Varicella-Related Hospitalization In Children: A Retrospective Study In The Pre-Vaccine Era In Ankara, Turkey

Çocuklarda Suçiçeğine Bağlı Hospitalizasyon: Türkiye'de Ankara'da Aşı Öncesi Dönemde Retrospektif Bir Çalışma

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Summary

Aim: Varicella is predominantly a childhood disease in non-vaccinated populations. The purpose of the study is to evaluate the indications of hospital admissions, complications of varicella infection and their clinical characteristics among previously healthy and children. with underlying illness

Material and Methods: Hospital records of children hospitalized for varicella between January 2000 and August 2007 were reviewed.

Results: A total of 34 children were hospitalized during the study period, 38% of the patients were previously healthy and 62% were previously ill patients. Previously well children were hospitalized because of varicella-related complications and previously ill children were usually hospitalized for antiviral therapy or for observation. There were 25 complications in 21 patients. The most common complication was secondary bacterial infections reported in 8 children (23%) and was more common in healthy children ($p<0.01$). Hepatitis and arthritis were present in 3 (9%), thrombocytopenia, varicella pneumonia and stomatitis were present in 2 (6%) and disseminated varicella and encephalitis were present in 1 (3%) patient. There was no statistically significant difference in the frequency of hepatitis, arthritis, stomatitis, varicella pneumoniae, thrombocytopenia, encephalitis, and disseminated varicella between previously ill and well children ($p<0.05$). Varicella-related complications observed in healthy children were more severe than the ones observed in previously ill patients.

Conclusion: Our study confirms that healthy children are at risk for severe complications of varicella, especially secondary bacterial infections, leading to hospitalization. Thus, an universal childhood varicella immunization may reduce the rate of varicella-related complications and admissions in our country.

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Key words: Tick, Crimean-Congo Hemorrhagic Fever

Özet

Amaç: Suçiçeği aşısız toplumlarda çocukluk çağının sık görülen bir hastalığıdır. Bu çalışmanın amacı sağlıklı ve altta yatan hastalığı olan çocuklar arasında suçiçeğine bağlı hastaneye yatış endikasyonlarını, komplikasyonlarını ve klinik özelliklerini değerlendirmektir.

Gereç ve Yöntem: Ocak 2000 ve Ağustos 2007 arasında suçiçeği nedeniyle yatırılan çocuk hastaların dosyaları gözden geçirildi.

Bulgular: Çalışma boyunca toplam 34 çocuk hastaneye yatırıldı, hastaların %38'i daha önceden sağlıklı ve %62'si altta yatan hastalığı olan çocuklardı. Sağlıklı çocuklar suçiçeğine bağlı komplikasyonlar, altta yatan hastalığı olan çocuklar ise antiviral tedavi veya gözlem için yatırıldı. 21 hastada 25 komplikasyon gözlendi. En sık gözlenen komplikasyon sekiz çocukta bildirilen sekonder bakteriyel enfeksiyondu (%23) ve sağlıklı çocuklarda daha sıktı ($p <0.01$). Hepatit ve artrit üç hastada (%9), trombositopeni, suçiçeğine bağlı pnömoni ve stomatit iki hastada (%6) ve dissemine suçiçeği ve ensefalit bir hastada (%3) gözlendi. Sağlıklı ve altta yatan hastalığı olan çocuklar arasında hepatit, artrit, stomatit, suçiçeğine bağlı pnömoni, trombositopeni, ensefalit ve dissemine suçiçeği sıklığında istatistiksel olarak anlamlı fark yoktu ($p<0.05$). Sağlıklı çocuklarda gözlenen suçiçeğine bağlı komplikasyonlar altta yatan hastalığı olan çocuklara göre daha şiddetli idi.

Sonuç: Çalışmamız sağlıklı çocukların hospitalizasyona neden olan ağır komplikasyonlar, özellikle sekonder bakteriyel enfeksiyonlar, açısından riskli olduğunu göstermektedir. Bu nedenle ülkemizde rutin suçiçeği aşı uygulaması suçiçeğine bağlı komplikasyonları ve hastaneye yatışları azaltabilir. *(Çocuk Enf Derg 2009; 3: 1-4)*

Anahtar kelimeler: Suçiçeği, komplikasyon, çocuk

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Introduction

Varicella is a common contagious disease caused by primary varicella-zoster virus (VZV) infection. Varicella infection usually results in mild to moderate illness. However, it is more severe in immunocompromised people and it can result in high morbidity and mortality. Potentially life-threatening complications include pneumonitis, secondary bacterial infections, encephalitis, and hemorrhage. The varicella vaccine prevents most of the morbidity caused by primary varicella in children and is recommended by The American Academy of Pediatrics and the Advisory Committee on Immunization (1,2). In Turkey, routine vaccination against varicella has not become standard practice, despite the commercial availability of the varicella vaccine and data on varicella complications are scant. The purpose of the study is to evaluate the indications of hospital admissions, complications of varicella infection and their clinical characteristics among previously healthy and ill children.

Material and Methods

Hospital records of children hospitalized for varicella between January 2000 and August 2007 were reviewed. Patients' demographics, immune status of the cases, clinical features, microbiological findings, varicella-related complications and the outcomes were analyzed. The diagnosis of VZV infection was based on typical physical findings. Children were included in the study if varicella-zoster virus infection resulted in hospitalization, either for a varicella-related complication/event or for antiviral treatment or observation. Children were categorized as previously ill, including immunocompromising conditions, and previously well. Pre-existing illness was defined as any condition requiring continuous medical attention.An immuncompromising condition was defined as any congenital or acquired immunodeficiency, malignancy, or receipt of corticosteroids or chemotherapy within 30 days before the onset of varicella. A varicella-associated complication was defined as a condition or event occurring within 14 days of onset of varicella that may have been caused by varicella-zoster virus infection. The presence of skin and soft tissue bacterial infections was established by clinical findings or confirmed by bacterial cultures. The diagnosis of pneumonia required appropriate clinical and radiographic findings. Hepatitis was defined as elevation of serum alanine aminotransferase and aspartate aminotransferase values at least two times greater than normal. Thrombocytopenia was defined as a platelet count below 100.000/mm^3. The diagnosis of primary encephalitis was accepted if the clinical course was characterized by fever and altered level of consciousness, along with compatible cerebrospinal fluid findings and no reasonable alternative diagnosis in a patient with varicella. Disseminated varicella required abnormalities in at least two parenchymal organs.

Statistical analysis was performed via SPSS program. We compared the frequency of complications between previously ill and well children using chi-square and/or Fisher's exact test. Differences were considered significant at a value of $p<0.05$.

Results

The hospital records of 35 children with varicella admitted to the Ankara University Medical School, Department of Pediatric Infectious Diseases between January 2000 and August 2007 were examined. One child who was hospitalized for pyelonephritis and in whom varicella developed during the hospital stay was excluded. The mean age was 57.4±48.4 months (range, 4 months to 17 years), with a male predominance (2.4:1). At admission, 82% of patients had a profuse vesicular rash (>100), 64% fever, 23% mucosal involvement, and 18% fewer than 10 skin lesions (Table 1).

Overall, 38% (13/34) of the patients were healthy before onset of varicella and 62% (21/34) of the patients were previously ill. Of 21 previously ill children, 18 (86%) were immunocompromised. Ten patients with malignancy (lymphoma in five, neuroblastoma in two, rhabdomyosarcoma in one, Ewing sarcoma in one, acute myeloid leukaemia in one) received chemotherapy at the time of primary varicella. Five patients received immunosuppressive treatment; two for juvenile rheumatoid arthritis, one for immune hemolytic anemia, one for bone marrow transplantation for thalassemia major, and one for Crohn's disease. Two patients had immune deficiency. Three other pre-existing diseases were, one Lennox-Gastaut syndrome, one congenital toxoplasmosis and one congenital myopathy. One patient was considered immunocompromised since she had malnutrition.

Of the children hospitalized for varicella, 21 (62%) had one or more varicella-related events; 13 (62%) were previously well and 8 (38%) were previously ill. The other 13 (38%) patients were hospitalized for initiation of intravenous acyclovir or for observation, they did not

Table 1. Demographic and clinical characteristics of patients

Charalteristics	
Male/female no	24/10
Mean age (months; SD)	57.4±48.4
Mean hospital stay (days;SD)	6.7±6.2
Healthy/previously ill patients (n)	13/21
Clinical manifestations (n:%)	
Profuse vesicular rash	28; 82%
Fever	22; 64%
Fewer than 10 skin lesions	6; 18%
Mucosal involvement	8; 23%

experience complications and all of them had pre-existing illness. There were 25 varicella-associated complications experienced by 21 children (Table 2).

The number of complications exceeded the number of patients because more than one complication was seen in some patients. Secondary bacterial infection was the most common complication identified and occurred in 8 patients (23%). All children with bacterial infections except one were previously well ($p<0.01$). The most common secondary bacterial infection was skin/soft tissue infection, cellulitis in four and necrotizing fasciitis in one patient. Of five patients with invasive bacterial infections, three had septicemia (after cellulitis due to *Staphylococcus aureus* in one patient, after necrotizing fasciitis due to group A β-hemolytic streptococcus in one patient, and due to *Haemophilus influenzae* type b in one patient), and three had pneumonia (with bacteraemia as a result of *Haemophilus influenzae* type b in one patient). *Staphylococcus aureus* was isolated from two patients with cellulitis. Children with cellulitis and septicemia were significantly more likely to be previously healthy than previously ill ($p<0.05$).

Three children had arthritis, two of whom with exacerbation of juvenile rheumatoid arthritis. Hepatitis was diagnosed in three children, two of whom were previously ill. Although arthritis and hepatitis were more frequent in ill children (2/21, 9.5%) compared with healthy children (1/13, 7.7%), this difference was not statistically significant ($p>0.05$). In two healthy patients, inadequate oral intake was the main reason for admission. Feeding difficulties were attributed to severe mucosal involvement. One healthy and one previously ill patient had viral pneumonia. Thrombocytopenia was diagnosed in two children, both were immunocompromised and thrombocytopenia occurred independently of the underlying diseases. One child had clinical manifestations consistent with primary viral encephalitis and he was previously healthy. One patient was admitted temporarily to the intensive care unit due to disseminated varicella. There was no statistically significant difference in the frequency of stomatitis, varicella pneumoniae, thrombocytopenia, encephalitis, and disseminated varicella between previously ill and well children ($p <0.05$).

The average length of hospital stay was 6.7±6.2 days (2 to 37 days). Of the 34 children hospitalized for varicella, 21 (62%) received acyclovir; 18 (86%) were immunocompromised and 3 (14%) were previously well. Among the previously well children who received acyclovir one had disseminated varicella, one had encephalitis, and one had pneumonia. The mean duration of antiviral therapy was 2.2±2.2 days. All children with secondary bacterial infections were treated with antibiotics.

None of the patients required surgical intervention. All patients survived and major sequelae at hospital discharge and follow-up were not recorded.

Discussion

Varicella is a common infectious disease and complications are believed to be rare. A live attenuated varicella vaccine is shown to be safe and effective. In Turkey, varicella vaccine is not recommended for routine administration to children despite the commercial availability of the vaccine. The aim of the study was to describe the indications for hospital admissions, varicella complications and their clinical characteristics among healthy and previously ill children hospitalized for varicella. From 2000 to 2007, 34 children were hospitalized for varicella, 62% of them were previously ill and 38% of them were previously healthy. The proportion of previously

Table 2. Type and frequency of complications in patients admitted due to varicella infection

Complication*	Well children (n=13)	Ill children (n=21)	Total (n=34)
Secondary bacterial infection	7 (54)	1 (5)	8(23)
Cellulitis	4 (30)	0	4
Necrotizing fasciitis	1 (7)	0	1
Septicaemia	3 (23)	0	3
Pneumonia	2 (15)	1 (5)	3
Hepatitis	1(7)	2 (10)	3 (9)
Arthritis	1 (7)	2 (10)	3 (9)
Varicella pneumonia	1 (7)	1 (5)	2 (6)
Thrombocytopenia	0	2 (10)	2 (6)
Stomatitis	2 (15)	0	2 (6)
Disseminated varicella	1 (7)	0	1(3)
Encephalitis	1 (7)	0	1 (3)
Total	17 (68)	8 (32)	25 (100)

*Some children had more than one complication

ill patients among children hospitalized for varicella was higher than the reported proportions in literature. The reason was the higher number of immunocompromised patients due to the presence of bone marrow transplantation unit in our hospital. Indications for admission differed for previously well and ill children. The majority (62%) of previously ill children were admitted for acyclovir therapy or for observation and not for complications. Previously well children hospitalized for varicella were admitted mainly for management of complications.

The spectrum of complications was consistent with previous studies (3-9). Secondary bacterial infections were the most common complications. They were mostly confined to the skin and soft tissue, and were present in previously healthy children similar to the studies in the literature. Peterson et al. (3) found skin/soft tissue infections to be the most common complications experienced by 574 children hospitalized patients for varicella. In their study, nearly half of the patients were previously ill, as in our study. Koturoğlu et al. (4) reported that infectious complications were the most common complications of varicella requiring hospitalization in healthy children in a study carried out in our country. Alnuneef et al (5) followed 3802 cases of chickenpox, and skin and soft tissue infections were the most common complications.

Hepatitis and arthritis were second in frequency among our patients and usually occurred in previously ill patients. Elevation of aminotransferase values in previously healthy children with varicella is well recognized (10). Arthritis was detected in two patients with juvenile rheumatoid arthritis who were in remission. These may have been manifestations of underlying disease or activation of underlying disease due to varicella infection in these patients, rather than complications of varicella.

Pneumonia is a well-recognized complication of varicella in immunocompromised children and adults; however, documented varicella pneumonia in healthy children is rare. In our study, one of two patients with varicella pneumonia was previously healthy and the other was previously ill.

Neurological complications are usually reported second in order of frequency, and in the healthy older age children (3,4,11). We found only one previously healthy case of encephalitis, considerably fewer than noted in earlier reports, presumably because of the low proportion of the healthy children or low mean age of children in our study.

Varicella infection is more severe in immunocompromised people and leads to the development of much more severe conditions than in healthy children (1). In our study, the spectrum of complications in previously ill patients was different from the previously healthy children. Secondary bacterial infections were observed mainly in previously healthy children, whereas hepatitis, arthritis and thrombocytopenia were the most common complications in previously ill patients. In addition, varicella-related complications observed in healthy children were more severe than the ones observed in previously ill patients. This is most likely due to increased risk awareness and prompt administration of antivirals, which were administered to all immunocompromised patients.

In conclusion, previously well children were hospitalized due to varicella-related complications and previously ill children were usually hospitalized for antiviral therapy or for observation. Secondary bacterial infections were the most common complications and were observed mainly among healthy children. Varicella complications occurred in immunocompetent children were more severe than in previously ill children. Our study confirms that healthy children are at risk for severe complications of varicella leading to hospitalization. Thus, a universal childhood varicella immunization may reduce the rate of varicella-related complications and admissions in our country.

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