Ege Tıp Dergisi 41 (4): 225 - 228, 2002

THE EFFICACY OF MONODOSE VARICELLA VACCINE IN PEDIATRIC CANCER PATIENTS

KANSERLİ HASTALARDA TEK DOZ SUÇİÇEĞİ AŞISININ ETKİNLİĞİ

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Key Words: varicella vaccine, immunization, cancer
Anahtar Sözcükler: suçiçeği aşısı, bağışıklama, kanser

SUMMARY

In this study the efficacy of a single dose varicella vaccine was evaluated in 20 patients with acute lymphoblastic leukemia and lymphoma. AH patients were serologically negative by the absence of antivaricella antibody. AH cases were in remission for at least 6 months and their absolute lymphocyte count at the time of immunization was ≥ 700/mm^3. For patients receiving maintenance therapy, chemotherapy was suspended for 1 week before and 1 week after immunization. Antivaricella antibody concentration was determined 3 and 24 months after immunization to evaluate antibody response. İn cancer group geometric mean antibody concentration was found 42.78 HU on the 3rd month and 29.3 HU on the 24th month and in the control group the values were 45.98 HU and 31.8. The seropositivity rates were found 90% on the 3rd and on the 24th months in each group. Unserious side effects due to varicella vaccination were determined in 40% of the pediatric cancer group and in 10% of the control group. İn conclusion we can say that single dose varicella vaccine is effective and safe in patients with acute lymphoblastic leukemia and lymphoma.

ÖZET

Bu çalışmada tek doz suçiçeği aşısının etkinliği akut lenfoblastik lösemili ve lenfomalı 20 hastada değerlendirildi. Tüm hastalarda antivarisella antikorları negatif idi. Tüm olgular en azından 6 ay süre ile remisyonda idiler ve aşının yapıldığı günkü lenfosit sayıları 700/mm^3 ve üzerinde idi. İdame tedavisi alan hastalarda aşıdan 1 hafta öncesinden, 1 hafta sonrasına kadar kemoterapiye ara verildi. Antivarisella antikor tayinleri aşıdan 3 ve 24 ay sonra antikor yanıtının belirlenmesi amacıyla elde edildi. Kanser grubunda antivarisella antikor geometrik ortalaması 3. ayda 42.8 HU ve 24. ayda 29.3 olarak bulundu. Kontrol grubunda ise bu değerler sırasıyla 42.3 ve 31.8 HU idi. Her iki grupta da 3 ve 24. aylardaki seropozitivite oranları %90 olarak belirlendi. Suçiçeği aşısına bağlı ciddi olmayan yan etkiler hasta grubunda %40, kontrol grubunda ise %10 olarak belirlendi.

Sonuç olarak tek doz varisella aşısının akut lenfoblastik lösemili ve lenfomalı olgularda etkin ve güvenli olduğunu söyleyebiliriz.

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Makalenin geliş tarihi: 25. 10. 2002 ; kabul tarihi: 14.01. 2003

INTRODUCTION

Varicella usually a benign disease of childhood is a significant concern for the child with cancer because the mortality rate in untreated patients ranges from 7% to 20% owing to visceral dissemination to the liver, lung and

central nervous system. Although the availability of antiviral therapy and postexposure prophylaxis with varicella zoster immunglobulin have reduced the frequency of severe disease, these interventions have limitations. The goals of immunizing children with acute lymphoblastic leukemia and lymphoma against varicella are to confer protection from severe chickenpox and also to avoid disruption of chemotherapy schedules because of exposure to chickenpox. In this study the efficacy and safety of a single dose varicella vaccine was evaluated in children with acute lymphoblastic leukemia and lymphoma.

MATERIAL AND METHODS

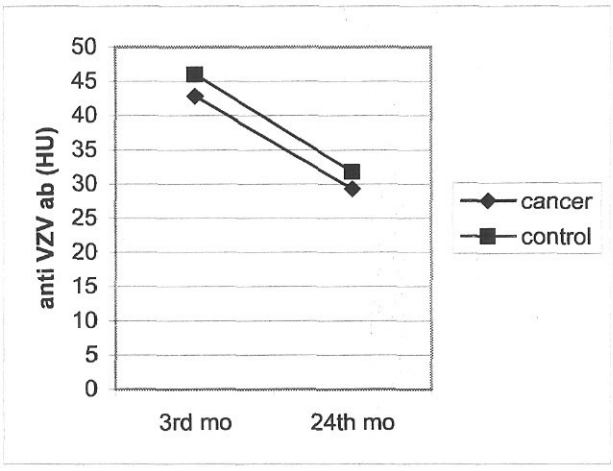
Twenty patients with pediatric malignancies who were attending the pediatric oncology clinic at our hospital and seronegative for antibodies to varicella infection were selected for vaccination. Ten healthy children also seronegative for varicella infection were taken as the control group. Seventeen patients with acute lymphoblastic leukemia (ALL), 1 with Hodgkin lymphoma (HL) and 2 with non-Hodgkin lymphomas (NHL) constituted the cancer group. AH of the cancer patients were in remission for at least 6 months and they had an absolute lymphocyte count of equal or over 700/mm^3 at the time of immunization. Nine patients with ALL were receiving maintenance therapy (6 mercaptopurine 50 mg/m^2/day, methotrexate 20 mg/m^2/once in a week). All chemotherapy was suspended for 1 week before and 1 week after immunization for patients receiving maintenance therapy. Eight patients with ALL, one patient with HL and two patients with NHL no therapy.

A single 0.5 mi dose of Oka strain of varicella vaccine (Varilrix®, Smith Kline Beecham, Belgium) was administred subcutaneously in ali age groups. Anti VZV antibody concentrations were determined 3 and 24 months after immunization to evaluate the duration of the humoral response. Anti VZV antibody concentrations were determined by using micro ELISA tecnique (Sorin, KIT LOT No: 2325600-084) and human varicella IgG test concentrations equal or greater than 20 human unit (HU) were accepted as seropositive. ann Whithney U test and Fisher exact chi-square test were used in statistical analyses.

RESULTS

Nine (45%) of the patients were boys and 11 (55%) were girls with a mean age of 10.6 years (5-17 years). Seven boys (70%) and 3 girls (30%) constituted the control group with a mean age of 8.5 years (4 to 15 years).

Three months after vaccination, geometric mean anti VZV antibody concentrations were 42.78 HU in cancer patients and 45.98 HU in the control group. Twentyfour months after vaccination, these values were 29.3 HU and 31.8 HU respectively (Figüre 1). No statistically significant difference was found between the values of the cancer patients and the control group on the 3rd and 24th month ($p>0.05$). Eighteen of the 20 cancer patients (90%) and 9 of the 10 control group (90%) were found seropositive on the 3rd and the 24th month.



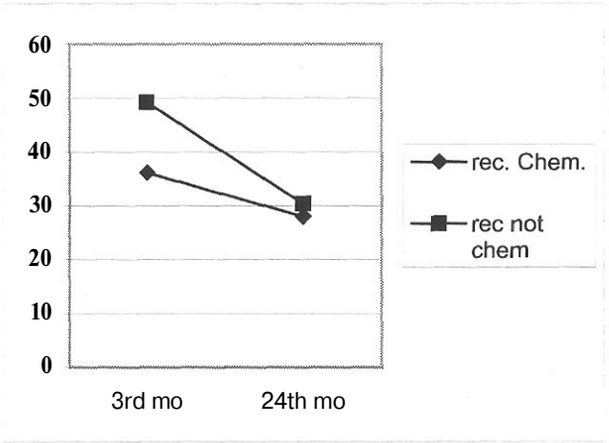
Figüre 1. The geometric mean anti VZV ab concentrations in cancer patients and controls

Two of the 20 cancer patients were found to be seronegative. Among these seronegative patients, one was a 5 years old ALL case receiving maintenance therapy and the other one was a 7 years old Hodgkin lymphoma patient receiving no therapy. Five of the 18 seropositive patients were older than 13 years. No correlation was found for seropositivity in cancer patients between their age, sex and chemotherapy status.

The geometric mean anti VZV ab concentrations of 9 patients receiving maintenance chemotherapy were 36.14 HU on the 3rd month and 28.0 HU on the 24* month. The geometric mean anti VZV ab values of 11 patients not receiving chemotherapy were 49.16 HU on the 3rd month and 30.4 HU on the 24th month (Figüre 2). Although the antibody titers of the patients not receiving chemotherapy were higher, no statistically significant difference was found between these two groups ($p>0.05$). Eight of the 9 patients (88.9%) receiving maintenance therapy and 10 of 11 patients (90.9%) receiving no chemotherapy were found to be seropositive after 3 and 24 months of vaccination and the difference was not statistically significant ($p>0.05$).

Mild vesicular lesions (17-28 lesions) occured in 4 patients (40%) of the cancer group and in 1 child (10%) of the control group 10-15 days (median 12 days) after

vaccination and low grade fever in one cancer patients. Ali children required no spesific treatment.



Figüre 2. The geometric mean anti VZV ab concentrations in patients receiving chemotherapy and not receiving ehemotherapy.

DISCUSSION

The prognosis of acute lymphoblastic leukemia and lymphoma becomes prominently better with more intensive chemotherapy protocols in recent years. But both the cancer itself and the intensive chemotherapy protocols make the patient more sensitive to infeetions such as varicella. Exposure of immunosuppressed children to varicella infection complicates their çare, interferes with treatment, adds vericella related morbidity and inereases the cost of medical çare (1).

Varicella is usually a mild disease that is rarely associated with serious complications. The important exception is when the disease oecurs in those who are immunocompromised. In these circumstances the infection may disseminate to organs such as to lungs and brain and has been associated with mortalities ranging from 7% to 30%. Although the availability of antiviral therapy and postexposure prophylaxis with varicella zoster immunglobulin have reduced the frequency of severe disease, these interventions have limitations. To improve immmunization against varicella by vaccination seems the most benefical aspect in immunocompromised children (2,3,4).

Among healthy children high seroconversion rates are obtained by a single dose of varicella vaccine and the immunization continues for 10 years (5,6,7,8).

İn many studies responses to the vaccine was found lower in immunocompromised patients than in healthy children with a single dose vaccine and administration of two doses of vaccine with one month interval was recommended. İn other studies no differences was found in seronegativity between patients who received single or double doses and the second dose was recommended only for those in whom the seroconvertion did not oecur. Wİth a single dose of vaccine the rates of seroconversion in patients with ALL and immunocompromised children were reported by Arbeter et al (9) as 91%, by Takahashi et al (10) as 86% and by Morales et al (11) as 90.3%. Gershon et al (12) found the seroconversion rate as 85% with a single dose and after the second dose this value inereased to 97%. Ecevit et al (13) deseribed 95% seroconversion rate with double doses of vaccine. Lou et al (14) reported the seroconversion rate as 62.5% with a single dose of varicella vaccine in patients with ALL and with the second dose of vaccine the seropositivity rate inereased to 87.5%. Navajas et al (15) obtained the seroconversion rate in 76% after one dose and 92 after the second dose. İn a collaborative study ineluding 557 children with ALL in remission, La Russa et al (16) reported that the vaccine proteeted completely against severe varicella and coneluded that the vaccine was extremely beneficial for leukemic children. Gershon et al (17) emphasized the importance of proteeting high risk children against severe varicella by the use of vaccine.

In our study we evaluated the efficiacy of a single dose varicella vaccine and found the seroconversion rate as 90% at 3 and 24 months postimmunization. There was no difference in the seroconversion rate or magnitude of serum antivaricella antibody in cancer patients and the healthy control group. The seroconversion was 89% in patients receiving maintenance therapy in whom chemotherapy was suspended and 91% in patients receiving no therapy and we coneluded that seroconversion was not effected negatively with chemotherapy. We applied single dose in ali our patients without considering their ages. Ali of the five patients who were older than 13 years were found seropositive. Among 3 patients who were seronegative, one was ALL and receiving maintenance therapy, one was a Hodgkin case in remission and the other one was a healthy child from the control group. Mild side effects were noted in 4 patients (40%) and in 1 healthy child (10%). On the average, only antiviral therapy was found fivefold expensive than one dose varicella vaccine.

We coneluded that a single dose of Oka strain live attenuated varicella vaccine did provide prominent immunity and it is safe and cheap for patients who are in remission and receiving maintenance chemotherapy.

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"This study was presented at "XXXV. Ulusal Pediatri Kongresi, 19-23 Mayıs 1999, Ankara" and "XXVII. Ulusal Hematoloji Kongresi. 11-13 Kasım 1999, İstanbul".