

Correlation of vaginal micro-ecology and human papilloma virus infection to cervical lesions.

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Abstract

Objective: Correlation of vaginal micro-ecology and human papilloma virus infection to cervical lesions.

Methods: From May 2014 to May 2017, 40 patients with cervical lesion enrolled in our hospital were collected and set as the research group. Meanwhile, another 40 patients without the lesion were collected in the control group. Patients in both groups were given determinations of vaginal flora followed by further detection of the high-risk Human Papilloma Virus (HPV). The correlation between HPV and the result of vaginal flora determinations in both groups was analysed with the logistic regression model.

Results: The rate of micro-ecological imbalance in the research group was higher than that in the control group ($P < 0.05$). There was no significant difference in the detection rate of *Trichomonas* infection between these two groups ($P > 0.05$). The detection rate of *Lactobacilli*, *Candida* and lead cells between these two groups turned out to be significantly different ($P < 0.05$). In addition, the positive rate of HPV in the research group was significantly higher than that in the control group ($P < 0.05$). The logistic regression model analysis showed that the independent risk factors of cervical lesions included HPV infection, lactobacillus and vaginal micro-ecological imbalance.

Conclusion: There are many characteristics in the case of cervical lesions, including significant vaginal imbalance, lower detection rate of *Lactobacilli* and positive rate of HPV.

Keywords: Vagina microenvironment, Human papillomavirus infection, Cervical lesions, Correlation analysis.

Accepted on August 23, 2017

Introduction

Cervix Intraepithelial Neoplasia (CIN), also called cervical dysplasia is the term for abnormal changes in cells on the surface of the cervix. CIN does not usually cause any symptoms. Abnormal cells are found only after a routine Pap smear test. CIN usually occurs after a woman becomes infected with the Human Papilloma Virus (HPV), a virus that is spread through sexual contact. However, the mechanism of how HPV exactly cause CIN is unknown. Recently, some researches demonstrated that CIN disease progression is associated with imbalance of vaginal micro-ecology caused by increased vaginal microbiome diversity. Meanwhile, other studies showed that the micro-ecological imbalance in the vagina may cause damages on the immune protection mechanism of the vaginal microenvironment, enhance abnormal adhesion of HPV and lead to epithelial cell injury [1,2]. But the correlation of vaginal micro-ecology and human papilloma virus infection to cervical lesions is not clear. In our study, we analysed the

correlation of vaginal micro-ecology and human papilloma virus infection to cervical lesions and determined the high-risk factors that lead to cervical lesions by logistic regression model.

Material and Methods

General materials

From May 2014 to May 2017, 40 patients with cervical lesion enrolled in the Third Affiliated Hospital of Sun Yat-Sen University were collected and set as the research group. Meanwhile, another 40 patients without the lesion were collected in the control group. All patients in the research group were diagnosed as Cervical Intraepithelial Neoplasia (CIN) by the histopathological examination of the cervix. There was no history of cervical conization in both groups and all the patients did not receive relevant treatment within four weeks. The patients with severe heart and kidney dysfunction,

lactation and pregnant women and the patients of mental disorders, immune diseases or malignant tumors were excluded. The study was approved by the ethics committee of the hospital and the consent were obtained from both patients and their families. In the research group 18 cases were type I CIN, 14 type II and 8 type III with the age ranging from 22 to 45 y old, 35.80 ± 3.25 y old on average and the average gravidity and parity of the patients were respectively 2.56 ± 1.03 and 1.62 ± 1.20 times. In the control group, the patients were aged from 24 to 43 with an average age of 34.79 ± 3.45 , the average gravidity and parity were 2.48 ± 1.52 and 1.40 ± 1.18 times.

Methods

First, all cases were given vagina micro-ecology detection with such procedures as: the patient's vulva was strictly cleaned to the degree of fully displaying the cervical and vaginal area through sterile speculum. Items like leukocyte esterase, hydrogen peroxide and sialidase activity (LE, H_2O_2 and SNA) were detected in use of the joint determination kit provided by Beijing Zhongsheng Jinyu Company followed by the implementation of the vaginal micro-ecology evaluation [3,4]. SNA showed no color under normal circumstance and purple or red SNA turned out to be positive; LE showed no color under normal circumstance and blue or green LE turned out to be positive; if the H_2O_2 showed purple or red with the dosage of 2 mmol/L or above, the result turned out to be negative. Whereas it showed blue with the dosage below 2 mmol/L, it turned out to be positive [5,6]. If the current micro ecological environment was normal, it turned out that the H_2O_2 was negative, SNA negative and LE negative; With the micro ecological imbalance, the result displayed that H_2O_2 was negative, SNA negative and LE positive or H_2O_2 was positive, SNA negative and LE positive [7-9].

Secondly, the vaginal flora was detected in all cases. The detection of all the patients were conducted by way of sterile speculum to have the cervical site fully exposed, two specialized sterile cotton swabs with a depth of about 1.5 cm were respectively inserted into the cervical canal [10]. Meanwhile, the swab was turned around counter clockwise or clockwise for a circle with a stay time of 10 seconds. The swab, after being taken out, was sent to the gynecology laboratory for scientific examination. The data about such indicators as *Candida*, lactic acid bacteria, lead cells and *Trichomonas* were carefully observed and summarized.

Finally, HPV detection was implemented. Multiplex HPV testing, type 18 and the other 12 high-risk HPV subtypes, namely HPV31, HPV33, HPV35, HPV39, HPV45 and HPV51, HPV52, HPV56, HPV58 and HPV59, HPV66 and HPV68 [11,12].

Statistical methods

The relevant data were analysed and processed by SPSS21.0 statistical software. The count data were expressed in the form of number and percentage and tested by chi-square test. The

measurement data were described as mean \pm SD and tested by t-test. Logistic stepwise regression method was used to analyse the risk factors. $P < 0.05$ suggested that the differences had statistical significance.

Results

Comparison of vagina micro-ecology between two groups

The rate of micro-ecological imbalance of the research group was higher than that of the control group, $P < 0.05$ (Table 1).

Table 1. Comparison of vagina micro-ecology between two groups (n (%)).

Group	Case	Rate of micro-ecological imbalance
Research	40	28 (70.0)
Control	40	6 (15.00)
P		<0.05

Comparison of vaginal flora between two groups

The detection rates of lactobacillus and lead cells in the research group were obviously higher than those in the control group ($P < 0.05$) and the *Candida* infection rate of the research group was lower than that of the control group ($P < 0.05$). There was no significant difference in the detection rate of *Trichomonas* infection in the two groups ($P > 0.05$) (Table 2).

Table 2. Comparison of vaginal flora between two groups (n (%)).

Group	Case	Lactobacillus	Candida	Lead cells	Trichomonas
Research	40	26 (65.00)	8 (20.00)	29 (72.50)	2 (5.00)
Control	40	10 (25.00)	28 (70.00)	11 (27.50)	4 (10.00)
P		<0.05	<0.05	<0.05	>0.05

Comparison of HPV positive rate between two groups

The HPV positive rate of the research group was significantly higher than that of the control group of statistical significance, $P < 0.05$ (Table 3).

Statistical analysis of the risk factors of cervical lesions

Cervical lesion was set as the variable of the study with the independent variables including the patient's clinical data, vaginal micro-ecology and HPV infection. The result of logistic regression analysis showed that the main factors causing cervical lesions included HPV infection, *Lactobacillus* and micro-ecological imbalance, which were independent risk factors of much importance (Table 4).

Table 3. Comparison of HPV positive rate between two groups (n (%)).

Group	Case	HPV positive rate
Research	40	30 (75.00)

Control	40	12 (30.00)
P		<0.05

Table 4. Statistical analysis of the risk factors of cervical lesions.

Independent variables	Partial regression coefficients	Standard error	χ^2	P	OR (95% CI)
Micro-ecological imbalance	1.329	0.136	10.596	<0.05	2.098 (1.335-3.236)
HPV infection	2.268	0.445	26.489	<0.05	9.125 (4.123-23.146)
<i>Lactobacillus</i>	0.527	0.238	4.960	<0.05	1.658 (1.097-2.746)

Discussion

Cervical Intraepithelial Neoplasia (CIN) is the precancerous lesion in the period of cervical lesions and it is now widely believed that HR-HPV continuous infection is the most dangerous factor of cervical cancer occurrence [13]. For some cases of HPV infection, the CIN can make its own progression and will not cause cervical cancer, but there may be other factors involved in the development of cervical cancer. Inside of the vagina, a microbial system is formed by endocrine mechanism, microflora and anatomical structure of the organism with the presence of different microorganisms. On normal condition, the ratio of anaerobes and aerobic bacteria in the vagina keeps being 5:1 to provide normal function of vaginal flora, which is also an important way of assessing the normality of vaginal flora [14]. In addition, the vagina mucosa contains many immune cells to display the function of good immune barrier, but microbial invasion can cause cervical lesions with full exposure of the cervix inside the vagina [15-17].

The rate of micro-ecological imbalance of the research group was higher than that of the control group, $P < 0.05$. There was no significant difference in the detection rate of *Trichomonas* infection in the two groups, $P > 0.05$; the comparison of the detection rate of *Lactobacilli*, *Candida* and lead cells between the two groups turned out to be of statistical significance, $P < 0.05$; in addition, the positive rate of HPV in the research group was significantly higher than that in the control group, $P < 0.05$; with the analysis by logistic regression model, it turned out that the independent risk factors of cervical lesions included HPV infection, *Lactobacillus* and micro-ecological imbalance. The results also suggested that the imbalance of vaginal flora can enhance the expression of HPV and cause the change of cervical cancer cells [18].

Cervical cancer is one of the common malignancies that threaten the health of women. Therefore, it is of great significance to effectively explore the occurrence of cervical lesions and its correlation with the host immune defense mechanism for effective interruption of the progression of cervical lesions [19]. As a typical microbial ecosystem, the vagina contains numerous microorganisms that exhibit interaction and restriction as well as dependent relatedness, allowing the ecosystem to be in a state of equilibrium. The research results show that the soluble immune mediators within the microbial floras and vaginal secretions belong to the main

components of the innate immune defense of the host and the change of vaginal micro-ecology therefore plays a key role in the case of cervical disease [20]. Besides, high-risk HPV infection is also an important early warning of cervical cancer. Many studies show that continuous infection of high risk HPV serves as an important risk factor for the development of cancer and its phase. And low risk HPV infection is an important reason for producing recurrent respiratory papillomatosis of the genital. The balance of vaginal micro-ecology is an important part of the body immunity and cervical lesions can be attributed to HPV infection, the formation of vaginal micro-ecology bacteria and the important link between overgrowth of anaerobic bacteria and HPV infection.

Conclusion

To sum up, cervical lesion evolves significant vaginal micro-ecology imbalance and importance performances such as the decrease of detection rate of *Lactobacillus* and the rising positive rate of HPV. Due to the complexity of vaginal microenvironment with several bacteria involved, the research on the distribution of various bacteria in the cervix needs to be further expanded in scale.

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