



Role of Vaccines in Preventing Cancer



Imran Akram*

King Edward Medical University, Pakistan

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*Correspondence Address: Imran Akram, King Edward Medical University, 39 Brandon road, Upper darby, Lahore, Pakistan, Tel: 00923336109240; Email: i_akram@ymail.com

Abstract

In recent time, great progress in understanding and regulating the immune system have led to new hope specifically destroying cancer cells without affecting normal tissues. Following review describes fundamental immunologic advances and the latest vaccine strategies arising from these advances, as well as the early clinical trials studying new approaches to treat or prevent cancer. Despite all these advances, cancer remains a major cause of death worldwide. Using radiotherapy or chemotherapy to treat cancer affect normal cells and result in side effects that limit treatment. In principle, the specificity of the immune system could be used to precisely target cancer cells without harming normal cells. This hope has motivated much research over several decades but has only got limited success. However, the huge increase in knowledge of the immune system and its regulation have led to a revival of interest in immunologic approaches to target and eliminate cancer. Two important vaccines to prevent cancer approved by FDA are Hepatitis B virus vaccine and Human Papilloma virus HPV.

Introduction and Background

Cancer is a group of diseases involving abnormal cell growth with the ability to invade or spread to distant parts of the body from origin of cancer [1]. These are unlike to benign tumors, which do not spread to other parts of the body [2]. Deaths from cancer were 5.8 million in 1990 [3]. Deaths are mainly increasing primarily due to longer lifespans and lifestyle changes in the developing world and longer life span due to decreased mortality in cardiac events due to much progress in cardiac field and increased awareness of risk factors of cardiac diseases [4]. The biggest risk factor for developing cancer is age [5]. Although it is possible for cancer to hit at any age, most patients with invasive cancer are over 60 [6]. According to a cancer researcher Robert A. Weinberg, "If we lived long enough, sooner or later we all would get cancer [7]. Some of the associations between aging and cancer is attributed to immunosenescence damage to DNA over a lifetime [8,9] and changes in the endocrine system with age [10]. Effect of aging on cancer is increased by factors such as DNA damage and inflammation promoting it and factors such as vascular aging and damage and, endocrine changes inhibiting it [11]. Attitudes toward vaccines, in general, were the strongest predictors of the acceptance of any vaccine in preventing the cancer [12].

Cancer Treatment Strategy

As Cancer is a class of diseases [13,14], so there cannot be single treatment for it, as there is no single treatment for all infectious diseases [15]. Angiogenesis inhibitors were once thought to inhibit cancer and having a role in cancer treatment but it all proved to be false theories [16]. Angiogenesis inhibitors and some other cancer therapeutics are used in combination

to decrease somehow cancer morbidity and mortality [17]. If one treatment strategy results in some successful results, we can try it for some other cancer too [18]. Diagnostic tests are under development to target the therapies to relevant patients, based on their individual biology [19]. Better understanding of Molecular and cellular biology due to cancer research has led to new treatments for cancer since US President Richard Nixon declared the "War on Cancer" in 1971. Since then, the country has spent over \$200 billion on extensive cancer research, including resources from public and private sectors. [20] The cancer death rate (adjusting for size and age of the population) declined by seven percent between 1950 and 2005 but stats are different in different studies and in fact in some recent studies cancer incidence and deaths related to cancer have increased [21].

Huge financial burden appears to have suppressed the creativity, cooperation, risk-taking and original thinking required to make fundamental discoveries and more innovative research. One other big obstacle in advancement in research on cancer studies is that many of studies claim some dramatic results but later can't be proved and replicated and this discourages the institutions to put sufficient investment in studies [22-27]. Virotherapy, which uses convert viruses, is being studied and it may be of extreme advancement in cancer treatment and decreasing the morbidity and mortality. There have been few Vaccines developed that prevent infection by some viruses which lead to chronic infection and causing cancer over period of time, thus decreasing the risk of cancer [28]. Human papillomavirus (HPV) vaccine (Gardasil and Cervix) decrease the risk of developing cervical cancer [29]. The hepatitis B (HBV) vaccine prevents infection with hepatitis B virus and thus decreases

the risk of liver cancer [30]. The administration of human papillomavirus and hepatitis B vaccinations is recommended to decrease the risk of Cervical cancer and Hepato-cellular carcinoma [31].

Human papilloma virus (HPV) vaccine

Human papilloma virus (HPV) vaccine is a vaccine that prevents infection by some types of human papillomavirus. Available vaccines protect against different types of HPV by decreasing the risk of infection [32]. All vaccines protect against at least HPV type 16 and 18 and some other types that cause the greatest risk of cervical cancer. It is estimated that they may prevent 70% of cervical cancer, 80% of anal cancer, 60% of vaginal cancer, 40% of vulvar cancer [33]. They additionally prevent some genital warts with the vaccines against 4 and 9 HPV types providing greater protection and prove to be of great benefit.

The World Health Organization (WHO) recommends HPV vaccines as part of routine vaccinations in all countries. The vaccines require two or three doses depending on a person's age and immune status. Vaccinating girls around the ages of nine to thirteen (09 to 13) is typically recommended. The vaccines provide protection for at least 5 to 10 years. Cervical cancer screening by PAP smear is still required following vaccination. Vaccinating a large portion of the population may also benefit the unvaccinated. In those already infected the vaccines are not effective.

HPV vaccines are very safe. Pain, Redness and swelling at the site and fever may also occur. No link to Guillain-Barré syndrome has been found in many studies. The first HPV vaccine was introduced in 2006 and in 2007 it was widely spread to other parts of the world and gained a mandatory role at least for girls. They are considered one of the most effective and safe medicines needed in a health system by World Health Organization (WHO). The wholesale cost in the developing world is about US\$50 a dose as of 2014. In the United States it costs more than US\$200. Vaccination may be cost effective in the developing world and it is one of the major hurdle in under developed and developing countries [34].

Role for Males

HPV vaccines are approved for males in many countries of the world. In males HPV Vaccine decreases the risk of genital warts and precancerous lesions caused by HPV. This reduction in precancerous lesions reduces the rates of penile cancer in men. Gardasil has been shown to also be effective in preventing genital warts in males. [35] Since penile and anal cancers are much less common than cervical cancer, HPV vaccination of young men is likely to be much less cost-effective than for young women. [36] In early 2013 the two companies who sell the most common vaccines announced a price cut to less than US\$5 per dose to poor countries, as opposed to US\$130 per dose in the US to encourage the increase use of HPV vaccine and to reduce the risk of cancer [37].

Role in older Women

It was concept in start that HPV vaccine prevents cancer only in young females but after new studies and new evidence that HPV vaccine is also effective in preventing the cancer in women over 45 years of age too [38]. In November 2007, Merck presented new data on Gardasil after investigational studies. In an investigational study, Gardasil reduced the incidence of HPV types 6, 11, 16 and 18-related persistent infection and disease in women through age 45. The study evaluated women who had not contracted at least one of the HPV types targeted by the vaccine by the end of the three-dose vaccination series.

Merck planned to submit this data before the end of 2007 to the FDA, and to seek an indication for Gardasil for women of age 45. Neither vaccine prevents any other sexually transmitted diseases, nor do they treat existing HPV infection or cervical cancer, that is main reason to administer vaccine at early age [39] There are high-risk HPV types, that are not covered by available vaccines. Recent researches are focusing on the development of HPV vaccines that will provide protection against a broader range of HPV types. One such method is a vaccine based on the minor capsid protein L2, which is highly conserved across HPV genotypes at molecular level. Efforts for this have included boosting the immunogenicity of L2 by linking together short amino acid sequences of L2 from different oncogenic HPV types or by displaying L2 peptides on a more immunogenic carrier [40]. There is also subsequent research interest in the development of therapeutic vaccines, which seek to elicit immune responses against established HPV infections and HPV-induced cancers and future seems to be bright and hopeful in this regard.

Hepatitis B virus vaccine

Hepatitis B is an infectious liver disease caused by the Hepatitis B virus (HBV). It can lead to mild illness, lasting a few weeks (acute) or long-term (chronic) illness that over the period of time can lead to liver disease or liver carcinoma by its carcinogenic ability. The hepatitis B (HBV) vaccine is used in all age groups to prevent HBV infection but early administration is recommended before the infection can hit [41]. The very first evidence of cancer prevention by vaccination in was provided by HBV vaccination in infants. Chronic HBV is related to more than 80%of hepatocellular carcinomas (HCC) in adults and nearly 100% of childhood HCC in areas endemic for HBV infection. HCC prevention failure is mainly related to vaccine failure to inhibit chronic HBV infection. The main reason of vaccine failure have included intrauterine infection, vaccine escape mutants, genetic hypo responsiveness, cost in under developed countries and poor compliance. Advance efforts to reduce vaccine failure by thorough research and new modifications will improve the efficacy of liver cancer prevention by HBV vaccination. This experience of HCC prevention by HBV immunization may also be applied to the prevention of other infection-related cancers [42].

Injectable Hepatitis B vaccines requires processes and refrigeration making them costly, which can make them difficult

to access in developing countries. To tackle this issue, researchers have been working to engineer plants capable of producing the ingredients necessary to make vaccines so that people can eat these plants to receive the vaccine in as simple process as possible making it available to large number of people in under developed countries. Potatoes, bananas, lettuce, carrots, tobacco and few other plants are being genetically engineered to produce the Hepatitis B vaccine ingredients.

Future

In the recent past, the approach to cancer prevention has moved forward from population and epidemiological studies to molecular targeting and immunological approaches and to look for high-risk pre-cancerous lesions in individuals using latest detecting technologies. Worldwide implementation of these scientifically proven sound and medical-based cancer prevention strategies has the potential to reduce global cancer incidence, prevalence and mortality rates in the decades ahead. As much more is being explored about the mechanisms and pathways that are affected by genetic and molecular changes that lead to cancer or encourage its progression, targeted therapies are being developed to stop these processes.

Conclusion

Vaccines have been among the most cost-effective agents, saving millions of lives. However, for treatment of cancer, vaccines have yet to access to worldwide population. Increased understanding of the immune system through advanced research studies have created new hopes to prevent cancer through vaccines before starting damage to tissues and modifying the pathway leading to cancer. HPV vaccine and HBV vaccines are the two most important vaccines which are approved to prevent cancer till to date. Tumor antigen identification and developing vaccine against them causing response from immune system has led to cancer prevention. A number of promising new cancer vaccine strategies have entered clinical trials, and we are waiting for them.

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