Exploring the Curative Effects of Anti-Human Papillomavirus Protein Dressing for High-Risk Human Papillomavirus Infection

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To explore the clinical effects of innovative anti-human papillomavirus biological protein dressing (Luke duokang) for high-risk human papillomavirus infection was the objective of this study. We collected the clinical information of 220 persistent high-risk human papillomavirus infection patients who were randomly divided into 2 groups according to their conditions (anti-human papillomavirus protein dressing and control groups) each with 110 individuals (n=110). Anti-human papillomavirus protein dressings group was using the one from Luke duokang antibody while the control group did not use any vaginal medication. Thin-layer cytology and human papillomavirus-deoxyribonucleic acid were re-examined after 3 mo of drug withdrawal. At the same time, the levels of interleukin-6, 8 and 17 were analyzed. Further, tumor necrosis factor-alpha and C-reactive protein were also measured by enzyme-linked immunosorbent assay. Respectively, white blood cells, neutrophils, lymphocytes, platelets, red blood cells, fibrinogen, D-dimer, total cholesterol, low and high density lipoproteins, triglycerides, n-terminal pro B type natriuretic peptide, creatinine, aspartate aminotransferase and alanine aminotransferase were also examined. Negative conversion rate of patients in the anti-human papillomavirus biological protein dressing group was 54.5 % (60/110), while the control group was 20 % (22/110). After using anti-human papillomavirus biological protein dressing, the expression level of inflammatory factors in the treatment group was significantly reduced, compared with the control group. Meanwhile, the expression levels of white blood cells, lymphocytes and alanine aminotransferase showed different patterns between the two groups ($p<0.05$). The incidence of adverse reactions in the anti-human papillomavirus biological protein dressing was similar to that in the control group. Anti-human papillomavirus biological protein dressing (Luke duokang) has achieved effective results in controlling high-risk human papillomavirus infection and protecting patients.

Key words: Human papillomavirus, Luke duokang antibody, interleukin, cervical cancer, neoplasia, thin-layer cytology

The incidence and mortality of cervical cancer remains extremely high in developing countries[1]. Even with the advances in techniques as well as new raising methods, the overall outcomes of the disorder are still far from satisfaction, worldwide[2]. Cervical cancer is a serious threat to women's health and the quality of life. It is now well established that persistent high-risk Human Papillomavirus (HPV) infection is the cause of cervical intraepithelial neoplasia leading to cervical cancer. However, the transition from high-risk HPV infection to cervical intraepithelial neoplasia and then to invasive cancer can take a long time, which may take (15-20) y[3-5]. The longer the course of the disease, the more time is provided for the prevention and treatment of cervical intraepithelial neoplasia and cervical cancer[6-8]. In order to eliminate HPV in a timely manner, the use of anti-HPV therapy is the key to block the cervical intraepithelial neoplasia and prevent the development of cervical intraepithelial tumors into invasive cancer. The drug treatment for high-risk HPV infection includes local application of anti-HPV bioprotein dressings and interferon, etc.[9,10]. Anti-HPV biological protein dressing is an emerging drug product for treating high-risk HPV infections. Compared with traditional interferon administration, the incidence of side effects of anti-HPV biological protein dressing is lower. However, little is known

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about the overall results of this product. Here, our laboratory has developed a new type of anti-HPV biological protein dressing and conducted in-depth discussions on the efficacy of this drug product in clinical applications. 220 individuals with persistent high-risk HPV infection were recruited from the Fourth Hospital from June 2021 to June 2023. Liquid-based Thin-Layer Cytology (TCT) was abnormal; colposcopy and biopsy were performed. Among them, 160 individuals were diagnosed as low-grade Cervical Intraepithelial Neoplasia (CIN1) lesions and high-risk HPV positive by pathological examination, and 60 individuals were diagnosed as high-grade lesions (CIN II and III) by Loop Electrothermal Excision Procedure (LEEP) or cold knife conization. The pathological diagnosis was still CIN II and III with negative margin and high risk HPV positive in 60 individuals. The patient's age ranged from (30-60) y. Patients with drug allergy, acute vaginal inflammation, pregnancy, lactation, severe liver and kidney dysfunction and mental disorders were excluded. They were randomly divided into 2 groups according to their conditions. anti-HPV protein dressing group (n=110), with an average age of (37.5±6.5) y and control group (n=110) with mean age (37.1±6.7) y. There was no significant difference in age among the 2 groups ($p>0.05$). This study was approved by the Fourth Hospital Ethical Committee. Anti-HPV protein dressings group was using the one from Luke duokang antibody (Hunan) Medical Technology Co. Ltd., (Luke duokang). The high-risk HPV infection patients took 1 dose every time (3 g per dose), once every other day, 3 mo as a course of treatment. The medication was administrated at night before bed use so as to reach the posterior fornix of the vagina for 3 courses of treatment, thereby avoiding menstrual periods. The control group did not use any vaginal medication. TCT and HPV-Deoxyribonucleic Acid (DNA) were reexamined 3 mo after drug withdrawal. We studied the observation indicators. TCT was normal and HPV-DNA was negative after 6 mo of treatment. Further, before and after 3 mo of drug treatment, 5 ml of peripheral venous blood was collected on an empty stomach in the morning and the supernatant was obtained by routine centrifugation to determine the levels of Interleukin-6 (IL-6), IL-8, IL-17, Tumor Necrosis Factor-Alpha (TNF-α) and C-Reactive Protein (CRP) using Enzyme-Linked Immunosorbent Assay (ELISA). All the tests were performed with ELISA kits (Puteick Biotechnology, Co. Ltd., Suzhou). Subsequently, 5 ml of peripheral venous blood from each individual was collected from the patient under fasting state, centrifuged routinely. We collected the supernatant and routine blood test was performed. Ultimately, we studied the incidence of drug-related adverse reactions in the two groups which was analyzed statistically. The experimental data of this study was analyzed and studied using the Statistical Package of Social Sciences (SPSS) (https://www.ibm.com/spss) version 21.0. The measured data was represented by mean±standard deviation ($\bar{x}\pm s$). We analyzed study group data and control group data using t-test while the comparison between the two groups was performed using Chi-square (χ^2) test where $p<0.05$, was considered to be statistically significant. Primarily, the curative effect between the two groups was studied. The negative conversion rate was 54.5 % (60/110) in anti-HPV biological protein dressing group and 20 % (22/110) in the control group. There was significant difference between the treatment group and the control group ($p<0.01$) (Table 1). The inflammatory factors were analyzed comparatively between the two groups. Before treatment, there was no significant difference in inflammatory factors between the two groups ($p>0.05$). However, after treatment the expression levels of inflammatory factors in the anti-HPV biological protein dressing group were significantly decreased compared with the control group and the difference was statistically significant ($p<0.01$) (Table 2). Further, the relationship between grouping and blood routine indices in patients with high-risk HPV infection was studied. The levels of White Blood Cells (WBC), lymphocyte and alanine aminotransferase were significantly different among the two groups ($p<0.05$). The levels of Neutrophils (N), Lymphocytes (L), Platelets (PLT), Red Blood Cells (RBC), Fibrinogen (FIB), D-dimer, Total Cholesterol (TC), Low-Density Lipoprotein (LDL) Cholesterol (C) and High-Density Lipoprotein (HDL)-C, Triglyceride (TG), n-Terminal pro-Brain Natriuretic Peptide (nT-proBNP), Creatinine (CREA), Alanine aminotransferase (ALT) and Aspartate Transaminase (AST), where we found no significant difference ($p>0.05$) (Table 3). Finally, we compared the adverse reactions between the two groups where we found no significant difference ($p>0.05$), suggesting that the treatment of anti-HPV biological protein dressing group is safe and effective (Table 4). As suggested by several studies, cervical cancer is mainly caused by

HPV infection. HPV is actually a common covalent double chain in clinical practice. The circular DNA virus not only has strong tissue specificity, but also has a strong epithelial tropism, with humans being its only host[11-13]. Other scholars have emphasized that when the HPV in the body remains at a high level for a long time, it is easy to induce cervical cancer[14]. It should be pointed out that in general, it is impossible to completely eliminate HPV infection. To this end, it is necessary to actively seek a method that can effectively treat HPV. Recent research findings support that after immunization of laying hens with antigens, chickens can produce corresponding antibodies and transfer as well as accumulate them in the yolk[15]. This antibody is called Immunoglobulin of Yolk (IgY). Compared with mammalian antibody IgG and IgY has many characteristics, such as high production, good homogeneity, no activation of mammalian complement system, no non-specific binding to rheumatoid factors, no fixing to *Staphylococcus* A protein and no undergoing cross serotype reactions with mammalian immunoglobulins, etc.[16,17]. Here, in this study, we used the specific product (Luke duokang) anti-HPV protein dressing group from Leke antibody. Beside the general characteristics of anti-HPV bioprotein dressing, it also has anti-virus, anti-tumor and immunomodulatory effects. It targets the lesion site and inhibits viral nucleic acid replication, transcription and protein synthesis. In addition, it has multiple regulatory effects on the body's immune system, promoting variety of immune cell functions such as macrophages, lymphocyte and so on, thereby achieving anti-tumor and immunomodulatory effects. Here, from our study, we could demonstrate that compared with the control group, the expression levels of inflammatory factors in the anti-HPV biological protein dressing group were significantly decreased where the difference was statistically significant ($p<0.01$). Meanwhile, the levels of WBC, lymphocyte and alanine aminotransferase were significantly different between the two groups ($p<0.05$). Furthermore, there was no significant difference in the incidence of adverse reactions between anti-HPV biological protein dressing and the control groups ($p>0.05$), supporting that the treatment of anti-HPV biological protein dressing group is safe and effective. Special anti-HPV protein dressing has multiple pharmacological effects, including anti-tumor, anti-virus, anti-inflammatory and analgesic effects. It could also inhibit the proliferation of HPV16 positive cervical cancer cell lines, affect the DNA replication of tumor cells and inhibit the expression of viral gene fragments integrated into the host genome. The results of this study showed that the therapeutic effects of special anti-HPV protein dressing were significant. The pharmacological effects of anti-HPV bioprotein dressings are more specific. In conclusion, this study included a subset of patients with high-grade cervical intraepithelial neoplasia (CIN II and III) who had no indication for clinical hysterectomy and who were persistently at high risk for HPV positivity. It brings anxiety and tension, which has negative effect on the body's ability to resist the disease. Therefore, it is beneficial for patients to be given feasible drug treatment while emphasizing positive and regular examination. Overall, special anti-HPV protein dressing had certain curative effect on high-risk HPV infection and it had more advantages in turning HPV negative.

TABLE 1: COMPARISON OF CURATIVE EFFECTS BETWEEN THE TWO GROUPS

Group (n=110)	CIN I		CIN II and III		Negative conversion rate (%)
	Before treatment	After treatment	Before treatment	After treatment	
Anti-HPV bioprotein dressing	80	48	30	12	54.5
Control	80	17	30	5	20

TABLE 2: COMPARISON OF INFLAMMATORY FACTORS BETWEEN TWO GROUPS BEFORE AND AFTER TREATMENT (x̄±s)

Group (n=110)	IL-6		IL-8		IL-17		TNF-α		CRP	
	Before	After	Before	After	Before	After	Before	After	Before	After
Anti-HPV bioprotein dressing	32.66±4.23	15.76±2.58[ab]	8.81±1.26	6.74±1.03[ab]	54.28±8.23	38.46±5.48[ab]	15.64±3.01	7.45±1.88[ab]	10.64±3.13	2.89±0.76[ab]
Control	31.82±4.03	29.21±2.84	8.76±1.96	8.83±1.02	53.71±7.99	54.26±5.87	15.21±3.18	16.01±2.15	10.21±3.14	10.22±1.15
t	0.76	8.23	0.34	1.93	0.33	4.90	0.70	6.67	0.70	6.78
p	0.44	<0.01	0.71	<0.01	0.74	<0.01	0.48	<0.01	0.49	<0.01

Note: [a]p<0.05 and [b]p<0.05, compared with the two groups before and after treatment

TABLE 3: RELATIONSHIP BETWEEN GROUPING AND BLOOD INDICES IN PATIENTS WITH HIGH-RISK HPV INFECTION (x̄±s)

Blood indices	Group		p
	Anti-HPV bioprotein dressing	Control	
WBC (×10^9/l)	9.06±1.23	9.32±1.26	0.02*
N (×10^9/l)	6.52±2.03	6.66±1.96	0.34
L (×10^9/l)	1.56±0.23	1.78±0.26	0.01*
PLT (×10^9/l)	241.75±58.81	246.89±60.18	0.40
RBC (×10^{12}/l)	4.71±0.52	4.42±0.58	0.58
FIB	2.87±0.38	2.71±0.46	0.67
D-dimer	332.82±74.16	372.18±79.03	0.54
TC (mmol/l)	4.71±0.79	4.89±0.82	0.57
LDL-C (mmol/l)	3.40±0.53	3.42±0.57	0.66
HDL-C (mmol/l)	1.02±0.31	1.11±0.41	0.71
TG (mmol/l)	1.77±0.37	1.83±0.43	0.65
NT-proBNP (pg/ml)	98.33±23.81	88.15±20.13	0.11
CREA (umol/l)	73.17±17.81	86.21±22.18	0.22
AST (U/l)	28.02±5.19	24.16±3.42	0.19
ALT (U/l)	18.617±3.39	22.15±4.18	0.02*

Note: *p<0.05

TABLE 4: COMPARISON OF ADVERSE REACTIONS BETWEEN TWO GROUPS, n (%)

Group (n=110)	Vulval discomfort	Vaginal discomfort	General discomfort	Rate (%)
Anti-HPV bioprotein dressing	2	2	4	8 (7.27)
Control	1	0	2	14 (2.73)
χ^2	-	-	-	0.46
p	-	-	-	0.51

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Zhichao Sun and Yiyi Zhang have equally contributed for this study

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