tumors [17], 22]. These studies showed that some patients with bladder cancer associate HPV infection, yet still we do not know which patients are at risk of HPV infection, very valuable information in clinical practice, in order to establish an appropriate therapeutic management in these patients.

A recent review published in 2014 about the prevalence of HPV infection in men, that included 31 studies from all Europe, except eastern Europe, reports that the prevalence of HPV infection in general population is 12.4 % and in high risk population is 30.9 % [9], meaning that the virus is present with or without pathological implication in men.

Risk factors for HPV infection were reported before to be: anal sex [2], multiple sexual partners [10], sexual behavior [16–17] and young age at first intercourse [14], [16].

2. Objectives

The purpose of this study was to observe from the application of anonymous questionnaires on sexual behaviour, knowledge about HPV infection, contact with HPV infection in patients with confirmed NMIBC in our clinic, in compare with a control group of healthy voluntaries and if we can identify risk factors for an eventual HPV infection in the group of patients with non-muscle invasive bladder cancer (NMIBC). Secondary purpose was to identify patients at risk in which we suspicion an HPV infection and identify the opportunity of making HPV testing using PCR determinations in these patients.

3. Material and Methods

Between 1 July 2014 to15 March 2015 we applied an unvalidated questionnaire consisting of 37 questions about sexual behaviour, knowledge about HPV infection and contact with HPV infection in a group of 25 patients with NMIBC at first manifestation and a control group of 17 volunteers without bladder tumour. The questionnaires were anonymous, only data on the patient's age, sex, education, and ethnicity were collected. Statistical analysis was performed with SPSS 17 and statistical tests chi square, t student and Mann Whitney test were applied to compare the two groups.

The level of statistical significance was set at $p<0.05$.

4. Results and Discussions

Mean age was 64.32 in NMIBC (group A) and 48.0 yr. in control (group B) (p=0.0001). 88.0% were male in group A and 76.5 % in group B (p=0.32). With high school education were 44.0 % in group A and 47.1% in group B (p=0.35). Hungarians ethnics were 32 % in group A and only 11.8 % in group B (p=0.14). Age at first pollution or menstruation was similar in both groups 14 yr. (p=0.75).

4.1. Sexual behaviour

First intercourse was at 18 and 19 yr. (p=0.70). In terms of length of first relation in months we noticed a higher stability in group A with a mean of 37.2 months (range 23 to 55 months) than in group B, 24.11 months (range 18 to 40 months) (Fig.1).

The mean months until first intercourse with the first partner was 6 months in group A and 12 months in group B but not statistically significant (Test Mann Whitney, p-0.87). 76 % in group A and 70.6 % in group B reported an unprotected first intercourse (p=0.69).

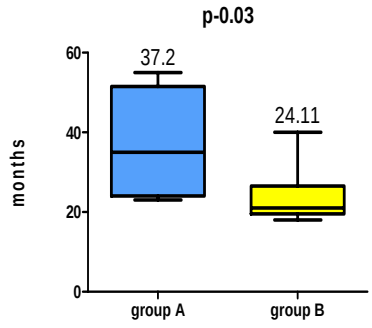

Fig. 1 *Deference between means regarding duration in months of the first relation, group A (non-muscle invasive patients) and group B (controls)*

Related to knowledge of contraception methods 52 % and 41.2 % reported no knowledge of any (p=0.11), among contraceptive known methods condom is most known with 60 % in both groups. Only 44 % and 41 % of responders consider that condom is very efficient in preventing STD (p=0.89). In terms of types of sex practice 12 % and 11.8 % of patients reported that they practiced vaginal, anal and oral sex (p=0.85). 32 % of the patients with NMIBC reported more than 10 sex partners during life and only 17.6 % in control group (p<0.11) and 24 % from responders reported that had frequent sexual relations outside the couple in group A in compare with only 11.8% in group B (p=0.64).

4.2. STDs (sexual transmitted diseases) history and knowledge

First information about sex and STD was receved at mean at 14 yr. in both groups (p=0.54). All patients in group B and 92% in group A consider that it is not the case to visit a doctor after an extraconjugal sex relation (p=0.49). Meanwhile 72 % in group A and 64.7 % in control consider that the urological examination schould be yearly (p=0.61). Only 16 % form NMIBC group had knowledge that there is a reproduction health outpatient clinic in our city and none of the controls (p=0.08). In terms of reasons for adresing to a doctor bleading was the most common simptom with 28 % in group A and 17.6 % in group B.

4.3. Knowledge and risk of infection with HPV

Regarding knowlegde of HPV infection, 44% and 52.9% repectively in group B did not know about HPV infection, or the existance of the virus (p=0.56). Futhermore 32% in group A and 41.2 % of controls did not know if HPV infection represents any kind of risk for health. In terms of preventing infection with HPV, 48 % in NMIBC group and 64.7% of controls reported one sexual partner durring life, condom use 48 % and 58.8% and personal hygine 32 % and 29.4 % in control group. None of the responders in NMIBC group knows that genital warts represents a way of HPV transmision (Table 1).

Table 1

Transmisson ways of HPV infection

Transmission ways of HPV infection	Yes % A	No % A	Yes % B	No % B
WC	20.0	20.0	35.3	29.4
Bath-pool	12.0	20.0	17.6	35.3
Kiss	16.0	20.0	29.4	35.3
Intimal touch	16.0	12.0	17.6	35.3
Insect stings	16.0	16.0	11.8	41.2
Vaginal sex	28.0	12.0	47.1	5.9
Anal sex	32.0	8.0	47.1	5.9
Skin/warts	0.0	24.0	11.8	35.3
Blood transfusions	40.0	8.0	41.2	29.4
Unsterile needles	40.0	8.0	41.2	17.6
Contaminated objects	24.0	16.0	35.3	23.5
Food	4.0	20.0	5.9	41.2

Among with HPV, syphilis and gonoreea are the most knowen sexual transmited deseases in both groups (Table 2), but only 16 % of the responders in NMIBC group heard about genital warts, compared with 47.1 % in control group.

Table 2

Knowledge of STDs in groups

STDs that you heard of?	Yes Gr.A	No Gr.A	Yes Gr.B	No Gr.B
Syphilis	92.0	4.0	94.1	0.0
HPV	76.0	8.0	64.7	29.4
Gonoreea	48.0	3.0	64.7	17.6
Trichomonas	28.0	36.0	11.8	70.6
Genital warts	16.0	48.0	47.1	41.2
Genital herpes	28.0	48.0	47.1	41.2
Candidosis	20.0	48.0	58.8	29.4
Uretritis	20.0	44.0	29.4	52.9
Prostatitis	20.0	44.0	41.2	41.2
Vulvo-vaginitis	16.0	48.0	23.5	58.8
Balanititis	4.0	56.0	11.8	70.6
Others	0.0	4.0	23.5	41.2

We noticed very poor knowledge about HPV infection in both groups and also a poor rate of response becouse of the lack of knowledge about the subject. Half of the NMIBC responders were sure that they did not receive a HPV vaccine and 3 quarters in control group. The low percentages are due to the fact that the ones that never heard about HPV infection did not ask to these questions about the HPV infection, so the response rate was between 20 to 76.5 %. The results practicaly highlights that patients in both groups know very little about HPV infection (Table 3).

From these results we noticed a lack of information and knowledge about HPV infection in both groups, in terms of ways of transmission and pathological role of the virus. Furthermore only 56 % in NMIBC group heard about HPV and 47.1 % of controls; similar results were reported in other populations ranging from 17.7 % to 66.5 % [6], [7], [8], [12-15], [19], [21], but none about the patients with bladder cancer. These findings represent and important tool for further research in order to identify the patients at risk and also to develop predictive models for determine HPV infection (ex. validated questionnaires in large cohorts).

Knowledge about HPV infection Table 3

Knowledge about HPV infection	Yes Gr.A	No Gr.A	Yes Gr.B	No Gr.B
Most of the infection has spontaneous remission?	4.0 %	24.0 %	11.8 %	41.2 %
Treatment for cervical cancer treats the infection?	4.0 %	16.0 %	0 %	35.3 %
Genital warts are caused by the same type of HPV as cervical cancer?	4.0 %	16.0 %	0 %	29.4 %
Almost all cases of cervical cancers are due to HPV infection?	12.0 %	16.0 %	23.5 %	17.6 %
At women that were diagnosticated with HPV the anti-HPV vaccine is useless?	12.0 %	8.0 %	11.8 %	11.8 %
Do you receive any anti-HPV vaccine?	0.0 %	48.0 %	0.0 %	76.5 %

An interesting fact is that NMIBC patients consider that genital warts is not a way of transmission of HPV infection 0 % compared with controls 11.8 %, but even so this percentages are lower that the ones reported in other patient cohorts 65.7 % [12], or with a general practitioners cohort 79 % [20].

In terms of risk factors reported before for HPV infection: unprotected sex, high number of sexual partners, anal sex and low education were the most common [2], from our results we can include NMIBC patients at high risk for having HPV infection those that practice unprotected and anal sex, with more than 10 sex partners, low education and history of STDs, in which could be indicated PCR determination for HPV detection.

5. Conclusion

From this study results a lack of knowledge about HPV infection in NMIBC patients, but also in control group. Risk factors for HPV infection could be unprotected and anal sex, more than 10 sex partners, low education and history of STD. In order to increase the knowledge level about HPV infection in general population public campaigns about the risk of infection are needed.

Acknowledgements

This paper is supported by the Sectoral Operational Programme Human Resources Development (SOP HRD), financed from the European Social Fund and by the Romanian Government under the contract number POSDRU/159/1.5/S/133377 and Research Grant nr. 04/2014 financed by Romanian Dermatological Society (SRD), beneficiary University of Medicine and Pharmacy, Târgu Mures, Romania

References

1. Badawi, H., Ahmed, H., et al.: *Role of human papillomavirus types 16, 18, and 52 in recurrent cystitis and urinary bladder cancer among Egyptian patients.* In: Medscape J Med, 2008 10(10), p. 232.
2. Bell, M.C., Schmidt-Grimminger, D., et al.: *Risk factors for HPV infection among American Indian and withe women in the Northern Plains.* In: Gynecol Oncol. 2011 Jun 1; 121(3), p.532-6.
3. Ben Selma, W., Ziadi, S., et al.: *Investigation of human papillomavirus in bladder cancer in a series of Tunisian patients.* In: Pathol Res Pract, 206 (2010), p. 740–743.
4. Berrada, N., Al-Bouzidi, A., et al.: *Human papillomavirus detection in Moroccan patients with bladder cancer.* J Infect Dev Ctries, 7 (2013), p. 586–592.
5. Cai, T., Mazzoli, S., et al.: *Human papillomavirus and non-muscle invasive urothelial bladder cancer: potential relationship from a pilot study.* In: Oncol Rep, 25 (2011), p. 485–489.
6. Capogrosso, P., Ventimiglia, E., et al.: *Awareness and knowledge of human papillomavirus-related diseases are still dramatically insufficient in the era of high-coverage vaccination programs*. In: World J Urol. 2014 Sep. [Epub ahead of print]
7. Colon-Lopez, V., Ortiz, A.P., et al.: *Awareness and knowledge of human papillomavirus (HPV) infection among high-risk men of Hispanic origin attending a sexually transmitted infection (STI) clinic.* In: BMC Infect Dis. 2012 Dec 12;12, p. 346.
8. Deriemaeker, H., Michielsen, D., et al.: *Knowledge about human*

papillomavirus and the human papillomavirus vaccin in Belgian students. In: Cent European J Urol. 2014; 67(4), p. 410-7.

9. Hebnes, J.B., Olesen, T.B., et.al.: *Prevalance of genital human papillomavirus among men in Europe: systematic review and meta-analysis.* In: J Sex Med. 2014 Nov; 11(11), p. 2630-44.
10. Liu, Z.C, Liu, W.D, Liu, Y.H, Ye, X.H, Chen S.D.: *Multiple Sexual Partners as a Potential Independent Risk Factor for Cervical Cancer: a Meta-analysis of Epidemiological Studies.* In: Asian Pac J Cancer Prev. 2015;16(9):p.3893-900
11. Kim, S.H., Joung, J.Y., et al.: *Detection of human papillomavirus infection and p16 immunohistochemistry expression in bladder cancer with squamous differentiation.* In: PLoS One, 9 (2014), p. e93525.
12. Kuznetsov, L., Reitmaier-Weber, C.M., et al.: *Awareness of human papillomavirus infection,genitoanal warts and cancer in a dermatological outpatient clinic setting.* In: Acta Derm Venereol. 2013 Mar 27;93(2), p. 218-22.
13. Makwe, C.C., Anorlu, R.I., et al.: *Human papillomavirus (HPV) infection and vaccines: knowledge, attitude and perception among female students at the University of Lagos, Nigeria.* In: J Epidemiol Glob Health. 2012 Dec; 2(4), p.199-206.
14. Nielsen, A., Kjaer, S.K., Munk, C., Iftner, T.: *Type-specific HPV infection and multiple HPV types: prevalence and risk factor profile in nearly 12,000 younger and older Danish women.* In: Sex Transm Dis 2008, 35:276–282.
15. Osazuwa-Peters, N., Wang, D.D., et al.: *Sexual Behavior, HPV knowledge, and association with head and neck cancer among a high-risk group.* In: Oral Oncol. 2015 May; 51(5), p. 452-6.
16. Rathfisch, G., Güngör, İ., et al.: *Human papillomavirus vaccines and cervical cancer: awareness, knowledge, and risk perception among Turkish undergraduate students.* In: J Cancer Educ. 2015 Mar;30(1), p.116-23.
17. Remschmidt, C., Fesenfeld, M., Kaufmann, A.M, Deleré, Y.: *Sexual behavior and factors associated with young age at first intercourse and HPV vaccine uptake among young women in Germany: implications for HPV vaccination policies.* In: BMC Public Health. 2014 Dec 5; 14:1248.
18. Shigehara, K., Sasagawara T., et al.: *Human papillomavirus infection and pathogenesis in urothelial cells: A mini-review.* In: J Infect Chemother 20 (2014), p.741-747.
19. Shigehara, K., Sasagawa, T., et al.: *Etiologic role of human papillomavirus infection in bladder carcinoma.* Cancer, 117 (2011), p. 2067–2076.
20. Signorelli, C., Odone, A., et al.: *Human Papillomavirus infection and vaccination: knowledge and attitudes of Italian general practitioners.* In: Epidemiol Prev. 2014 Nov-Dec; 38 (6 Suppl 2), p. 88-92.
21. Tu, Y.C., Wang, H.H., et al:. *HPV Knowledge and Factors Associated with Intention to Use Condoms for Reducing HPV Infection Risk among Adolescent Women in Taiwan.* In: Women Health. 2015 Feb-Mar; 55(2), p.187-202.
22. Yavuzer, D., Karadayi, N., et al.: *Role of human papillomavirus in the development of urothelial carcinoma.* In: Med Oncol, 28 (2011), p. 919–923.