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IMMUNOMODULATORY THERAPY OF PRECANCERS OF THE CERVIX – OPINION OF MEDICAL PROFESSIONALS AND STUDENTS

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ИММУНОМОДУЛИРУЮЩАЯ ТЕРАПИЯ ПРЕДРАКОВЫХ ЗАБОЛЕВАНИЙ ШЕЙКИ МАТКИ – МНЕНИЕ МЕДИЦИНСКИХ РАБОТНИКОВ И СТУДЕНТОВ

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Objective. To assess the relevance of immunomodulatory therapy of precancerous diseases of the cervix among medical professionals and students. Precancerous diseases of the cervix combine pathological processes characterized by the structural changes in the epithelium of the cervix. If not treated, they lead to the development of cervical cancer. At present there are no selective drugs for the human papillomavirus. To administer immunotropic medicines it is necessary to know the mechanism of effect on the immune system.

Materials and methods. The study was conducted using an anonymous online questionnaire on the Google Forms platform (<https://vk.com/away.php?utf=1&to=https%3A%2F%2Fforms.gle%2FRtT7PknCrLqBB1x8>). The

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questionnaire is presented as part of a one-stage (cross-sectional) study. Data analysis was carried out using Microsoft Excel 2010 graphs and tables. Empirical, sociological and statistical research methods were used. The indicators of the structure of the respondents were calculated, the reliability of the differences was determined by the Student's *t*-criterion, confidence differences were considered at significance of $p < 0.05$.

Results. The average age of the respondents was 30.4 ± 10.8 years. 46 people (75.4 %) are aware of the possibility of using immunomodulation as therapy for precancerous diseases of the cervix, and 15 people (24.6 %) are not aware of it. 41 respondents (67.2 %) would administer the therapy themselves and their close people; 12 people (19.7 %) find it difficult to answer; 8 respondents (13.1 %) do not agree to administer the therapy.

Conclusions. Medical students have an idea about immunomodulatory therapy in gynecology in 55.9 % of cases. Doctors of different specialties in 100 % of cases are aware of the treatment, see the benefits of prescribing drugs. Students' awareness of the possibilities of immunomodulatory therapy is sufficient, they get additional knowledge from clinical recommendations on the specialty in the practical course.

Keywords. Precancer of cervix, human papilloma virus, papilloma-viral infection, cervical intraepithelial neoplasia (CIN).

Цель. Оценка актуальности использования иммуномодулирующей терапии предраковых заболеваний шейки матки среди медицинских работников и студентов. Предраковые заболевания шейки матки объединяют патологические процессы, характеризующиеся наличием структурных изменений эпителия шейки матки. Без лечения приводят к развитию рака шейки матки. Сегодня нет препаратов, избирательно действующих на вирус папилломы человека. Назначение иммуностропных препаратов требует знаний механизма действия на иммунную систему.

Материалы и методы. Исследование проводилось при помощи анонимного онлайн-анкетирования с помощью Google-формы (<https://vk.com/away.php?utf=1&to=https%3A%2F%2Fforms.gle%2FRt77PktCrLqBB1x8>).

Анкета представлена в рамках одномоментного (кросс-секционного) исследования. Анализ данных проводился с использованием графиков и таблиц Microsoft Excel (2010). Оценка распределения признаков на нормальность проводилась с помощью критерия Шапиро – Уилка. Использованы эмпирический, социологический и статистический методы исследования. Рассчитаны показатели структуры опрошенных, достоверность различий определена *t*-критерием Стьюдента, доверительные различия считались при пороге значимости $p < 0,05$.

Результаты. Средний возраст опрошенных составил $30,4 \pm 10,8$ г. Ознакомлены с возможностью применения иммуномодуляции в качестве терапии предраковых заболеваний шейки матки 46 человек (75,4 %), и не знакомы – 15 (24,6 %). Назначили бы себе и своим близким – 41 человек (67,2 %); 12 (19,7 %) – затрудняются ответить; нет, не согласны назначить – 8 (13,1 %).

Выводы. Студенты медицинского вуза имеют представление об иммуномодулирующей терапии в гинекологии в 55,9 % случаев. Врачи разных специальностей в 100 % случаев знакомы с лечением, видят пользу в назначении препаратов. Информированность о возможностях иммуномодулирующей терапии обучающихся в вузе достаточная, дополнительные знания они получают в процессе практической деятельности из клинических рекомендаций по специальности.

Ключевые слова. Предрак шейки матки, вирус папилломы человека, папилломавирусная инфекция, цервикальные интраэпителиальные неоплазии (CIN).

INTRODUCTION

The concept of “precancerous diseases of the cervix” first occurred in the last century [1]. These are pathological conditions manifested by the presence of structural changes in the epithelium of the cervix.

Without treatment, cervical cancer may develop [2], but there is some positive aspect to the problem – the development of the disease takes from 3 to 8 years [3; 4]. To date, the statistics for the Russian Federation are disappointing: 15.1 cases per 100 thousand population. The incidence of

precancerous pathology is steadily increasing [5; 6]. A preventive measure for cervical cancer is the timely detection and treatment of background and precancerous conditions [7].

Non-specific antiviral, restorative therapy, desensitizing agents, tranquilizers, interferon preparations and their inducers, ozone therapy, adaptogens, synthetic immunomodulators are often prescribed additionally [8; 9]. It would seem prudent to determine the role of immunotropic therapy in the complex treatment of precancerous pathology of the cervix [10; 11].

The objective of the study was to assess the relevance of the use of immunomodulatory therapy for precancerous diseases of the cervix among medical professionals and students.

MATERIALS AND METHODS

61 people were interviewed using an anonymous online survey, conducted on the Google Forms platform. The sample size was not calculated beforehand. The questionnaire was presented as part of a one-stage (cross-sectional) study, which included the collection of information and analysis of data at a certain point in time.

Two groups were selected for comparative analysis: Group 1 comprised 34 people, and Group 2 – 27 people.

The data analysis was conducted using Microsoft Excel graphs and tables (version 2010). The age of the respondents was calculated using formulas for determining the

average value and standard deviation. The assessment of the distribution of signs for normality was carried out using the Shapiro–Wilk test. The distribution was normal. The results were presented in figures and tables with conclusions.

Empirical, sociological and statistical research methods were used. Indicators of the structure of respondents were calculated. Reliability of differences was determined using the Student's t-test. Confidence intervals were considered at a significance level of $p < 0.05$, i.e. the confidence level for the data is 95 %.

RESULTS AND DISCUSSION

The average age of the respondents was 30.4 ± 10.8 years, the vast majority of respondents were 23 years old, the minimum age was 22 years, the maximum age was 55 years.

First, the authors determined the general attitude towards immunomodulatory therapy in gynecology among practitioners and students. It was found that 46 people (75.4 %) were aware of the possibility of using immunomodulation as therapy for precancerous diseases of the cervix; 15 people (24.6 %) were not aware of it; 47 people (77.0 %) saw benefits in treating precancerous cervical diseases associated with HPV and supported this approach, while 14 people (23.0 %) had a different opinion; almost half of the doctors – 27 respondents (44.3 %) – used these drugs in addition to treatment for cervical dysplasia (associated

with HPV), in particular, 20 of them (32.8 %) did it after surgical manipulations on the cervix. 37 people (60.7 %) justified the use of immunomodulators based on clinical recommendations; 8 respondents (13.1 %) rely on books on obstetrics, gynecology, immunology, and oncology; the other 8 (13.1 %) follow articles in medical journals; 5 (8.2 %) respondents rely on their colleagues and acquaintances; the remaining 3 (4.9 %) people responded that they didn't prescribe these medications at all.

Specialists were also asked if their patients were satisfied with taking immunomodulatory drugs. 27 (44.3 %) respondents said that their patients were satisfied, 23 (37.7 %) people had no experience with immunomodulatory drugs, 8 (13.1 %) people did not use this kind of drugs, and 3 (4.9 %) respondents stated that their patients were not satisfied with taking immunomodulatory drugs.

Indications for the use of immunomodulatory therapy included: cervical dysplasia, according to 31 people (50.8 %); no such diseases – 15 respondents (24.6 %); acceleration of recovery after surgical treatment – 6 respondents (9.8 %); after an unsuccessful in vitro fertilization attempt – 4 (7.3 %); miscarriage – one person (1.2 %); chronic endometritis – one person (1.3 %); cervicitis and vaginitis – 3 respondents (5 %).

Five of the surveyed doctors (8.2 %) claimed that their patients experienced side effects from therapy; 24 respondents (39.3 %) reported no side effects in their

patients; and 32 people (52.5 %) have no personal experience with immunomodulators.

In general, the attitudes towards immunomodulatory therapy are shown in the figure: 21 people (34.4 %) find it acceptable to use, 17 respondents (27.9 %) consider it possible, 15 people (24.6 %) think it is safe to use, 5 people (8.2 %) see it as unsafe, and 3 people find it completely unacceptable (4.9 %).

When conducting a comparative analysis of the responses of doctors and students, the authors found no significant differences in the following parameters: familiarity with immunomodulatory therapy; reliance on books on obstetrics and gynecology and scientific articles when prescribing this type of therapy by doctors; opinion that immunomodulatory therapy is safe and/or completely unacceptable (table).

Drawing an analogy to the above conclusion, we have characterized all other sample indicators accordingly.

Statistically significant differences were obtained in the answers to the questions about the use of immunomodulatory drugs, planning to use them; their use in combination with CIN therapy; the presence of side effects; reference to the opinions of colleagues and clinical recommendations as well as medical journals when prescribing these drugs; attitude to immunomodulatory therapy as safe; the possibility of self-prescription of treatment and/or prescribing it to relatives; refusal to prescribe such treatment.

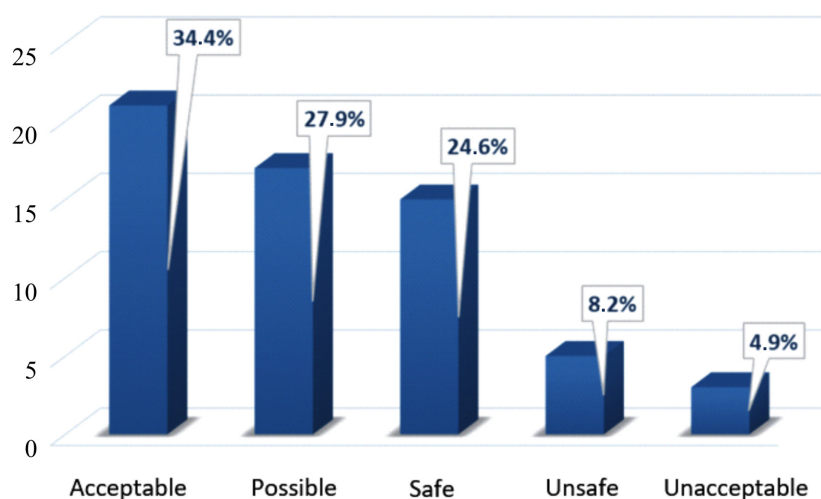


Fig. Attitude of the respondents to immunomodulatory therapy

Attitude of the respondents in the study groups to immunomodulatory therapy

Parameter	Group 1 (<i>n</i> = 34), %	Group 2 (<i>n</i> = 27), %	Reliability of differences, <i>R</i>
Respondent is familiar with immunomodulatory therapy	55.9	100	0.2
Respondent sees benefit from immunomodulatory therapy	58.8	100	0.01
Respondent uses of immunomodulatory drugs in practice	0	77.8	0.01
Respondent is planning to use immunomodulatory drugs	64.7	0	0.01
Respondent uses immunomodulators in therapy (besides CIN)	0	100	0.0001
Respondent registered side effects of immunomodulators	70.6	0	0.01
Respondent refers to clinical guidelines when administering immunomodulators	29.4	100	0.01
Respondent refers to books on obstetrics and gynecology when administering therapy	11.7	14.8	0.5
Respondent refers to the opinion of colleagues in the therapy	23.5	0	0.003
Respondent refers to scientific articles when administering therapy	17.6	7.4	0.2
Respondent refers to the medical journals in the appointment of therapy	23.5	0	0.003
Respondent considers therapy with immunomodulators as safe	79.4	100	0.001
Respondent is satisfied with the price of immunomodulatory drugs	0	100	0.0001
Respondent is not satisfied with the price of immunomodulatory drugs	26.5	0	0.002
Respondent finds it difficult to give an answer on the price of immunomodulatory drugs	73.5	0	0.01
Respondent would prescribe immunomodulatory treatment to themselves and/or their family	41.2	100	0.002

End of the Table

Parameter	Group 1 (<i>n</i> = 34), %	Group 2 (<i>n</i> = 27), %	Reliability of differences, <i>R</i>
Respondent would not prescribe immunomodulatory therapy to anyone	23.5	0	0.003
Respondent considers therapy with immunomodulators acceptable	23.5	48.1	0.05
Respondent considers therapy with immunomodulators possible	50	0	0.05
Respondent considers therapy with immunomodulators safe	2.9	51.9	0.15
Respondent considers therapy with immunomodulators unsafe	14.7	0	0.02
Respondent considers therapy with immunomodulators totally unacceptable	8.8	0	0.08

This study showed a high level of awareness of immunomodulatory therapy among the medical community – 75.4 % (*n* = 46). This confirms information from Russian publications on the commitment of physicians to this type of treatment [8;9].

Modern Russian clinical guidelines recommend the use of immunological drugs for the treatment of precancerous cervical diseases only in the presence of human papillomavirus, in addition to excisional treatment methods. In the study, 77 % of medical professionals believed that this type of therapy was effective against human papilloma virus (confirming information in clinical recommendations), while 23 % believed it was ineffective. At the same time, 34.4 % (*n* = 21) actively used these drugs to treat HPV infections, while 29.5 % (*n* = 18) did not consider them effective presumably based on literature reports about the lack of evidence supporting their effectiveness against HPV [10].

According to the respondents, 44.3 % (*n* = 27) often use immunomodulators in

the treatment of gynecological pathology unrelated to cervical dysplasia – miscarriages, unsuccessful IVF attempts, chronic endometritis, etc. This helps preserve the reproductive health of women, as this issue is considered a strategic one for healthcare in many official statistics.

Doctors who perform surgical procedures on the cervix often prescribe immunomodulators to help promote tissue healing after surgery and provide complex treatment for human papillomavirus. 66.7 % of them recommend using immunomodulators, while 33.3 % do not. Medical literature has shown that vaccination and proper treatment for precancerous conditions can be effective in preventing cervical cancer [7–10].

It was gratifying to learn that medical professionals adhered to clinical guidelines (60.7 %), as well as books and journals in their field, thereby enhancing their expertise.

When comparing the two groups, we found a generally favorable attitude towards the administration of immunomodulatory

therapy. 100 % of respondents from group 2 saw the benefit of prescribing immunomodulators, and 77.8 % used this type of therapy in practice. However, only 58.8 % of respondents in group 1 saw the benefits of prescribing it ($p = 0.01$), and did not use it in practice ($p = 0.05$).

In addition, doctors tend to recommend treatments based on clinical guidelines (100 %), while students find it acceptable to consult with their colleagues (23.5 %) and read journal articles on the subject ($p = 0.003$).

CONCLUSION

77 % ($n = 47$) of medical workers see benefits from the use of immunomodulatory therapy, while 34.3 % ($n = 21$) actively utilize this type of treatment in practice. Medical students have a good understanding of immunomodulation in gynecology in 55.9 % of cases. Doctors of various specialties are aware of this treatment in 100 % of the cases, they see benefits in prescribing it for their patients, as well as recommending it to relatives. Overall, medical professionals have a sufficient understanding of the potential of this therapy during their studies, and they gain additional knowledge about indications, contraindications, and potential complications through practical training, primarily through clinical guidelines.

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