Assessment of Unwanted Side Effects of Vaccines in Cancer Patients: Where Do We Stand in Vaccination? Where Should Our Next Step Be?

Asli GECGEL[1], Derya KAYA[2], Sevgi EROL[3], Oguzcan OZKAN[1], Tansu YAMAZHAN[2], Erhan GOKMEN[1], Meltem ISIKGOZ TASBAKAN[2]

[1] Ege University Faculty of Medicine, Department of Medical Oncology
[2] Ege University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology
[3] Ege University Faculty of Medicine, Department of Internal Medicine

ABSTRACT

For cancer patients, vaccination against diseases that can be prevented by vaccination is a crucial but often disregarded matter. Our aim was to find out how adult immunization guidelines were being used and to investigate undesirable effects after vaccination. Vaccination status against hepatitis A and hepatitis B virus, tetanus-diphtheria, pneumococcus, influenza and meningococcus of 535 patients with solid organ malignancies who were referred to the Adult Vaccination Polyclinic from oncology outpatient clinic between July 2020 and March 2024 were documented retrospectively. Data collection and statistical analyses were performed with SPSS statistical software version 22.0. The patients' mean age±SD was 56.8±12.3. Of the patients, 329 (61.4%) are women. Breast cancer (n= 184, 34.3%), urogenital cancers (n= 89, 16.6%), and lung cancer (n= 69, 12.8%), are the most prevalent cancers among patients applying for vaccination. Pneumococcal vaccine was the most frequently administered vaccine in 515 patients (96.2%), while influenza vaccine was the least frequently administered vaccine in 12 patients (2.2%). Fifty-three (9.9%) patients had grade 1 side effects. Pain at the injection site was the most common side effect and occurred most frequently after tetanus-diphtheria vaccination. Undesirable side effects were more frequent in 7.9% (n= 42) of patients who were under treatment (p= 0.016). However, no significant relationship was found between age, sex, the disease stage and the types of treatment received and the incidence of side effects (p> 0.05). None of the participants experienced any moderate or serious post-vaccination side effects serious enough to require medical attention. Although the pneumococcal vaccination rates in our study are greater than to the literature, the application rate of other vaccines, especially influenza vaccine, is low according to current guidelines. Increased awareness of this issue among oncology physicians is suggested by the fact that about 1/5 of patients were referred to vaccination outpatient clinics. This study is extremely valuable in demonstrating to oncology physicians the rarity of vaccine side effects.

Keywords: Vaccination, Immunization, Cancer patient, Solid tumor, Post-vaccination unsiderable effect

INTRODUCTION

As the number of cancer diagnoses rises and more patients experience compromised immune systems, infection prevention becomes increasingly important.[1] Vaccination is regarded as one of the most significant advancements in public health. The incidence of vaccine-preventable diseases has grown because patients with solid organ cancers have greater immune system suppression as a result of treatments including chemotherapy, radiation therapy, and corticosteroid use.[2] It is well known that during intensive anticancer therapy, antibody titers for vaccine-preventable diseases decline even in immunized patients.[3] By decreasing the incidence and severity of illness and avoiding the interruption of anticancer therapy, vaccinations can assist these patients experience a decrease in morbidity and mortality from vaccine-preventable infections. Patients receiving cancer therapy should be evaluated for age- and indication-appropriate vaccinations, and the responsibility for administering these vaccines should be shared between the oncologist and the primary care provider.

Especially after Corona virus disease (COVID) vaccines, prejudice against vaccines has developed in the society. At the same time, oncology patients are a more specialized group and making decisions about vaccination can sometimes be difficult for both the physician and the patient. The decline in vaccination rates and the rise in the likelihood of vaccine-preventable disease outbreaks and epidemics are thought to be caused by vaccine hesitancy. The refusal of a sizable percentage of healthcare personnel to get the flu vaccine despite strong advice to do so and the availability of free vaccines at work in many countries serves as another excellent example of vaccine hesitation among experts.[4] Data from the Behavioral Risk Factor Surveillance System found that 42% of cancer survivors did not receive an influenza vaccination, and 52% reported never receiving a pneumococcal vaccination.[5]

Under the category of immunosuppression, a number of national, international, and local guidelines include vaccination advice for cancer patients. In actuality, immunization rates are extremely low.[6] The belief that immunizations have unsiderable side effects is one of the main causes of vaccination refusal. Despite the fact that symptoms are frequently reported after vaccines, their reasons are not always obvious. While some side effects could be directly related to the vaccination, others might be the result of pre-existing conditions or unintentional symptoms that are mistakenly linked to the vaccines. In a study looking at side effects after pediatric influenza vaccination, parental reporting of side effects was strongly associated with pre-vaccination expectation of side effects, and perceived side effects reduced future intention to vaccinate.[7] In any immunocompromised patient, live attenuated viral vaccines have the potential to cause disease; however, inactivated vaccines can be safely administered. All non-live vaccines can be administered safely to persons with altered immunocompetence, whether the vaccine is a killed whole-organism or a recombinant, subunit, split-virus, toxoid, polysaccharide, or polysaccharide protein-conjugate vaccine.[7] Vaccine-preventable diseases such as influenza, pneumococcal disease or herpes zoster have the highest incidence and severity in older adults due to comorbidities and immunosenescence, but may also need to be administered to younger populations with immunosuppressed cancer diagnoses.[8,9] According to National Comprehensive Cancer Network (NCCN) guidelines; Hemophilus influenza b (Hib), hepatitis A and B, tetanus, diphtheria, and acellular pertussis (dTP), human papilloma virus (HPV), pneumococcal, meningococcal, and influenza vaccinations are advised for cancer patients.[10] Although guidelines may offer general recommendations for immunization schedules, each vaccine's safety and effectiveness should be assessed to determine how best to customize the plan for each individual.

Antigen-derived vaccinations have the potential to provide protection, even if that protection is limited in immunocompromised patients. Nevertheless, any protection is preferable to none at all if the vaccine is withheld. The recommended vaccinations should ideally be given before cancer treatment begins to achieve the best possible protection before a patient's immune system is affected by cancer treatment.[11] Influenza, Respiratory Syncytial Virus (RSV) and COVID-19 vaccines should be received before the temporal regional spread of these viruses. Programs that implement routine assessment of vaccine status during the fall-winter season provide a critical opportunity to engage, educate and improve vaccine access and use. Seasonal vaccinations can be given concurrently with chemotherapy, immunotherapy or radiation therapy. Changing the timing of influenza vaccination to avoid vaccination during treatment or with cytopenias is not recommended and may result in missed vaccination opportunities with no clear benefit. Cytotoxic therapy may decrease the proliferative lymphocyte responses necessary for protective immunity, hence vaccinations shouldn't generally be administered on the same day as the treatment.[12] An individualized vaccination program should be implemented taking into account underlying diseases, age, and treatments administered during vaccination. Undesirable side effects after vaccination is any adverse medical event that occurs after vaccination in a person who has been vaccinated, either as a known vaccine side effect or as a suspected vaccine-related medical event. Common side effects include fever, malaise, myalgia, headache, loss of appetite, which are not specific to any disease symptoms. They can develop

due to vaccination or other causes.[13] Pain, swelling and redness at the injection site can be observed in varying proportions (5-60%) after all vaccines. This reaction is more common with repeated doses of tetanus vaccine. The symptoms usually resolve spontaneously within 24-48 hours. Allergic reactions can occur due to the vaccine antigen or vaccine components such as cell culture material, preservatives, stabilizers or antibiotics used to inhibit bacterial growth. Serious effects such as anaphylaxis can be life-threatening. Anaphylaxis is very rare (0-1 cases per million vaccine doses) in people who are severely allergic to one of the vaccine ingredients.[14] With this study, we think that by presenting data from one of the largest hospitals in the Aegean Region, we will contribute to the literature by providing real-life data on vaccine side effects, which is one of the biggest hesitations about vaccination. We also think that we will raise awareness about vaccination rates and lead to an increase in vaccination rates. Our study's objectives were to assess the real-life immunization status of solid organ cancer patients who applied to the Adult Vaccination Outpatient Clinic of our hospital and to investigate the adverse effects after vaccination.

PATIENTS AND METHODS

This was a retrospective single-center cohort study. Between July 2020 and March 2024, 535 patients with solid organ malignancies who were referred to the Adult Vaccination Polyclinic from the oncology outpatient clinic were included in the study. These patients were selected from those referred to the vaccination outpatient clinic by the oncology outpatient clinic and successfully underwent the vaccination procedure. Hepatitis A virus (HAV), hepatitis B virus (HBV), tetanus-diphtheria (dT), pneumococcal, influenza and meningococcal vaccination statuses of the patients were obtained from the hospital's electronic database. The patients' age, sex, diagnosis, stage and post-vaccination side effects data were analyzed retrospectively. Patients were classified as stage 1 early, stage 2-3 locally advanced and stage 4 metastatic disease. Patients were classified as under treatment or under observation according to their status at the start of vaccination. Oncology patient files and adult vaccination outpatient clinic files were obtained from the hospital electronic data system and vaccine tracking system. In patients receiving systemic treatment, an optimal waiting period of two week was left between the day of vaccination and the day of treatment. However, in patients requiring urgent treatment, inactivated vaccines were administered with an interval between the two courses of treatment or postponed until the end of treatment, taking into account the individual's underlying diseases, age and treatments. No live vaccine was administered in patients receiving treatment. Only inactivated vaccination rates were evaluated in our study.

Side effects written in the vaccine outpatient clinic notebook at the control visit of the patients were recorded as data. Side effects seen in patients were classified using the Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 Grade 1 side effects are classified as mild, grade 2 as moderate and grade 3 and above as serious. Local reactions at the vaccination site (pain, erythema and swelling) was considered grade 1 if asymptomatic and no need for medication. [15] Moderate and serious adverse events after vaccination include persistent fever, cellulitis, ecchymosis and pain at the injection site, gastrointestinal disorders such as vomiting and diarrhea, hypotension, urticaria, uvula edema, development of severe allergic reaction (e.g. anaphylaxis, angioedema) and shortness of breath which requiring hospitalization. Before vaccination, immune system viability and history of allergic reactions to vaccines assessed. All individuals were monitored for immediate vaccine reactions. This period was 15 minutes for patients with no previous history of vaccine reaction, 30 minutes for people who have experienced a vaccine reaction.

Descriptive statistics are expressed as mean±standard deviation, median [minimum (min)-maximum (max)], distribution, and percentage. The Pearson chi-squared test and Fisher's exact probability test were used to analyze the categorical variables. P value < 0.05 was considered statistically significant. Data collection and statistical analyses were performed with SPSS statistical software version 22.0.

Approval fort he study was received from the Ege University Faculty of Medicine ethics committee with application number 2024-2814.

RESULTS

Of the 2455 patients who applied to the oncology outpatient clinic between 2020-2024, 535 patients were referred to the vaccination outpatient clinic and could be vaccinated. The study excluded 105 patients whose data could not be reached. During this time period, 1815 (73.9%) of the 2455 patients who applied to the oncology outpatient clinic and were diagnosed with cancer could not reach the vaccination outpatient clinic and be vaccinated. In this vaccination outpatient clinic immunized 11270 adult patients between 2020 and 2024. Cancer patients make up 21.7% of the total vaccinated patient population. The mean age of the patients was found 56.8 ± 12.3 (mean ± SD), and the median age was 58 (min-max 18-85). Of the patients 329 (61.4%) are women. Breast cancer (n:184, 34.3%), urogenital cancers (n= 89, 16.6%), lung cancer (n: 69, 12.8%), colon cancer (n= 60, 11.2%), and head and neck cancer (n= 35, 6.5%) are the most prevalent cancers among patients applying for vaccination. The distribution of patients according to baseline characteristics is shown in Table 1. Additionally, the distribution of patients according to cancer type shown in the Figure 1. Of the patients, 44 (8.2%) were in early stage, 179 (33.4%) in locally advanced stage and 330 (61.6%) in metastatic stage. Of the 311 (58.1%) patients were on active treatment, the rest were on surveillance. Of the patients, 157 (29.3%) patients were receiving chemotherapy, 55 (10.2%) patients were receiving immunotherapy, 54 (10%) patients were receiving palliative treatment, 45 (8.4%) patients were receiving targeted therapy (tyrosine kinase inhibitors, endocrine therapy, drug-antibody conjugates, etc.). Pneumococcal vaccine was administered to 515 patients (96.2%), dT vaccination to 429 patients (80.1%), hepatitis B vaccination to 304 patients (56.6%), hepatitis A vaccination to 30 patients (5.6%), influenza vaccination to 12 patients (2.2%), and meningococcal vaccine to 44 patients (8.2%). Vaccination rates are shown in Figure 2. Vaccine side effects were learned verbally from the patients during the visit and graded. When side effects were classified according to CTCAE Version 5.0, no patient experienced grade 2 or more side effects. Fifty-three (9.9%) patients had grade 1 side effects. Injection site pain was observed in 29 (5.4%) patients, fatigue in 13 (2.4%) patients, swelling in 7 (1.3%) patients and subfebril fever in 4 (0.7%) patients. No other moderate or serius side effects were reported. Of the 29 patients with injection site pain, 86.2% (n= 25) developed it after tetanus-diphtheria vaccination. These minor side effects developed within 1 week after vaccination, no late side effects were observed Undesirable side effects were more frequent in 7.9% (n= 42) of patients who were under treatment (p= 0.016). The frequency of side effects was numerically greater with increasing disease stage, but there was

Table 1. Baseline characteristics of study population

Variables	n	%
Sex		
Female	329	61.4
Male	206	38.6
Age		
<65	384	71.8
65 and older	151	28.2
Cancer type		
Breast cancer	184	34.3
Urogenital cancers	89	16.6
Lung cancer	69	12.8
Colon cancer	60	11.2
Head and neck cancer	35	6.5
Pancreatic cancer	29	5.4
Gastroesophageal cancer	24	4.4
Bone cancer	13	2.4
Skin cancer	10	1.8
Central nervous system tumors	4	0.7
Other cancers	22	4.1
Disease stage		
Early stage	44	8.2
Locally advanced stage	179	33.4
Metastatic stage	330	61.6
Treatment status		
Under treatment	311	58.1
In surveillance	224	41.8
Treatment type		
Chemotherapy	139	26
Immunotherapy	54	10.1
Palliative therapy	54	10.1
Targeted therapy	47	8.8

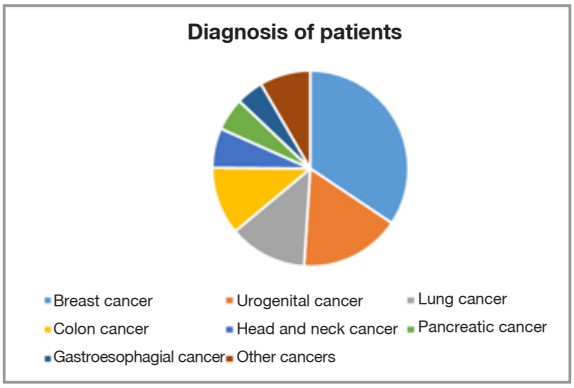

Figure 1. Distribution of patients according to cancer type

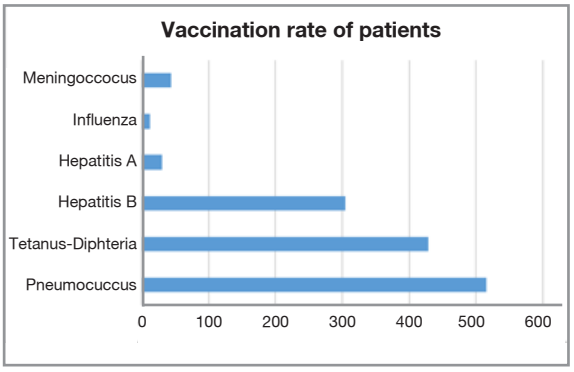

Figure 2. Distribution of vaccines administered in patients with solid organ malignancy

no significant statistical difference between them (p= 0.056). No significant relationship was found between age, sex, the disease stage and the types of treatment received and the incidence of side effects (p> 0.05). The incidence of side effects and the relationship between variables are summarized in Table 2. None of the patients experienced any post-vaccination side effects moderate or serious enough to require medical attention. No immediate vaccine reaction was observed in any patient included in the study.

DISCUSSION

Adult immunization is becoming increasingly crucial due to the rise in chronic illnesses and cancers associated with our nation's aging population to the dawning of a new era.Combined medicines (immunotherapies, chemotherapeutic medications, drug-antibody conjugates, etc.) has enhanced the treatment of many tumors in recent years, increasing the likelihood of better patient outcomes.[1]

Nonetheless, during this time, very few studies on vaccination and immunization have been published.

Table 2. Incidence of side effects and association between variables

		Side effect (+)		Side effect (–)		p
Sex	Female	32	6%	297	55.6%	0.623
	Male	21	3.9%	184	34.5%	
Age	< 65	33	6.2%	350	65.4%	0.113
	65 and older	20	3.7%	132	24.7%	
Disease stage	Early stage	3	0.6%	40	7.5%	0.056
	Locally advanced stage	10	1.9%	160	29.9%	
	Metastatic stage	40	7.5%	282	52.7%	
Teatment status	(–)	14	2.6%	210	39.3%	0.016*
	(+)	39	7.3%	272	50.8%	
Treatment type	Chemotherapy	19	3.6%	120	22.4%	0.067
	Immunotherapy	7	1.3%	47	8.8%	
	Palliative	8	1.5%	46	8.6%	
	Targeted	5	0.9%	42	7.9%	

Immunization recommendations for cancer patients under the category of immunosuppression are provided by a number of international organizations including the NCCN, the United States Advisory Committee on Immunization Practices (ACIP), the Infectious Diseases Society of America (IDSA), and the Centers for Diseases Control and Prevention (CDC).[2,10,16] In our country, the Vaccınatıon Cırcular of the Mınıstry of Health and associatıons related to vaccınatıon make recommendatıons on this issue, such as Infectious Diseases and Clinical Microbiology Specialty Society of Turkey (EKMUD).[17]

Patients with solid tumors are at risk of infection due to weakness, malnutrition and in some cases anatomical obstruction (e.g. lung masses blocking bronchial drainage). Urinary tract infection is more common in patients with at least one comorbidity and immunosuppressant drug use. Parenteral antibiotic therapy and hospitalization should be necessary in this situation. As a result, both the patient's rate of comorbidity and the national economy's costs rise.[18] Compared to the immunocompetent host, this patient population's infections frequently result in excess morbidity and mortality, and antimicrobial therapy is frequently less successful.[3] While immunization seems like an obvious way to prevent infection, many immunocompromised patients are also less likely to mount a protective immune response to active vaccination.[19] Furthermore, attenuated versions of the virus may proliferate uncontrollably as a result of live viral vaccination. Chemotherapy causes both quantitative and qualitative T and B cell depletion, which results in immunodeficiency and lasts for months after treatment is finished.[20] Due to the possibility of vaccine-induced infection, cancer patients undergoing chemotherapy or other immunosuppressive treatments should not get live virus vaccinations. For cancer patients, the inactivated form of a vaccination is recommended when both live and inactivated formulations are available. However, the effectiveness of such vaccinations might be suboptimal in this patient group. For cancer patients, vaccinations are essential, but ideally they shouldn't be administered while the patient is receiving chemotherapy-induced immunosuppression because live vaccines can result in vaccine-induced infections and they may not be effective at this time.[21] Adult cancer patients should have all recommended vaccinations prior to beginning chemotherapy, using other immunosuppressive medication, receiving radiation therapy, or having a splenectomy. Indicated inactivated vaccines should be given ≥ 2 weeks prior to chemotherapy and indicated live virus vaccines should be given ≥4 weeks prior to chemotherapy.[16]

Patients whose disease is in remission, who have not received anti-B cell antibodies (e.g. rituximab, alemtuzumab) and whose chemotherapy has been stopped for at least three months can receive live virus vaccines such as measles, mumps, rubella, chickenpox vaccines and live attenuated zoster vaccine, as well as inactivated vaccines. When patients are receiving potent immunosuppressive medications like fludarabine or anti-B cell antibodies like rituximab or alemtuzumab, the administration of both inactivated and live vaccinations should be postponed for a minimum of six months.[22] If other inactivated vaccines are given during chemotherapy, these should not be considered valid doses unless protective antibodies are documented. Vaccines should be re-administered after immune competence is restored in such patients. Antibody titers to the polio, tetanus, hepatitis B, rubella, mumps, and measles vaccines were measured after chemotherapy in a study by Zignol M, et al., on 192 patients. [19] It was found that the type of vaccine administered affected the rate at which protective antibody titers were lost during chemotherapy. Nintey three percent of individuals who had lost their protective antibody titer responded well to booster vaccination administration. Inactivated vaccinations are underutilized while being typically safe and effective. Unfortunately, vaccination of this patient group is not at the desired level due to physicians' concerns about the safety and efficacy of vaccines in cancer patients and patients' prejudice against vaccines due to adverse effects after vaccination. In a study conducted in France, 92.6% of general practitioners support vaccination. However, only one-third of them reported that they had vaccinated their patients undergoing chemotherapy; The main reason for this was the lack of proper training.[23] In the study by Ding J. et al. 805 cancer patients were

included in the study and vaccine hesitancy was observed in 27.08%. In this study, the mass media accounted for almost 66% of the patients' vaccine knowledge, and the reluctant group's vaccine knowledge was significantly biased. One significant contributing reason to vaccine hesitation was the perception that vaccinations exacerbate tumor prognoses.[24] Fear of side effects can lead to avoidance of vaccination. In a study looking at vaccination rates in the cancer population, pneumococcal vaccination rate was 5.1%, inluenza 28.6% (47% in patients over 65 years of age), HBV vaccination 27.4% in 148 patients.[25]

Vaccination rates in our study were greater than most studies in our country. In our study, of the 2455 patients who applied to the oncology outpatient clinic between 2020-2024, 535 (21.7%) were referred to the vaccination outpatient clinic and could be vaccinated. We believe that this might have happened as a result of the extensive training programs that the adult vaccination outpatient clinic, which was founded before many hospitals in our area, offered to doctors and nurses who worked with immunosuppressive patient groups. In actuality, this outpatient clinic immunized 11270 adult patients between 2020 and 2024. In a study conducted by Akın S. and colleagues, only 9% of 229 patients could be vaccinated after cancer diagnosis.[26] Although pneumococcal (96.2%) and dT (80.1%) vaccinations were high, our influenza (2.2%) vaccinations were very low compared to the literatüre.[25,27,28] We think that the low rate of influenza vaccination in our study was due to the fact that patients received this vaccine in other centers. For vaccine-preventable diseases, the World Health Organization (WHO) aims for immunization coverage rates of ≥ 95% depending on age. For the influenza virus, the immunization rate should be at least 75%.[29] According to guideline recommendations, patients should be advised that influenza vaccine should be repeated annually and dT vaccine should be repeated every 10 years.[10,30]

Patients with solid tumors receiving chemotherapy are at risk for influenza complications. In addition to adjuvant treatments like antiviral medication prophylaxis during influenza A outbreaks, effective protection of the immunocompromised adult may necessitate the use of vaccinations and/or passive immunization (i.e., immune globulin).[31] A comprehensive analysis of 20 nonrandomized serological studies involving patients undergoing chemotherapy for various cancer types revealed that while the patients' antibody response (seroconversion) following influenza vaccination was not as high as that of healthy controls, most patients nonetheless exhibited a timely and protective immune response, independent of chemotherapy schedule, comparable to that of healthy individuals. It has been observed that it can create (i.e. seroprotection).[32] According to a recent research, influenza vaccination reduces mortality and improves infection-related outcomes in immunocompromised persons with cancer.[33] According to the PRISMA trial, among 1778 high-risk adults aged over 65, immunization against the influenza averted 87% of hospital admissions and 78% of deaths.[34] Regretfully, influenza vaccination rates are extremely low despite all recommendations. The fact that COVID vaccinations were prioritized during the COVID-19 pandemic might be one of the causes of this. Furthermore, because of the increased use of masks, vaccination against influenza may not have been necessary because of the possibility of lower influenza transmission. Receiving at least three doses of the COVID-19 vaccination is more protective against severe illness and the requirement for hospitalization than receiving less than two doses, according to a research assessing 403 individuals with COVID-19 PCR-positive solid tumors.[35]

Pneumococcal vaccination rates have significantly increased since clinical vaccine guidelines were put into practice; yet, long-term improvements will need to be made through persistent efforts. Vaccination uptake initiatives for patients 65 years of age and older are worthwhile.[36] In a study conducted by Monier A, et al., despite specific recommendations for immunocompromised patients, anti-pneumococcal and influenza vaccines could only be administered to 47% of patients > 65 years of age.[25] In our country, 13-valent pneumococcal vaccine is administered free of charge to adults in the risk group. 20- or 21-valent vaccines are not yet included in the routine vaccination schedule in our country. However, we think that people in the risk group vaccinated with 13-valent vaccine should

be vaccinated again with 20 or 21-valent vaccine. Adults who have just received a cancer diagnosis and have never received a pneumococcal vaccine ought to receive the PCV20/21 pneumococcal conjugate vaccine. Additional pneumococcal polysaccharide vaccine (PPSV23) is not needed for those receiving PCV20/21, according to the CDC.[10] In contrast to the literature, we administered the influenza vaccination at a very low rate in our study, while having a higher application rate for the pneumococcal vaccine. Although the fact that influenza vaccination is mostly administered by family physicians in our country explains the serious low rate, the vaccination rate is still below optimal. In this specific group of patients diagnosed with solid cancer, receiving treatment or under follow-up, influenza vaccination should be repeated annually. The addition of serogroup B meningococcal vaccine has been recommended for patients at high risk of meningococcal disease. Patients at high risk, such as those with asplenia, persistent Graftnversus host disease (GVHD), complement deficit taking complement C5 inhibitors (e.g., eculizumab, ravulizumab), or any combination of these conditions, should be evaluated for the meningococcal B vaccine. Both the monovalent meningococcal serogroup B vaccine series and the quadrivalent MenACWY vaccine series should be administered to patients.[10] After the vaccination series is finished, patients who are still at risk for meningococcal disease should get a booster dose every five years. In our study, meningococcal vaccination rate was 8.2%. The fact that there are strong recommendations in a limited patient group in the guidelines may explain this low rate. Having a vaccination outpatient clinic in institutions has many benefits such as providing the shortest and most reliable vaccination support to patients in the risk group who are treated and followed up, ensuring the follow-up and control of the vaccination status of patients, contributing to the increase of vaccine awareness and consciousness of non-infectious specialties, and providing a ready infrastructure in cases where emergency vaccination is required, such as during the pandemic period.[17]

Influenza vaccine is obtained in the culture medium of the allontoyis fluid of embryo chicken eggs. The influenza vaccine contains very little egg protein. It has been observed that the rate of reaction to the vaccine in people with egg allergy is the same as in the general population.[37] We did not observe an allergic reaction in any of the patients after the influenza vaccination. Against diphtheria, tetanus and pertussis vaccines containing toxoids hypersensitivity reactions are very rare. Most reports is related to enjection site reactions.[38] In our study, 86.2% of patients experienced pain at the injection site after dT vaccination, which is consistent with the literature. Following vaccination with HBV recombinant vaccine, local reactions (pain, redness, swelling), headache, fever and rarely anaphylaxis have been reported at the injection site.[39] In our study, pain, swelling and subfebrile fever at the injection site were observed in a limited number of patients after HBV vaccination. In a study in which 1,202 participants received both conjugated and polysaccharide pneumococcal vaccines and safety was assessed, the most commonly reported adverse events were injection site pain, fatigue and myalgia, with no serious adverse events.[40] We observed pain and fatigue in a very small number of patients (1.1%, n= 6) who received the conjugated pneumococcal vaccine.

In our study, the incidence of side effects was higher in patients receiving treatment compared to those not receiving treatment, which may have been due to the higher expectation of vaccine side effects in patients receiving treatment. Because more than half of the reported side effects were pain, which is a subjective symptom. The frequency of side effects did not change according to the disease stage and the type of treatment received. None of the side effects were more than grade 1 and did not require treatment. Therefore, we think that inactivated vaccines can be safely administered in this patient group.

The limitations of our study are the possibility of false low vaccination rates in this patient group because we could not follow the vaccination rates administered outside our hospital (family medicine, other hospitals, etc.). Secondly, since this study is single centered and limited in number, it may not be generalizable to the population of Turkey. Thirdly, vaccine side effects may be subjective since they are learned verbally from patients and physical examination cannot be performed.

Conclusion

Oncology patients can safely get the vaccine, as evidenced by the fact that none of our trial participants experienced any moderate or serius side effect following vaccination. Low levels of immunization in this high-risk group may be explained by lack of communication between health care providers and the physician's lack of recommendation. Increasing physician awareness of this concern, especially among oncologists, may lead to a rise in vaccination rates. We think it is critical to establish an institutional vaccine management plan in cancer centers and to expand the database through randomized, observational studies including certain patient demographics and treatment modalities.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68: 394-424, 2018.
2. Rubin LG, Levin JM, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 58: 44-100, 2014.
3. Schreiber RD, Old LJ, and Smyth MJ. Cancer immunoediting: integrating immunity's roles in cancer suppression and promotion. Science 331: 1565-1570, 2011.
4. Hollmeyer HG, Hayden F, Poland G,et al. Influenza vaccination of health care workers in hospitals—a review of studies on attitudes and predictors. Vaccine 27: 3935-3944, 2009.
5. Underwood JM,Townsend JS, Stewart SL, et al. Surveillance of demographic characteristics and health behaviors among adult cancer survivors—Behavioral Risk Factor Surveillance System, United States, 2009. MMWR Surveill Summ 61: 1-23, 2012.
6. Bonanni P, Steffen R, Schelling J, et al., Vaccine co-administration in adults: An effective way to improve vaccination coverage. Hum Vaccin Immunother 19: 2195786, 2023.
7. Smith LE, Weinman J, Amlôt R, et al., Parental expectation of side effects following vaccination is self-fulfilling: a prospective cohort study. Ann Behav Med 53: 267-282, 2019.
8. Vousden N, Bunch K, Knight M. Incidence, risk factors and impact of seasonal influenza in pregnancy: A national cohort study. PLoS One 16: 0244986, 2021.
9. Nasreen S, Wang J, Kwong JC, et al. Population-based incidence of invasive pneumococcal disease in children and adults in Ontario and British Columbia, 2002–2018: a Canadian Immunization Research Network (CIRN) study. Vaccine 39: 7545-7553, 2021.
10. Baden LR, Swaminathan S, Angarone M, et al. Prevention and treatment of cancer-related infections, version 2.2016, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 14: 882-913, 2016.
11. Hall E, Wodi AP, Hamborsky J, et al. Epidemiology and prevention of vaccine-preventable diseases. 14th edition. US Department of Health & Human Services, Centers for Disease Control and Prevention, 2021: 9-37.
12. Sommer AL, Wachel BK, Smith JA. Evaluation of vaccine dosing in patients with solid tumors receiving myelosuppressive chemotherapy. J Oncol Pharm Pract 12: 143-154, 2006.
13. Atay O, Karaman O. Asilamada alerjik reaksiyonlar ve yan etkiler. Alhan E, editor. Çocukluk Çagi Asilari. 1. Baski, Ankara: Türkiye Klinikleri; 2021: 46-54.
14. Chung EH. Vaccine allergies. Clin Exp Vaccine Res 3: 50-57, 2014.
15. Shah SM. Common terminology criteria for adverse events. https://www.uptodate.com/contents/common-terminology-criteria-for-adverse-events (Access date: 06/06/2024).
16. Kroger A, Bahta L, Long S, Sanchez P. CDC- General best practice guidelines for immunization : best practices guidance of the Advisory Committee on Immunization Practices (ACIP). https://stacks.cdc.gov/view/cdc/124166 (Access date: 06/06/2024).
17. Eriskin Bagisiklik Rehberi 2024. Türkiye Enfeksiyon Hastaliklari ve Klinik Mikrobiyoloji Uzmanlik Dernegi. 1. Baski, Ankara: Bilimsel Tip Yayinevi; 2024:18-80.
18. Ozbay BO, Bastug A, Oksuz E, Bodur H. Safety, efficacy and direct/indirect cost analysis of an outpatient antimicrobial therapy unit: A prospective cohort study from Turkey. Mediterr J Infect Microb Antimicrob 12: 16-26, 2023.
19. Zignol M, Peracchi M, Tridello G, et al. Assessment of humoral immunity to poliomyelitis, tetanus, hepatitis B, measles, rubella, and mumps in children after chemotherapy. Cancer 101: 635-641, 2024.
20. Mackall CL. T-cell immunodeficiency following cytotoxic antineoplastic therapy: a review. Stem cells 18: 10-18, 2000.
21. Teh, B.W. (2021). Vaccination Schedules. In: Cornely OA, Hoenigl M. (eds) Infection Management in Hematology. Hematologic Malignancies. Springer, Cham. 2021: 77-105.
22. Pierron A, Bozon F, Berceanu A, et al., Vaccination coverage in hematological patients undergoing chemotherapy: Should we move towards personalized vaccination? Vaccine 39: 7036-7043, 2021.
23. Glavier M, Puyade M, Roblot F, Rammaert B. Vaccination of cancer patients treated with chemotherapy: a survey among general practitioners. Med Mal Infect 49: 586-592, 2019.
24. Ding J, Liu XC, Hong J, et al. Knowledge about, attitudes toward and acceptance and predictors of intention to receive the mpox vaccine among cancer patients in China: A cross-sectional survey. Huma Hum Vaccin Immunother 20: 2337157, 2024.

25. Monier A, Puyade M, Hernanz MPG, et al. Observational study of vaccination in cancer patients: How can vaccine coverage be improved? Med Mal Infect 50(3): 263-268, 2020.

26. Akin S, Dizdar O, Ozisik L, et al. Vaccination attitudes among patients with cancer receiving chemotherapy. Int J Hematol Oncol 26: 167-172, 2016.

27. Loubet P, Kernéis S, Groh M, et al. Attitude, knowledge and factors associated with influenza and pneumococcal vaccine uptake in a large cohort of patients with secondary immune deficiency. Vaccine 33: 3703-3708, 2015.

28. Loulergue P, Mir O, Alexandre J, et al. Low influenza vaccination rate among patients receiving chemotherapy for cancer. Ann Oncol 19: 1658, 2008.

29. Bonanni P, Faivre P, Lopalco PL, et al. The status of human papillomavirus vaccination recommendation, funding, and coverage in WHO Europe countries (2018–2019). Expert Rev Vaccines 19: 1073-1083, 2020.

30. Wilson BJ, Zitella LJ, Erb CH, et al. Prevention of Infection. Clin J Oncol Nurs 22: 157-168, 2018.

31. Kutlay DY, TanrÞöver MD. Do we still need to vaccinate patients against flu after the flu infection? Mediterr J Infect Microb Antimicrob 13: 14-14, 2024.

32. Vollaard A, Schreuder I, Slok-Raijmakers L, et al. Influenza vaccination in adult patients with solid tumours treated with chemotherapy. Eur J Cancer 76: 134-143, 2017.

33. Bitterman R, Eliakim-Raz N, Vinograd I, et al. Influenza vaccines in immunosuppressed adults with cancer. Cochrane Database Syst Rev 2(2): CD008983, 2018.

34. Hak E, Buskens E, Van Essen GA, et al. Clinical effectiveness of influenza vaccination in persons younger than 65 years with high-risk medical conditions: the PRISMA study. Arch Intern Med 165: 274-280, 2005.

35. Iskender G, Mert D, Yapar Toros G, et al. COVID-19 in cancer patients: patient characteristics and outcomes in the post-COVID-19 vaccination period. Turk J Med Sci 53: 1744-1755, 2023.

36. Sever SO, Ozturk GZ. Evaluation of relationship between conjugated pneumococcal vaccine (PCV13) and respiratory tract infection frequency in inviduals aged sixty five and over. Flora J Infect Dis Clin Microbiol 28: 613-620, 2023.

37. Des Roches A, Paradis L, Gagnon R, et al. Egg-allergic patients can be safely vaccinated against influenza. J Allergy Clin Immunol 130(5): 1213-1216.e1. 2012.

38. Jackson LA, Yu O, Nelson JC, et al. Injection site and risk of medically attended local reactions to acellular pertussis vaccine. Pediatrics 127(3): e581-e587, 2011.

39. Echeverría-Zudaire LA, Ortigosa-del Castillo L, Alonso-Lebrero E, et al. Consensus document on the approach to children with allergic reactions after vaccination or allergy to vaccine components. Allergol Immunopathol 43: 304-325, 2015.

40. Platt HL, Cardona JF, Haranaka M, et al. A phase 3 trial of safety, tolerability, and immunogenicity of V114, 15-valent pneumococcal conjugate vaccine, compared with 13-valent pneumococcal conjugate vaccine in adults 50 years of age and older (PNEU-AGE). Vaccine 40: 162-172, 2022.

Correspondence:

Dr. Meltem TASBAKAN

Ege Universitesi Tip Fakultesi
Enfeksiyon Hastaliklari ve Klinik Mikrobiyoloji
Anabilim Dali
Bornova
IZMIR / TURKIYE

Tel: (+90-530) 875 93 24

e-mail: tasbakan@yahoo.com

ORCIDs:

Asli Gecgel	0000-0001-6942-9858
Derya Kaya	0009-0000-6675-1198
Sevgi Erol	0009-0009-2485-3140
Oguzcan Ozkan	0000-0002-4075-7775
Tansu Yamazhan	0000-0001-5950-0702
Erhan Gokmen	0000-0003-4596-2986
Meltem Tasbakan	0000-0002-4689-720X