Original Article

Assessment of Influenza Vaccine Immunogenicity in Immunocompromized Host During 2009 Influenza Season: A Single Institution Experience

Dong Hwan Kim, M.D., Bong Sup Song, M.D., Jun Ah Lee, M.D., and Dong Ho Kim, M.D.

Department of Pediatrics, Korea Cancer Center Hospital, Seoul, Republic of Korea

Purpose : Although influenza is regarded as one of the major causes of morbidity and mortality in children with cancer, the actual vaccine coverage remains poor. We conducted evaluation of immunogenicity and safety of influenza vaccine in children with cancer.

Methods : In this study, 25 children with cancer who received influenza vaccine (SK influenza IX vaccine®) at the Korea Cancer Center Hospital between October and December 2009 were analyzed. Blood samples of patients were collected twice (at the beginning of this study and at 30th day after vaccination) and their antibody titers were measured using the hemagglutination-inhibition (HI) assay. Immunogenicity of the influenza vaccine was assessed by seroprotection rate on days 0 and 30, seroconversion rate on day 30, and mean fold increase (MFI) of geometric mean titer (GMT) of HI between days 0 and 30.

Results : Any of the subjects in our study did not experienced serious adverse events after influenza vaccination. Seroprotection rates were 68% for H1N1, 40% for H3N2, and 36% for B. Seroconversion rates were 12% for H1N1, 16% for H3N2, and 20% for B. MFIs were 0.9 for H1N1, 1.2 for H3N2, and 1.8 for B.

Conclusion : In the study, we found a limited protective immune response to influenza vaccine, among subjects with cancer. However, some subjects showed seroconversion, and there were no severe adverse events among all subjects, supporting the recommendation of annual influenza vaccination in children with cancer. **(Korean J Pediatr Infect Dis 2012;19:1-11)**

Key Words : Influenza vaccine, Childhood cancer, Immunogenicity

Introduction

Influenza is a common cause of respiratory tract infection during the epidemic season. Influenza has a significant clinical impact on immunocompromised hosts such as children with cancer, possibly leading to severe complications. In particular, hematopoietic stem cell transplantation patients and chemotherapy patients for leukemia show a meaningful mortality rate and high morbidity of complications such as pneumonia[1]. Influenza represents a significant socio-economic burden on both the individual and the community. Although influenza vaccine annually shows different immunogenicity, it has been acknowledged that influenza vaccine can reduce morbidity and disease severity. In spite of weaker immunogenicity compared with the healthy population, influenza vaccine is recommended to immunocompromised hosts for prevention of a severe course or superimposed bacterial infections[2-5].

In Korea, the administration of influenza vaccine to children with cancer is recommended prior to the

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Correspondence : Dong Ho Kim, M.D.
Department of Pediatrics, Korea Cancer Center Hospital, Seoul, Republic of Korea
Tel : +82-2-970-1298, Fax : +82-2-6008-5748
E-mail : kdh281920@gmail.com

beginning of the winter season. However, the medical survey for vaccine coverage has not been conducted, and it is also supposed that the actual vaccine coverage remains poor in children with cancer. In the other countries, vaccine coverage remains poor in high risk patients[6-9]. Loulergue et al. reported that the main reasons for the absence of vaccination included lack of incitation by the treating physician (72%), fear of side-effects (33%), and concerns regarding vaccination efficacy (10%)[9]. Among the medical oncologists, the leading self-reported reason for the absence of vaccination was the lack of awareness of recommendations[9]. There was also a concern regarding the efficacy of influenza vaccination in immunocompromised patients[9]. The aim of this study was to evaluate influenza vaccine immunogenicity in children with cancer on the basis of a single institute experience at the Korea Cancer Center Hospital (KCCH), and to offer a reference for immunization guidelines in this population.

Materials and methods

1. Study design

Enrollment was conducted at KCCH from October 2009 to December 2009. Children and adolescents with cancer were included in this study. Also, we included adults diagnosed with childhood tumor. We enrolled children receiving chemotherapy or children within 24 months after off-treatment to assess the difference of effect for immunogenicity with respect to chemotherapy protocol and duration after chemotherapy. Subjects who showed severe allergy to influenza vaccine or egg protein, or acute febrile illness at the time of vaccination were excluded. Subjects who had received chemotherapy within 2 weeks or with neutrophil count below 1,000 were excluded.

For the evaluation of immediate local or systemic reactions, all subjects were observed for 30 minutes following vaccine administration. All subjects (of their guardians) were educated to report any serious adverse events occurring between vaccination day (day 0) and the 30th day of post-vaccination (day 30).

On day 0 and day 30 after vaccination, 5 mL of venous blood samples were obtained from all subjects. On day 30 after vaccination, all subjects reported any adverse events. Subjects were excluded from the immunogenicity analysis if there were found to be non-compliant with the immunization or blood sampling schedule. The protocol was approved by the Institutional Review Board (IRB) of KCCH, and the written informed consent was obtained from all participants or their parents prior to the participation of this study.

2. Vaccine

Trivalent split influenza vaccine was used for the study: SK influenza IX vaccine® (Trivalent split influenza vaccine). The vaccine 0.5 mL contain 15 μg of A/Brisbane/59/2007 IVR-148 (H1N1), 15 μg of A/Uruguay/716/2007 NYMCX-175C (H3N2), and 15 μg of B/Brisbane/60/2008. The vaccine was administered by intramuscular injection in the deltoid muscle or in the upper lateral thigh with a single dose or 2 doses (for unprimed subjects under 9 years with 1 month interval) of either 0.25 mL (for those 6 to 35 months of age) or 0.5 mL (for those above 36 months of age).

3. Antibody studies

The haemagglutination inhibition test (HI test) was performed for the determination of anti-haemagglutinin antibody titers. Anti-haemagglutinin titers to H1N1, H3N2, and B were measured by A/Brisbane/59/2007 IVR-148 (H1N1), A/Uruguay/716/2007 NYMCX-175C (H3N2), and B/Brisbane/60/2008, respectively.

4. Immunogenicity assessment

Seroprotection was defined as an anti-HI titer ≥1:40. Seroconversion was defined as a change from a baseline titer <1:10 to a post-vaccination titer ≥1:40 or a 4-fold or greater rise in titer in those with an initial HI titer ≥1:10. Immunogenicity of the vaccine was assessed based on these findings: ① seroprotection rate on days 0 and 30, ② seroconversion rate on day 30, ③ mean fold increase (MFI) of geometric mean titer (GMT) of HI between days 0 and 30.

In order to confirm protective immunogenicity of vaccine based on the European Medicines Agency (EMEA) criteria, one of the following criteria must be met: seroprotection rate >70%, seroconversion rate >40%, or MFI >2.5.

5. Statistical analysis

SPSS for windows (version 17.0) was used for performance of all analyses. Student T-test, one-way ANOVA, Kruskal-Wallis test, Tukey-b test and Levene's test were used to assess the immunogenicity of the vaccine.

Results

1. Characteristics of study subjects

Twenty five patients at KCCH were enrolled in this study between October and December 2009. Twenty patients were diagnosed with a solid tumor, and 5 patients were diagnosed with ALL. Twenty patients with solid tumor included 10 patients with osteosarcoma, 8 patients with Ewing sarcoma, and 2 patients with synovial sarcoma. Five patients of solid tumor had undergone high dose chemotherapy (HDCT) and stem cell transplantation (SCT). Among subjects of solid tumor, two adults diagnosed with osteosarcoma were enrolled. Ten patients were receiving chemotherapy while the other 15 had completed chemotherapy. Mean age of patients was 13 years old (median 13, range 5-21 years). The ratio of male to female was 18/7. Table 1 shows the characteristics of the patients.

2. Immunogenicity in overall patients

Prior to the vaccination, 72% (18), 32% (8), and 24% (6) of patients showed seroprotection (an antibody titer of 1:40 or more) against H1N1, H3N2, and B. After the vaccination, 68% (17), 40% (10), and 36% (9) of patients showed seroprotection against H1N1, H3N2, and B. Seroconversion was showed in 12% (3), 16% (4), and 20% (5) of patients against H1N1, H3N2, and B. MFI was 0.9, 1.2, and 1.8 against H1N1, H3N2, and B. In the consideration of seroprotection rate, the influenza vaccine was unsuitable for EMEA criteria against H1N1, H3N2 and B, but seroprotection rate was increased against H3N2 and B. In a view of seroconversion,

some patients showed seroconversion against H1N1, H3N2 and B, although influenza vaccine was unsuitable for EMEA criteria against H1N1, H3N2 and B (Fig. 1).

3. Immunogenicity according to the different types of malignancy

For the assessment of different effects for the immunogenicity with respect to types of malignancy, children and adolescents with cancers were divided into 4 groups (ALL, osteosarcoma, Ewing sarcoma, and synovial sarcoma). In a view of seroprotection rate, patients with osteosarcoma showed a protective immune response against H1N1 (post seroprotection rate 80%). Patients with the other types of malignancy showed a limited immune response against H1N1. However, there was no significant difference in the immune response according to the different types of malignancy.

Against H3N2 and B, a limited immune response was shown, and there was no significant difference in the immune response according to the different types of malignancy.

In a view of seroconversion, seroconversion was shown against each antigen although it was not suitable for EMEA criteria. However, there was no significant difference in immune response according to the different types of malignancy.

In a view of MFI, a limited immune response was shown against each antigen. Table 2, 3, and 4 show the immunogenicity according to the different types of malignancy responding to influenza vaccination.

Table 1. Patients Characteristics

Characteristics	
No. of patients	25
Age (year; mean/median/range)	13/13/5-21
Sex (male/female)	18/7
Type of malignancy	
Osteosarcoma	10
Ewing sarcoma	8
Synovial sarcoma	2
ALL	5
Chemotherapy protocol	
Two drugs*	5
Three drugs†	6
Recurrence‡	4
ALL protocol∫	5
High dose chemotherapy with stem cell rescue‖	5
Time after off treatment	
On treatment	10
<12 months	10
12-24 months	5

*two drugs: cisplatin and adriamycin
†three drugs: ifosfamide, adriamycin and etoposide or ifosfamide, adriamycin and dacarbazine
‡recurrence: cyclophosphamide and topotecan
∫ALL protocol: prednisolone, vincristine, daunorubicin, L-asparaginase, cytarabine and methotrexate
‖HDCT: carboplatin, thiotepa and etoposide or ifosfamide, cyclophosphamide and etoposide
Abbreviation: ALL, acute lymphoblastic leukemia

4. Immunogenicity according to different chemotherapy protocol

For the assessment of different effects for immunogenicity with respect to different chemotherapy protocol, children and adolescents with cancers were divided into 5 groups [two drugs (cisplatin and adriamycin, 6 cycles), three drugs (ifosfamide, adriamycin and etoposide, 6 cycles, or ifosfamide, adriamycin and dacarbazine, 6 cycles), recurrence protocol (cyclophosphamide and topotecan, 6 cycles), ALL protocol (prednisolone, vincristine, daunorubicin, L-asparaginase, cytarabine and methotrexate, induction, 4 weeks) and HDCT (carboplatin, thiotepa and etoposide or ifosfamide, cyclophosphamide and etoposide)]. However, the difference of chemotherapy protocol did not show a significant effect in immune response to each influenza antigens. Table

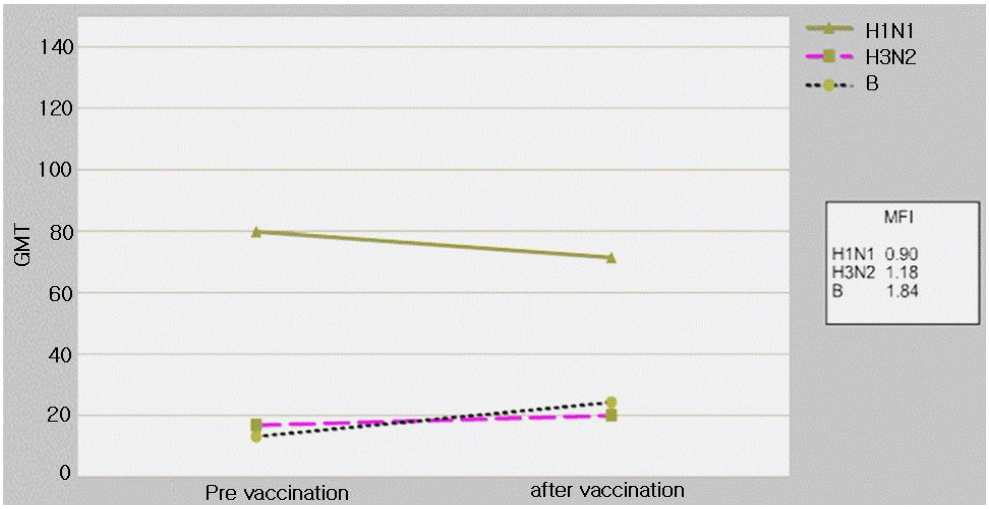

Fig. 1. MFI of GMT against each influenza antigen. Abbreviations : MFI, mean fold increase; GMT, geometric mean titer.

Table 2. Immunogenicity against H1N1

Characteristics	n	Pre seroprotection		Post seroprotection		Seroconversion	
		% (95% C.I.)	*P*-value	% (95% C.I.)	*P*-value	% (95% C.I.)	*P*-value
Total	25	72 (53-91)		68 (48-88)		12 (0-26)	
Type of cancer							
Osteosarcoma	10	70 (35-100)	0.656	80 (50-100)	0.784	20 (0-50)	0.563
Ewing sarcoma	8	88 (58-100)		63 (19-100)		0	
Synovial sarcoma	2	50 (0-100)		50 (0-100)		0	
ALL	5	60 (0-100)		60 (0-100)		20 (0-76)	
Chemotherapy protocol							
Two drugs*	5	100	0.455	100	0.399	0	0.091
Three drugs†	6	83 (40-100)		67 (12-100)		0	
Recurrence‡	4	50 (0-100)		75 (0-100)		50 (0-100)	
ALL protocol∫	5	60 (0-100)		60 (0-100)		20 (0-76)	
HDCT‖	5	60 (0-100)		40 (0-100)		0	
Time after off treatment							
On treatment	10	80 (50-100)	0.734	70 (35-100)	0.751	0	0.350
〈12 months	10	70 (35-100)		60 (23-97)		20 (0-50)	
≥12 months	5	60 (0-100)		80 (24-100)		20 (0-76)	
WBC							
≤3000/μL	5	60 (0-100)	0.524	40 (0-100)	0.145	0	0.083
〉3000/μL	20	75 (54-96)		75 (54-96)		15 (0-32)	
ALC							
≤500/μL	4	50 (0-100)	0.305	25 (0-100)	0.046	0	0.442
〉500/μL	21	76 (56-96)		76 (56-96)		14 (0-31)	

*two drugs : cisplatin and adriamycin
†three drugs : ifosfamide, adriamycin and etoposide or ifosfamide, adriamycin and dacarbazine
‡recurrence : cyclophosphamide and topotecan
∫ALL protocol : prednisolone, vincristine, daunorubicin, L-asparaginase, cytarabine and methotrexate
‖HDCT : carboplatin, thiotepa and etoposide or ifosfamide, cyclophosphamide and etoposide
Abbreviations : ALL, acute lymphoblastic leukemia; HDCT, high dose chemotherapy; ALC, absolute lymphocyte count

Table 3. Immunogenicity against H3N2

Characteristics	n	Pre seroprotection		Post seroprotection		Seroconversion	
		% (95% C.I.)	*P*-value	% (95% C.I.)	*P*-value	% (95% C.I.)	*P*-value
Total	25	32 (12-52)		40 (19-61)		16 (1-31)	
Type of cancer							
Osteosarcoma	10	30 (0-65)	0.905	50 (12-88)	0.777	20(0-50)	0.908
Ewing sarcoma	8	25 (0-64)		25 (0-64)		13 (0-42)	
Synovial sarcoma	2	50 (0-100)		50 (0-100)		0	
ALL	5	40 (0-100)		40 (0-100)		20(0-76)	
Chemotherapy protocol							
Two drugs*	5	60 (0-100)	0.431	80 (24-100)	0.365	20 (0-76)	0.889
Three drugs†	6	33 (0-88)		33 (0-88)		17 (0-60)	
Recurrence‡	4	0		25 (0-100)		25 (0-100)	
ALL protocol∫	5	40 (0-100)		40 (0-100)		20 (0-76)	
HDCT‖	5	20 (0-76)		20 (0-76)		0	
Time after off treatment							
On treatment	10	40 (3-77)	0.609	40 (3-77)	0.569	10 (0-33)	0.287
〈12 months	10	20 (0-50)		30 (0-65)		10 (0-33)	
≥12 months	5	40 (0-100)		60 (0-100)		40 (0-100)	
WBC							
≤3,000/μL	5	40 (0-100)	0.684	20 (0-76)	0.314	0	0.042
〉3,000/μL	20	30 (8-52)		45 (21-69)		20 (1-39)	
ALC							
≤500/μL	4	25 (0-100)	0.756	0	〈0.001	0	0.042
〉500/μL	21	33 (11-55)		48 (24-71)		19 (1-37)	

*two drugs : cisplatin and adriamycin
†three drugs : ifosfamide, adriamycin and etoposide or ifosfamide, adriamycin and dacarbazine
‡recurrence : cyclophosphamide and topotecan
∫ALL protocol : prednisolone, vincristine, daunorubicin, L-asparaginase, cytarabine and methotrexate
‖HDCT : carboplatin, thiotepa and etoposide or ifosfamide, cyclophosphamide and etoposide
Abbreviations) ALL; acute lymphoblastic leukemia, HDCT; high dose chemotherapy, ALC; absolute lymphocyte count

2, 3, and 4 show the immunogenicity according to the different protocols of chemotherapy responding to influenza vaccination.

5. Immunogenicity in the different chemotherapy status

For the assessment of different effects for immunogenicity with respect to the different chemotherapy status, children and adolescents with cancers were divided into 3 groups (patients with receiving chemotherapy, patients within 12 months after off-treatment, and patients over 12 months after off-treatment). However, the difference of chemotherapy status did not show a significant effect in immune response to each influenza antigens. Only in the analysis of seroconversion rate, patients over 12 months after off-treatment showed significantly higher seroconversion rate compared with patients receiving chemotherapy against B antigen. Table 2, 3, and 4 show the immunogenicity according to the difference of chemotherapy status responding to influenza vaccination.

6. Immunogenicity in the different immune states

Patients with any lymphocyte count showed a limited immune response against H1N1, H3N2, and B.

Table 4. Immunogenicity against B

Characteristics	n	Pre seroprotection		Post seroprotection		Seroconversion	
		% (95% C.I.)	*P*-value	% (95% C.I.)	*P*-value	% (95% C.I.)	*P*-value
Total	25	24 (6-42)		36 (16-56)		20 (3-37)	
Type of cancer							
Osteosarcoma	10	30 (0-65)	0.515	40 (3-77)	0.532	20 (0-50)	0.909
Ewing sarcoma	8	25 (0-64)		50 (5-95)		25 (0-64)	
Synovial sarcoma	2	50 (0-100)		0		0	
ALL	5	0		20 (0-76)		20 (0-76)	
Chemotherapy protocol							
Two drugs*	5	40 (0-100)	0.586	60 (0-100)	0.420	40 (0-100)	0.773
Three drugs†	6	17 (0-60)		17 (0-60)		17 (0-60)	
Recurrence‡	4	25 (0-100)		25 (0-100)		0	
ALL protocol∫	5	0		20 (0-76)		20 (0-76)	
HDCT‖	5	40 (0-100)		60 (0-100)		20 (0-76)	
Time after off treatment							
On treatment	10	20 (0-50)	0.864	20 (0-50)	0.325	0	0.020
〈12 months	10	30 (0-65)		40 (0-77)		20 (0-50)	
≥12 months	5	20 (0-76)		60 (0-100)		60 (0-100)	
WBC	25						
≤3,000/μL	5	20 (0-76)	0.824	20 (0-76)	0.413	0	0.021
〉3,000/μL	20	25 (4-46)		40 (16-64)		25 (4-46)	
ALC	25						
≤500/μL	4	0	0.010	0	0.001	0	0.021
〉500/μL	21	29 (8-50)		43 (20-66)		24 (4-44)	

*two drugs : cisplatin and adriamycin
†three drugs : ifosfamide, adriamycin and etoposide or ifosfamide, adriamycin and dacarbazine
‡recurrence : cyclophosphamide and topotecan
∫ALL protocol : prednisolone, vincristine, daunorubicin, L-asparaginase, cytarabine and methotrexate
‖HDCT : carboplatin, thiotepa and etoposide or ifosfamide, cyclophosphamide and etoposide
Abbreviations : ALL, acute lymphoblastic leukemia; HDCT, high dose chemotherapy; ALC; absolute lymphocyte count

However, patients with lymphocyte count >500/μL at immunization showed a significantly stronger immune response than patients with lymphocyte count ≤500/μL against H1N1, H3N2, and B. Although the EMEA criteria was not met, some patients with lymphocyte count >500/μL showed seroconversion against each antigen.

Patients with leucopenia (white blood cell count ≤3,000/μL) at immunization showed a somewhat weaker immune response against H1N1, H3N2, and B than patients with WBC count >3,000/μL, but the difference was partially reliable in statistics.

Neutrophil count did not affect a significant effect in immune response to influenza antigen. Table 2, 3, and 4 show the immunogenicity according to the different WBC and lymphocyte count responding to influenza vaccination (Fig 2).

7. Vaccine adverse effects

On day 30 after vaccination, any adverse events were reported from all participants or their parents. Reported side effects included some local adverse reactions. However, serious adverse events including Guillain-Barre syndrome were not reported. Overall, the vaccine was well tolerated in all subjects.

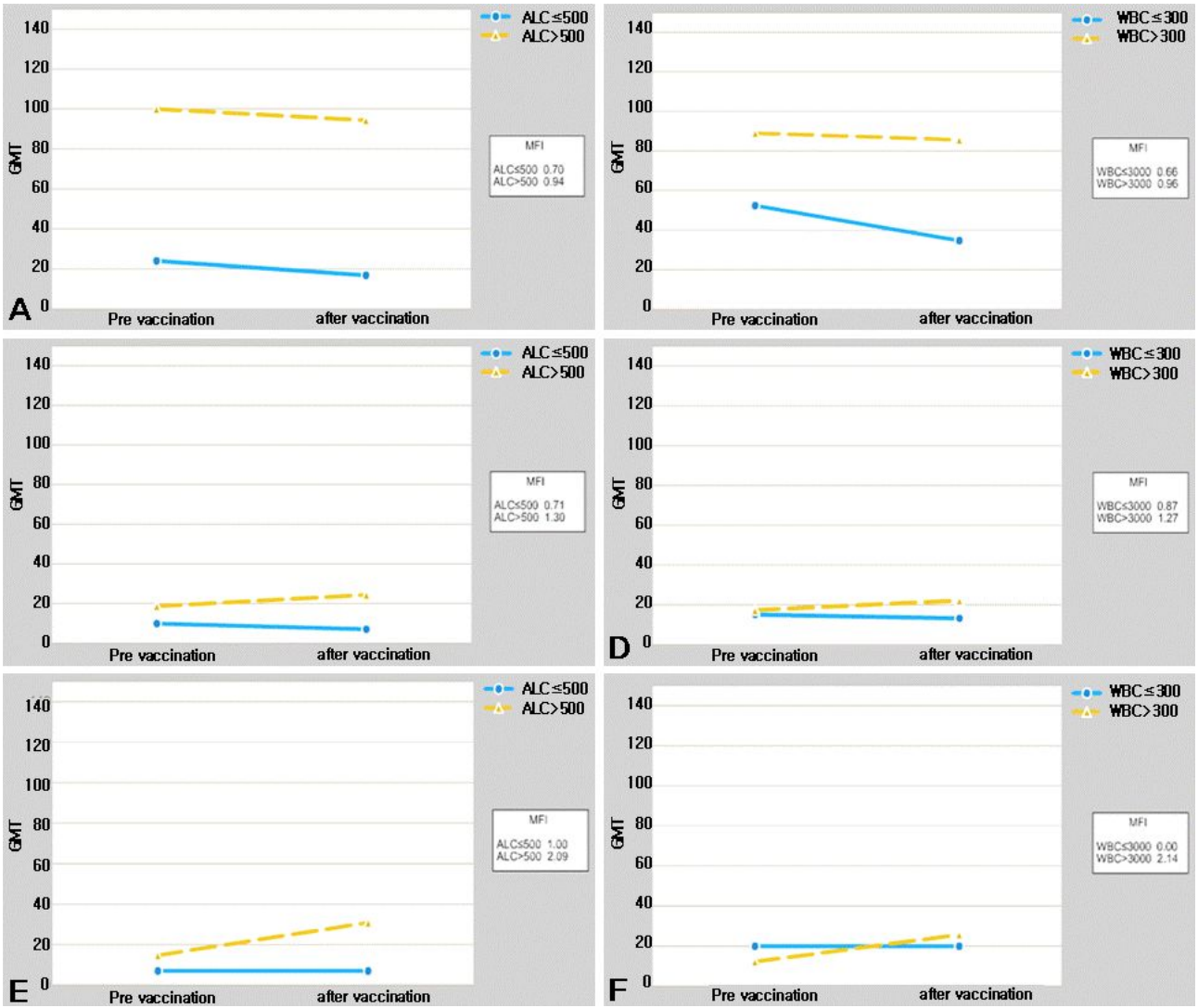

Fig. 2. MFI of GMT against each influenza antigen according to different immune state. (A) MFI of GMT against H1N1 antigen according to ALC count (MFI; ALC ≤500/μL: 0.70, ALC >500/μL: 0.94). (B) MFI of GMT against H1N1 antigen according to WBC count (MFI; WBC ≤3,000/μL: 0.66, WBC >3,000/μL: 0.96). (C) MFI of GMT against H3N2 antigen according to ALC count (MFI; ALC ≤500/μL :0.71, ALC >500/μL: 1.30). (D) MFI of GMT against H3N2 antigen according to WBC count (MFI; WBC ≤3,000/μL: 0.87, WBC >3,000/μL: 1.27). (E) MFI of GMT against B antigen according to ALC count (MFI; ALC ≤500/μL: 1.00, ALC >500/μL: 2.09). (F) MFI of GMT against B antigen according to WBC count (MFI; WBC ≤3,000/μL: 1.00, WBC >3,000/μL: 2.14). Abbreviations: MFI, mean fold increase; GMT, geometric mean titer; ALC, absolute lymphocyte count.

Discussion

This study demonstrated the safety and limited protective immune response of the trivalent inactivated influenza vaccine in children with cancer. The results correspond to other previous studies for immunocompromised patients, including children with cancer[10-12].

In this study, seroprotection rate against H1N1 was higher than those of H3N2 and B. High seroprotection rate against H1N1 was supposed to be

caused by a high pre-seroprotection rate against H1N1. In Korea, a high prevalence of H1N1 influenza was reported during the winter season in 2008[13].

Age, type of malignancy, white blood cell counts, lymphocyte counts, serum IgG level, and status of cancer therapy are well known factors responsible for the immune response after influenza vaccination[14].

Data for the correlation of the immunogenicity of influenza vaccines with white blood cell count or lymphocyte count are often conflicting. Chisholm et al. reported that the response to influenza antigen was not affected by total white blood cell counts at immunization[15]. Other reports have demonstrated a positive correlation of response to influenza antigen with total numbers of circulating lymphocytes or neutrophils on the day of immunization[16]. In this study, lymphocyte count showed a significant correlation with immune response, and white blood cell count showed some correlation with immune response. Lymphocyte count showed a strong positive correlation with response to influenza antigen. White blood cell count also showed a positive correlation with response to influenza antigen, but the correlation was weaker than lymphocyte count. Patients with a lymphocyte count ≤500/μL at immunization showed a significantly weaker immune response against each antigens. Patients with a white blood cell count ≤3,000/μL at immunization showed a somewhat weaker immune response against each antigens, but it was partially reliable in statistics. The better response rate in patients with a lymphocyte count >500/μL or white blood cell count > 3,000/μL is probably related to more B cells and plasma cells than patients with a lymphocyte count ≤500/μL or white blood cell count ≤3,000/μL. Ljungman et al. claimed that patients with poorer antibody-producing capacity and smaller numbers of B cells and plasma cells might be less able to mount an immune response with a lower affinity of antibody[17].

In this study neutrophil count did not affect a response to influenza antigen.

Some reports have demonstrated a better immunogenicity in children with solid tumors than in those with leukemia[15, 16, 18], although the others showed no correlation[10]. In this study, children with solid tumors did not show any difference in immunogenicity compared with those with leukemia.

Ljungman et al. reported lower serological response rates in SCT patients compared with healthy individuals, and they recommended two vaccine doses in children below the age of 9 years old, who have not been previously vaccinated against influenza[17]. In this study, HDCT with SCT did not show any statistically different effect in immunogenicity, and there was no significant difference in immunogenicity according to the different chemotherapy protocols.

Chemotherapy status and time after off-chemotherapy did not have any influence in immunogenicity. However, seroconversion rate against B antigen in patients over 12 months after off-chemotherapy was significantly higher than patients received chemotherapy, and we need more evaluation for this result.

In this study, influenza vaccine showed a limited protective response. Other strategies are needed to reinforce the efficacy of influenza vaccination in children with cancer. Family member vaccination, healthcare worker vaccination, two vaccine doses, and avoidance of immunization at leukopenia or lymphopenia might be suggested. However, further

studies in this respect are needed.

The lack of a control group and precise evaluation for side effects is a limitation of this study. Hence, no comparison could be made with healthy children, and we only partially recognized side effects of vaccine. We only partially recognized the absence of serious side effect in our study group. Small sample sized group is another limitation of this study. Further studies for the immunogenicity of influenza vaccines and strategies to reinforce immunogenicity in the immunocompromised host with a larger sample size and control group are deserved.

Immune response for influenza vaccination was limited. However, some patients showed seroconversion. There were no reported serious side effects, and only immune state at vaccination showed a significant influence in immunogenicity. Therefore, we recommend the annual influenza vaccination to childhood cancer patients with a lymphocyte count >500/μL or white blood cell count >3,000/μL at immunization. However, because of a limited immune response for vaccination, we need some other vaccination strategies in order to reinforce the efficacy of influenza vaccination.

한 글 요 약

면역저하환자에서 인플루엔자백신의 면역원성 평가

한국원자력의학원 소아청소년과

김동환 · 송봉섭 · 이준아 · 김동호

목 적: 인플루엔자는 소아암 환자에게 이환율과 사망률이 높은 질환이나 소아암 환자에 대한 예방 접종률은 낮은 상태이다. 본 연구에서는 소아암 환자를 대상으로 인플루엔자 예방접종의 면역원성과 부작용에 대한 평가를 시행하였다.

방 법: 2009년 10월부터 12월까지 원자력의학원에서 인플루엔자 예방접종(SK influenza IX vaccine®)을 받은 25명의 소아암 환자를 대상으로 연구를 시행했다. 예방접종일과 접종 후 30일 뒤 2회에 걸쳐 채혈하였고 혈구응집억제 항체가를 측정하였다. 백신의 면역원성은 접종 전과 접종 후 30일의 혈구응집억제 항체가 1:40 이상인 피험자 비율, 접종 후 30일의 항체 양전율, 접종 전과 접종 후 30일 사이의 GMT 증가 배수로 평가하였다.

결 과: 본 연구대상자 중에서 심각한 예방접종관련 부작용을 경험한 대상자는 없었다. 접종 후 혈구응집억제 항체가 1:40 이상을 보인 피험자의 비율은 H1N1 항원에 대해 68%, H3N2 항원에 대해 40%, B 항원에 대해 36%였다. 항체 양전율은 H1N1 항원에 대해 12%, H3N2 항원에 대해 16%, B 항원에 대해 20%였다. GMT 증가 배수는 H1N1 항원에 대해 0.9, H3N2 항원에 대해 1.2, B 항원에 대해 1.8이었다.

결 론: 본 연구의 대상자들은 인플루엔자 백신에 대해 제한적인 면역반응을 보였으나 일부 대상자들에게서 항체 양전이 나타났고 심각한 예방접종관련 부작용이 없었던 점을 고려할 때 소아암환자를 대상으로 매년 정기적인 인플루엔자 예방접종이 추천된다.

References

1) Lapinsky SE. H1N1 novel influenza A in pregnant and immunocompromised patients. Crit Care Med 2010;38:e52-7.
2) American Academy of Pediatrics Committee on Infectious Diseases. Prevention of influenza: recommendations for influenza immunization of children, 2008-2009. Pediatrics 2008;122:1135-41.
3) Fiore AE, Shay DK, Broder K, Iskander JK, Uyeki TM, Mootrey G, et al. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2008. MMWR Recomm Rep 2008;57:1-60.
4) Principi N, Esposito S. Are we ready for universal influenza vaccination in paediatrics? Lancet Infect Dis 2004;4:75-

83.
5) Esposito S, Marchisio P, Principi N. The global state of influenza in children. Pediatr Infect Dis J 2008;27: S149-53.
6) Cho BH, Kolasa MS, Messonnier ML. Influenza vaccination coverage rate among high-risk children during the 2002-2003 influenza season. Am J Infect Control 2008; 36:582-7.
7) Nakamura MM, Lee GM. Influenza vaccination in adolescents with high-risk conditions. Pediatrics 2008;122: 920-8.
8) Esposito S, Marchisio P, Droghetti R, Lambertini L, Faelli N, Bosis S, et al. Influenza vaccination coverage among children with high-risk medical conditions. Vaccine 2006;24:5251-5.
9) Loulergue P, Mir O, Alexandre J, Ropert S, Goldwasser F, Launay O. Low influenza vaccination rate among patients receiving chemotherapy for cancer. Ann Oncol 2008;19:1658.
10) Matsuzaki A, Suminoe A, Koga Y, Kinukawa N, Kusuhara K, Hara T. Immune response after influenza vaccination in children with cancer. Pediatr Blood Cancer 2005;45:831-7.
11) Shahgholi E, Ehsani MA, Salamati P, Maysamie A, Sotoudeh K, Mokhtariazad T. Immunogenicity of trivalent influenza vaccine in children with acute lymphoblastic leukemia during maintenance therapy. Pediatr Blood Cancer 2010;54:716-20.
12) Opstelten W, Rimmelzwaan GF, van Essen GA, Bijlsma JW. Influenza vaccination of immunocompromised patients: safe and effective. Ned Tijdschr Geneeskd 2009; 153:A902.
13) Korea Centers for Disease Control and Prevention. Korean Influenza Surveillance Report, 2007-2008. 2011.
14) Schafer AI, Churchill WH, Ames P, Weinstein L. The influence of chemotherapy on response of patients with hematologic malignancies to influenza vaccine. Cancer 1979;43:25-30.
15) Chisholm JC, Devine T, Charlett A, Pinkerton CR, Zambon M. Response to influenza immunisation during treatment for cancer. Arch Dis Child 2001;84:496-500.
16) Gross PA, Lee H, Wolff JA, Hall CB, Minnefore AB, Lazicki ME. Influenza immunization in immunosuppressed children. J Pediatr 1978;92:30-5.
17) Ljungman P, Avetisyan G. Influenza vaccination in hematopoietic SCT recipients. Bone Marrow Transplant 2008;42:637-41.
18) Bektas O, Karadeniz C, Oguz A, Berberoglu S, Yilmaz N, Citak C. Assessment of the immune response to trivalent split influenza vaccine in children with solid tumors. Pediatr Blood Cancer 2007;49:914-7.