

The evaluation of chickenpox in the post-vaccination period in Turkey

Habip Almis, Ibrahim Hakan Bucak, Fedli Emre Kilic, Davut Kayak, Mehmet Geyik, Mehmet Tekin, Capan Konca, Mehmet Turgut

Adiyaman University Faculty of Medicine, Department of Pediatrics, Adiyaman, Turkey

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Abstract

Aim: Chickenpox is a viral infectious disease capable of causing severe morbidity, and even mortality. The purpose of this study was to determine the current position and demographic characteristics of cases of chickenpox following the addition of chickenpox vaccination to the routine vaccine schedule in Turkey.

Material and Methods: Patients aged 0-17 years presented to Adiyaman University Training and Research Hospital Pediatrics clinics and diagnosed with chickenpox between January 2013 and December 2016 were included in the study. Data were analyzed on Statistical Package for the Social Sciences (SPSS, version 22.0, Chicago, IL, USA) software. $p < 0.05$ was regarded as statistically significant.

Results: 314 patients diagnosed with chickenpox were included in the study. Mean age of the subjects included was 84.76 ± 41.67 months, and 54.1% were males and 46.9% females. A significant difference was observed between the groups in terms of age ($p = 0.001$). Cases' ages decreased on a year-by-year basis. Fifty (15.9%) cases of chickenpox were identified as having been infected despite vaccine. A significant difference was determined between the mean ages of vaccinated and non-vaccinated patients with chickenpox.

Conclusion: Although the addition of a single dose chickenpox vaccine to the national immunization schedule in Turkey reduces both severe complication and the incidence of the disease. In the light of our study we think that the addition of a second dose of chickenpox vaccination to our routine vaccine schedule will further reduce hospitalization numbers resulting from chickenpox-related complications. More comprehensive studies on the subject are now needed.

Keywords: Chickenpox; Child; Varicella; Vaccine.

INTRODUCTION

Varicella (chickenpox) is a highly infectious disease involving diffuse vesicular eruptions caused by Varicella Zoster Virus (VZV) primary infection. Non-specific findings, such as listlessness, lack of appetite, headache and sub-febrile body temperature are generally seen in the initial stage. The disease usually resolves in 7-10 days. However, the risk of complications increases with age. There is a broad spectrum of potential complications capable of involving various systems, such as secondary skin infections, otitis media, pneumonia and encephalitis, with the potential to lead to severe morbidity and mortality (1,2).

Varicella vaccine was added to the National Immunization Schedule in Turkey in February 2013 and is administered in a single dose at the end of the 12th month. Single-

dose vaccine provides 97% protection against severe and moderate chickenpox infection; although its level of protection against any degree of severity is lower (80-85%). In other words, children receiving single-dose vaccine can still contract chickenpox infection.

The purpose of this study was to determine the current position by examining age at onset, sex distribution, case numbers requiring hospitalization and demographic characteristics of cases of chickenpox following the addition of chickenpox vaccination to the routine vaccine schedule in Turkey and to identify changes occurring.

MATERIAL and METHODS

Patients aged 0-17 years presented to Adiyaman University Training and Research Hospital Children's Health and Diseases clinics and diagnosed with

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Corresponding Author: Habip Almis, Adiyaman University Faculty of Medicine, Department of Pediatrics, Adiyaman, Turkey

E-mail: drhabipalmis@yahoo.com

chickenpox between January 2013 and December 2016 were included in the study. Groups were established on a year-by-year basis and compared by years by recording sociodemographic data such as age and sex, as well as hospitalization requirements, presence of chronic disease and complications.

Clinical diagnosis of varicella was based on history and the presence of acute onset of a diffuse papulovesicular rash and typical pruritic vesicular eruptions exhibiting polymorphism at physical examination. Ethical approval for the study was granted by the Adiyaman University Medical Faculty Clinical Research Ethical Committee.

Statistical analysis

Data analysis was performed on Statistical Package for the Social Sciences (SPSS, version 22.0, Chicago, IL, USA) software. $p < 0.05$ was regarded as statistically significant. Data were expressed as mean \pm standard deviation (SD) and median values. Since there were more than two study groups, One-Way ANOVA was used to compare means, and Tukey's test when variances were homogeneous post hoc. Tamhane's T test was used when homogeneity was not established. Student's t test was used in the analysis of quantitative data for vaccinated and non-vaccinated

patients when data were normally distributed, and the non-parametric Mann Whitney U test when data were not normally distributed. The chi square test and Fisher's exact chi square test were used to compare qualitative data.

RESULTS

Three hundred fourteen patients diagnosed with chickenpox between 2013 and 2016 were included in the study. Mean age of the cases included was 84.76 ± 41.67 months; 54.1% were male and 46.9% female (Table 1).

The largest number of diagnoses was made in 2015, followed by 2014 and 2016. No statistically significant difference was determined in terms of gender between the groups on a year-by-year basis ($p=0.805$), but a significant difference was observed between the groups in terms of age ($p=0.001$). The most significant difference in terms of age was between the years 2013 and 2016 ($p=0.001$). A significant difference in terms of age among patients diagnosed with chickenpox was determined between the years 2014 and 2016 ($p=0.023$). The chickenpox case group with the highest mean age was the 2013 group, followed by 2014. Cases' ages decreased on a year-by-year basis (Table 1, Figure 1).

Table 1. Demographic characteristics of cases of chickenpox

Year	2013	2014	2015	2016	Total	P value
N	62	75	112	65	314	
Vaccinated	0	0	28	22	50	
Unvaccinated	62	75	84	43	264	
Age (months) (Mean \pm SD)	97.16 \pm 37.92	88.48 \pm 34.21	84.75 \pm 42.89	68.66 \pm 46.36	84.76 \pm 41.67	0.001

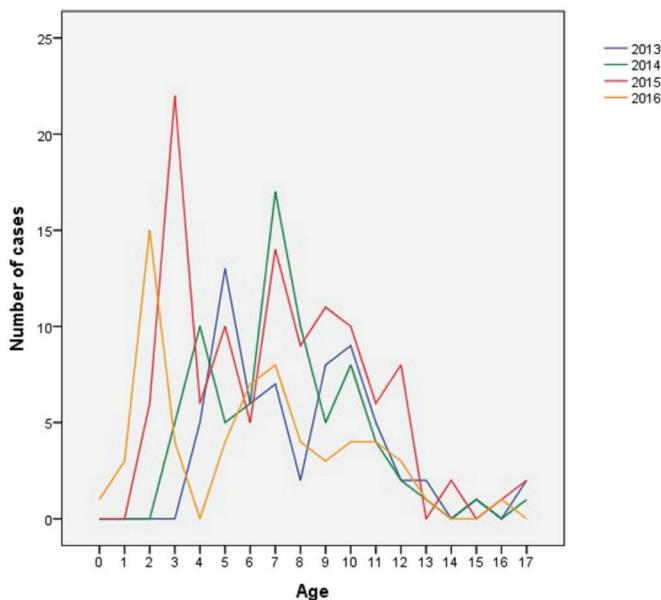


Figure 1. Age variation in varicella cases on a year-by-year basis

Fifty (15.9%) of the total 314 cases in the 4-year study period, 22 of the 65 cases of chickenpox determined in 2016 and 28 of the 112 cases in 2015, experienced infection despite having been vaccinated (Table 1). A

statistically significant difference was determined when the mean ages of the vaccinated and non-vaccinated patients with chickenpox were compared (Table 2).

Table 2. A comparison of the vaccinated and non-vaccinated chickenpox cases in terms of age

	Group	No.	Mean	P value
Age(months) (Mean \pm Standard Deviation)	Vaccinated	50	29.52 \pm 7.35	$p < 0.001$
	Unvaccinated	264	95.22 \pm 36.97	

When the groups were compared on a year-by-year basis, numbers of hospitalizations differed significantly ($p=0.016$). In terms of numbers requiring hospitalization, 26 patients (8 vaccinated subjects) were admitted over the 4-year period, 2 in 2013, 3 in 2014, 10 (4 patients contracted chickenpox despite being vaccinated) in 2015 and 11 (4 patients contracted chickenpox despite being vaccinated) in 2016. The estimated incidence of chickenpox-related admissions was calculated at a mean rate of 3.58/10.000 for our region.

In terms of diagnosis on admission of patients presenting to hospital due to chickenpox, the most common reason for admission was bronchopneumonia at 42%, followed by soft tissue infections at 26%. The level of patients admitted

due to gastroenteritis was 12%, with 8% of patients being admitted due to upper airway infection and urinary tract infection. The least common reason for admission was neurological complications, at 4%. The number of patients admitted after vaccine also increased on an annual basis.

DISCUSSION

The most important finding of our study was the increase in the number of cases of chickenpox as of February 2013, when Varicella vaccine was added to the National Immunization Schedule in Turkey, and that the number of admissions increased initially and then rose on an increasing basis. Age at onset also decreased progressively from the year when the disease was added to the vaccine schedule.

Kurugöl et al. investigated the incidence of chickenpox infection in non-vaccinated children and in children receiving single-dose vaccine in Izmir, Turkey, and reported that the disease developed in 27.7% of vaccinated children (3). Investigation of an outbreak of chickenpox in a nursery school with 144 children aged 6 months to 6 years in Istanbul determined that 6 (8.0%) out of 73 children vaccinated with a single dose developed the disease (4). Similarly, to previous studies, approximately 15.9% of patients in our study developed chickenpox despite having been vaccinated. As in other studies, this is significant in showing that single dose vaccine may not be sufficient. We think that the decrease in the mean age of cases of chickenpox following the addition of vaccination to the routine vaccine schedule is associated with the fact that a second dose was not added to the schedule. A statistically significant difference was determined in terms of age between children contracting chickenpox despite being vaccinated and non-vaccinated subjects ($p < 0.001$). The mean age of the children contracting chickenpox despite having been vaccinated was 29.52 ± 7.35 months.

The World Health Organization recommends the introduction of routine childhood Varicella vaccination and that the first dose should be administered at 12-18 months of age. The number of doses should be determined on the basis of the aims of the immunization. One dose is effective in reducing mortality and morbidity from Varicella, but is not sufficient to prevent limited virus circulation and outbreaks (5).

In the United States of America, two doses are administered for protection against Varicella, the first between the ages of 12 and 18 months and the second between 4 and 6 years (6).

The first of the two doses administered in Germany is administered at 11-14 months, and the second at 15-24 months. Two doses are administered in the Spanish province of Navarra, the first at 15 months and the second at 3 years. Two Varicella vaccinations are performed in Sicily, the first at 15 months and the second at 5 years (7). Since some Varicella vaccines and combine varicella vaccines are reported to increase the risk of febrile

seizures, it has been suggested that the second dose should be given after the age of 18 months (8-14).

Under the National Immunization Schedule in Turkey, Varicella vaccine is administered in a single dose at 12 months. Our study shows that children receiving Varicella vaccination in Turkey can still contract the disease at a mean age of 22-36 months. This may be due to antibody response not being at a good level, or to a gradual decrease over the years in antibody titers.

In a study involving the period 2008-2010, when Varicella vaccine had not yet been added to the routine vaccine schedule, Dinleyici et al. reported an estimated incidence of varicella-related hospitalization of 5.29-6.89 per 100,000 in all children aged 0-15 years of age in Turkey. They also reported that the most common complications requiring hospitalization were secondary bacterial infections, followed by neurological complications, and by respiratory complications in third place (15). Our study determined an estimated incidence of chickenpox-related admissions of 3.58/100,000 for our region. The complications most commonly requiring hospitalization in our study were respiratory complications, followed by secondary bacterial complications. The least common chickenpox complication requiring hospitalization was neurological complications. This was highly significant in showing that single-dose vaccine may have reduced the incidence of hospitalization and severe clinical conditions.

Another study performed at a time when Varicella vaccine had not yet been added to the vaccine schedule in Turkey assessed cases of chickenpox in terms of complications requiring hospitalization and identified pneumonia as the most common cause of chickenpox-related hospitalizations (16). Pneumonia was also the most common cause of hospitalization in our study.

A 6-year study from Spain involving hospitalization levels in chickenpox patients determined that approximately 8.5% of presentations required admission. The most common complication necessitating hospitalization in that study was soft tissue infection (17). The level of cases requiring hospitalization in our study was 8.2%, similar to the rate in that study and the most common complication necessitating hospitalization was bronchopneumonia.

Ziebold et al. reported that neurological complications were the complication most commonly seen in chickenpox patients in Germany (61.3%) (18). In our study, neurological complications were the least common factor. This suggests that single-dose vaccine protects against severe complications.

Theodoridou et al. reported that cutaneous infections were the most common cause of hospitalization in the period before the chickenpox vaccination Schedule (19). Cutaneous infections were the second most common cause of admission to hospital in our study.

The main limitation of this study is that it is based on data from a single region. Its retrospective nature is another limitation.

CONCLUSION

In conclusion, the addition of single-dose Varicella vaccine to the routine vaccine schedule in Turkey reduces severe complications and the incidence of the disease, although we know that children can still contract chickenpox despite having been vaccinated. Single-dose vaccine failing to provide the desired level of benefits has led to a second dose being added to vaccine schedules in several countries. As a result of our study, we think that the addition of a second dose of Varicella vaccine to our routine vaccine schedule will further reduce rates of hospitalization associated with chickenpox-related complications. Based on our findings, we think that if a second Varicella vaccine is to be administered in Turkey, this should be administered at 24-36 months. Wider-ranging studies are now needed on these subjects.

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Habip Almis ORCID: 0000-0001-9327-4876

Ibrahim Hakan Bucak ORCID: 0000-0002-3074-6327

Fedli Emre Kiliç ORCID: 0000-0002-0964-5572

Davut Kayak ORCID: 0000-0003-0328-7513

Mehmet Geyik ORCID: 0000-0001-5373-8007

Mehmet Tekin ORCID: 0000-0002-1157-1314

Capan Konca ORCID: 0000-0001-8625-9045

Mehmet Turgut ORCID: 0000-0002-2155-8113

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