ECONOMIC AND DIAGNOSTIC EFFICIENCY OF CERVICAL CANCER PREVENTION

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Abstract

Cervical cancer is a significant medical and social problem. In Bulgaria there is a tendency of morbidity and mortality rate increase. The values reached during the latest years are among the highest in Europe. Women of 35 to 65 years of age are the most affected, but all sexually active women are at risk.

Due to many factors – social, psychological, health and ethical alike – cervical cancer is frequently detected at a clinical stage that makes its treatment difficult.

Prevention is crucial for this disease when the aim is to preserve women's lives. It is efficient only by a combination of vaccination and regular preventive checkups.

Key words: *efficiency prevention, cervical cancer*

Introduction

Cervical cancer affects women in their prime.

According to WHO, it is responsible for 15% of all cancer cases in women. There are about 500 000 new cases each year and one woman dies each two minutes.

The severity of this problem is the biggest in Eastern Europe where cervical cancer mortality rate is twice as high as in the other parts of the continent.

Bulgaria features a sustainable tendency of increase of cervical cancer morbidity and mortality. Data from the National Cancer Register show that the new cases frequency has nearly tripled. It is indicative that only two countries in the world – Bulgaria and Thailand – report mortality rise. Mortality rate is an indicator of the efficiency of screening, early diagnostics, adequate treatment and follow-up (Mushmov, M., R. Raichev, 1996).

About 1200 new cases are registered each year and the share of advanced cancer forms is rising (Zlatkov, 2006).

This oncologic disease shows a tendency of affecting ever younger women. It is related to the younger age of the girls starting active sex.

Cervical cancer is a disease that has an impact on the family and profession and changes the lifestyle of the patients completely. Part of their established habits and traditions, their social and labor relations get broken. Cancer is a neoplasm which can be brought to a minimum by modern knowledge, technical facilities and a good organization of healthcare and the health insurance system (Karagyozov, 2005).

Presentation

Prevention in oncologic practice is performed to prevent disease and death from the various forms of malignant neoplasms. A necessary condition of its performance is the knowledge of the causes and the mechanism of occurrence and development of the respective disease. The risk factors include:

Early sexual activity and early marriage;

Promiscuity – frequent change of sexual partners. A study of K. Brock et al (1989) showed that women with more than seven partners are in six times greater risk of cervical cancer than those with one or no partner.

Low social and economic status – women of lower education and income;

Many births and abortions;

Sexually transmitted diseases – chlamydia, HSV-2, of which HPV infections come first.

Cervical cancer is curable. There are safe and efficient methods of protection that can successfully fight the disease. Prevention is considered to be a major method to improve this severe oncologic disease.

Prevention can be primary, secondary and tertiary (Zaridze, D. et al, 1987).

Primary prevention includes measures that influence the external and internal human environment and its aim is to preclude or reduce the influence of carcinogenic or predisposing factors. Primary prevention not only reduces the impact of such agents but also limits the contact of individuals with them. The improvement of health culture of the population and the acquisition of knowledge and skills also assist cancer prevention. The major task of primary prevention is to prevent the disease itself.

Cervical cancer is well known for the role of HPV (human papyloma virus) and the various sexual activity factors responsible for this disease. Unfortunately, due to the absence of real opportunities of sexual behavior regulation, primary prevention until recently recommended only later start of sexual behavior, limiting the number of partners and use of barrier contraception.

99.7% of cervical cancer cases are caused by a virus of the HPV group.

The HPV infection is easily transmitted immediately after the start of sexual life. Up to 80% of sexually active women get infected at certain moments of their lives.

The HPV infection is nowadays considered a major factor because out of the 460 000 patients registered annually by the WHO with cervical carcinoma in more than 200 cases there is a connection to the papyloma virus. Some authors have even found HPV infection in 99% of the cervical carcinoma cases.

That was made possible because the viral etiology of the disease was proved in the eighties of the 20-iest century by the German scientist professor Zurhousen. He was made Nobel laureate for his discovery which was followed by the development and implementation into practice of safe and highly efficient vaccines.

So far about 200 different HPV types have been reported and 50 of them are related to the genital tract. From a phylogenetic point of view, papyloma viruses are divided into five subgroups – A, B, C, D and E – and three of them are found in humans. The biggest group A is heterogeneous and is associated with benign and malignant genital infections.

Besides their structural differences, the papyloma virus genotypes can be divided depending on their clinical manifestations. The biological effect of these clinical manifestations is defined mainly by their oncogenic significance. They are divided into two groups. The first includes HPV types associated with benign skin and mucosal changes. The second one is associated mainly with pre-cancer and cancer changes, 20 of which are directly connected with cervical carcinoma. 16 and 18 are responsible for 70% of the cervical carcinoma cases.

Today's level of primary prevention includes:

Digene's HPV test for carriage of HPV virus. Modern testing technologies make it possible to discover the genetic (DNA) code of the virus. This test is recommended, together with the smear test, for women of 30 and above and is desirable for women below 30.

It is to be mentioned that the expensive equipment, the lack of experience and the labor intensity are all obstacles to the use of the HPV test for primary mass screening. (Dillner J., P. Sparen, M. Arbyn. 2003)

Cervical carcinoma vaccine

Cancer prevention vaccines are an important achievement of modern medicine. They protect the organism from infections by producing a specific immune response to the respective disease agent. The cervical cancer vaccine contains non-infectious virus-like particles and, when introduced into the organism it develops immunity against the disease agents.

The choice of primary prevention asks questions about the age when it should start and what part of the population to cover.

The vaccine is designed for the age group between 9 and 26. This is the age when the first sexual contacts start and the risk of infection with the virus is the highest.

According to Regulation 15 on immunizations in Bulgaria, HPV vaccination is recommended for girls and women between 12 and 25 years of age (National Immunization Calendar, 2005). Vaccination helps create a sustainable and lasting immunity against HPV types 6, 11, 16 and 18.

It is not indicated for the treatment of cervical carcinoma and cannot replace the standard prevention by gynecological examination and smear.

By the middle of 2012, on a world-wide level, more than 90 million doses have been administered. Vaccines have been authorized for use in more than 110 countries.

Vaccination programs are a part of the overall healthcare policy and are generally considered advantageous to society. Their economic value is estimated from the point of view of what they save to society and what will the losses be if people are not vaccinated.

Two vaccines have been authorized in Bulgaria: bivalent (HPV 16, 18) and quadrivalent (HPV 16, 18, 6, 11). Both of them are permitted for use in more than 80 countries. They have long proved their high efficiency, sustainability and safety – all requirements they must meet according to the European Centre for Disease Prevention and Control (ECDC, 2008). Both vaccines demonstrate above 95% efficiency against cervical cancer caused by HPV 16 and 18, which means that the vaccine is really capable to give protection against the virus it is intended for.

The health, social and economic price paid by society to cervical cancer disease is terribly high.

In 2007, WHO published technical instructions for ruling statesmen and politicians about cervical cancer vaccines. Having calculated the costs of vaccines, their delivery, consumables, screening and treatment of the disease and compared them to the costs and losses due to premature death, WHO experts found that **vaccination is more efficient and profitable** than screening which is performed twice to three times in life. Profitability depends on vaccine price but, at the price of 75 US dollars per a vaccinated person, the efficiency is 2000 US dollars per each life-year saved. (National Program of primary cervical cancer prevention).

Based on the data of profitability analysis, it was found that the price of the saved life of a vaccinated woman in Bulgaria is 62 573 BGN. The premature death of a 42-year-old woman would cost the country at least 288 000 BGN (16 000 BGN of GDP for 18 years of efficient life). (Petrova G., 2000)

Cervical cancer is the only oncologic disease that has been provided with a vaccine. However, there is still certain distrust and disapproval of it among the Bulgarian population. This negativism was proved by the results obtained from some activities performed in Vratsa District in relation to the National Program of primary cervical cancer prevention of 2012-2016. The program gives the parents the chance to make an informed decision to protect their child against the human papyloma virus and take advantage of the fact that the vaccine will be provided to their girl free of charge. The target of the Program is that by the end of the fifth year at least 75% of the liable girls should be vaccinated so that there will be a population effect to be measured and reported 10 or 15 years later.

The immunizations performed in 2013 in Vratsa District at the expense of the Program show a very low activity.

Immunizations reported: For 856 girls subject to immunization who turned 12 in 2013, there were 495 doses used from the beginning of January to the end of December 2013, as follows:

1st intake – 137; 2nd intake – 187; 3rd intake – 171

This makes 19.97% coverage of the complete immunization schedule.

Number of cervical cancer vaccine doses administered in Vratsa District for 2013 (data provided by the Vratsa Regional Health Insurance Fund)

	Glaxo	***Libra* AG**	**Total**
1st intake	105	32	137
2nd intake	128	59	189
3rd intake	120	51	171
Total			**495**

It was thought that the main reason of the insufficient use of the vaccination opportunity was the high price. But when vaccination was offered to the 12-year-olds free of charge, the results were not encouraging, either. This means that among the population there is still a lot of distrust to the vaccine or there are other reasons that have to be found by the experts.

According to information provided by the Vratsa Regional Health Inspectorate, there was little interest among the parents, which was obvious from their reluctance to attend the meetings organized by a group of experts of the Inspectorate. Moreover, many general practitioners signaled that parents who desired vaccination subsequently declined. That was partially influenced by opinions on cervical cancer vaccines on the Internet of incompetent persons without any medical education. The most common misconception is that vaccination threatens infection. It has a negative impact on the overall organization of the National Program of primary cervical cancer prevention. On the other hand, the competent persons and authorities are not sufficiently active in its support.

There exists another problem in the poorest region of Europe: many of the people of working age in Vratsa District work abroad. Their children are being raised by grandparents, aunts and even neighbors who are not their legal guardians. These people take the children to the required immunizations because they are compulsory for kindergartens and child benefits, but they cannot make decisions about a non-compulsory vaccine in the absence of the parents. In some cases this is the situation of all children subject to vaccination in some GPs' practices.

On the other hand, better results are achieved where there is active participation of several parties. Better vaccination coverage is registered when there is support from the municipal administration, the general practitioners, pediatricians, obstetricians, media and non-governmental organizations. (Report on activities performed for the National Program of primary cervical cancer prevention by the Vratsa Regional Health Inspectorate, 2013).

A major and very important moment in modern healthcare is patients' awareness. Informed patients are no longer passive and become active participants in the process of their health preservation.

According to the Consensus Declaration of the Bulgarian Association of Oncology and Gynecology, prevention by anti-HPV vaccination would have an impact on cervical cancer morbidity and mortality rates on a national level only if vaccination is performed on a population principle. This means that vaccination is to become part of the country's immunization calendar.

The same declaration describes that the anti-HPV vaccines do not guarantee prevention for the whole population threatened by the disease. Cervical cancer whose pathogenesis includes oncogenic HPV types that the vaccines do not build immunity against, preserves its potential independent of the vaccination. Therefore, women are subject to cytological cervical screening in compliance with the

accepted rules and norms. (Consensus Declaration of Bulgarian Association of Oncology and Gynecology, 2010)

Secondary prevention detects malignant tumors at an early stage or at a stage preceding cancer development. The purpose of this prevention is to reduce mortality and morbidity rates.

For gynecological locations, secondary prevention is most widely applied to cervical carcinoma by cytological screening and by specifying diagnostics by means of colposcopy by target or "blind" biopsy.

The choice of secondary prevention also asks questions about the age when it should start, the frequency of checkups and the accuracy of the methods.

The experience of many countries with screening programs shows that the programs are efficient and reduce the number of people suffering and dying of this cancer. All women between 30 and 59 years of age who have no diagnosed cervical changes should be screened.

Screening was defined first in 1957 by the Committee of Chronic Diseases of USA as: alleged identification of an unrecognized disease or defect by using tests, examinations or other procedures that can be applied quickly.

The screening principles defined by J. Wilson and G. Jungner in 1968 and included in the WHO enactments are still true today:

the disease subjected to screening must be a medical and social issue

its clinical course should be well known and its pre-clinical phase should correspond to a biologically less aggressive period of its development;

the screening test should be easy to perform, safe to investigate, of low price, high sensitivity, specificity and predictive value;

the treatment of the detected status should be effective and should reduce the mortality rate. (Wilson, J., G. Junger, 1968)

The cheapest and most efficient method of cervical cancer screening is the smear which has a proven diagnostic effect. The official authorization of cytology as a method of early finding and prevention of cervical cancer is performed on the strength of a 1962 decision of the World Health Organization which was confirmed ten years later by the International Union Against Cancer.

Preventive checkups of the genitalia in Bulgaria were introduced by order of the Ministry of Health in 1956 and cervical cytological screening was introduced in 1970.

Cervical screening is updated by: automation, preparation of a standard quality smear, HPV typing and prevention by vaccination. (Canavan, 2000) Some authors claim that these better-quality technologies reduce the number of errors and have a better "price to efficiency" ratio than standard screening. (Kostova, P., 2004).

The aim of the automated devices is to increase screening sensitivity and specificity, reduce the workload on cytological technicians and pathologists, decrease the screening program price and finally reduce cervical cancer morbidity and mortality rate.

The transformation of the modified cells into cancer ones is a slow process. As the early stages of development of the disease show no tangible symptoms, the modifications can be found only by screening. Regular prophylactic checkups for cervical cancer are designed to find modified cells in their early stage when the respective sections can be treated or removed without any malignant development. The later stages of the disease need surgery which sometimes is to be complemented by radiotherapy and chemotherapy. These highly specialized methods are costly to any healthcare system.

The task of oncologic screening is to find malignant tumors or their precursors before any symptoms appear. It is not designed to diagnose a case of clinical signs. It is an active search, among healthy

individuals, for people who probably have the disease or are at a risk of developing it. As screening is performed on a great number of apparently healthy persons, the test must be accurate to limit the chance of false results.

According to the recommendations of WHO and the professional organizations of pathologists, cervical smears must be examined by an accredited laboratory by qualified specialists under the direction of medical personnel with higher education, qualification and experience in the field of diagnostic cytology. (WHO, 1988)

There are various types of screening tests. Mass screening is designed to find pre-cancer conditions that can lead to cancer and is considered one of the possible and most successful public health measures to prevent malignant diseases. A well organized screening program can significantly reduce the morbidity and mortality rate of a number of malignant diseases.

Screening has long proved its efficiency. The number of the diseased and the dead in the countries that have national programs are reduced to 60%. (Antilla A, Ronco G, Clifford G, Bray F, Hakama M, Arbyn M, Weiderpass E.,2004)

Most of the analyses measure efficiency by years of saved life. They find that cervical screening does not save costs but its effect is to preserve the life of many women and to improve their life quality. (/Brawn, J., M. Sculpher, 1993)

The aim of screening is to identify modified cells in the earlier stages when the modified sections can be treated, so that cervical cancer does not develop. Once developed, its treatment is more difficult and less successful.

Organized checkups have proven to be a major method to fight cancer in most countries. In Great Britain, for example, cervical cancer screening was introduced in the eighties of the 20th century and saves 5000 lives each year. /Cancer Research UK, England/

Invitations for screening checkups in Bulgaria were dispatched in 2013. The initiative is included in the project “Stop and have a checkup! Your health is in your own hands!” of the Ministry of Health within the Operative Program “Development of human resources” funded by the European Social Fund of EU. The project will be finalized in 2013. Two million people have been informed via the social awareness and prevention campaigns. The project has many innovative components and is developed in compliance with European norms. The target group of cervical cancer screening are women of 25 to 60 years of age (250 000 checkups).

Tertiary prevention is intended for active follow-up of patients already treated. It provides rehabilitation activities and measures against recurrence. Rehabilitation is defined as: social and professional adaptation. Its best characteristics are early start, continuity, complexity and individual approach.

Conclusion

Cervical cancer prevention has a proven diagnostic and economic effect. The methods and means used in the preventive activities can help avoid the disease and reduce its morbidity and mortality rate. But despite the preventive measures, oncologic diseases hold second place among the causes of death in EU, just after cardiac diseases.

Preventive activities improve the working capacity, prolong the active working life of the population and help optimize health and social costs, which unavoidably leads to economic efficiency.

Primary prevention is intended to prevent the development of the disease by using measures that exclude the impact of carcinogenic and predisposing factors. There exists a unique opportunity of primary prevention by means of vaccination which, however, is not used well enough in Bulgaria. The

reasons for this situation are due to a number of social, economic, organizational and other factors and problems that can be solved with the implementation of a modern health reform.

Another important issue is vaccine efficiency depending on the virus type. The lack of multivalent HPV vaccine to guarantee 100% efficiency against the virus is much discussed. To reduce cervical cancer frequency, it is necessary to combine at least 8 to 10 oncogenic types.

It is also necessary to improve the social awareness of the population of the benefits of immunization. Good awareness is a guarantee of an efficient treatment process and adequate behavior in promotional programs.

One of the methods to enhance the active participation of the female population in such prevention checkups is the introduction of economic sanctions similar to the practices in most European countries.

Secondary prevention combines methods of diagnostics of malignant tumors on a pre-cancer stage. It is designed to reduce morbidity and mortality rates. An important precondition of its performance is the availability of efficient screening and early diagnostics methods.

Screening programs have long proved their efficiency in the reduction of the cervical cancer morbidity and mortality rates. They will certainly need investments. Prevention costs are justifiable not only from a medical but also from economic point of view. Preventive measures and early diagnostics are humane acts but they are also more profitable economically than long-term loss of working capacity or of human life.

The cytological examination for cervical cancer is the only method that fully meets the requirements and recommendations of WHO for a preventive screening program.

The implementation of projects and programs of cervical cancer prevention is a great challenge to our country. With time, they provide us with an opportunity to reduce the heavy toll of cancer diseases on our society. To function efficiently, however, they need the active participation of all stakeholders involved.

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