HIV & AIDS Review 14 (2015) 76–79

Contents lists available at ScienceDirect

HIV & AIDS Review

journal homepage: www.elsevier.com/locate/hivar

Original Research Article

Antibody response to VZV vaccination in HIV infected children

Agnieszka Ołdakowska [a,b,*], Urszula Coupland [a,b], Sabina Dobosz [a,b], Jolanta Popielska [a,b], Małgorzata Szczepańska-Putz [a,b], Magdalena Marczyńska [a,b]

[a] Department of Children's Infectious Diseases, Medical University of Warsaw, Poland
[b] Warsaw's Hospital for Infectious Diseases, Poland

ARTICLE INFO

Article history:
Received 25 September 2014
Received in revised form 17 March 2015
Accepted 18 March 2015
Available online 22 April 2015

Keywords:
HIV infection
Varicella vaccine
Post-vaccination antibodies

ABSTRACT

Aim: To evaluate the effectiveness of varicella vaccination based on the presence of VZV antibodies in HIV-infected children and to establish factors influencing vaccination response.
Background: VZV vaccination is recommended in HIV-infected children without severe immunodeficiency. This group of children may not produce sufficient immunologic response.
Materials and methods: Post vaccination antibodies were evaluated in 21 HIV-infected children who received 2 doses of varicella vaccine. VZV antibodies were checked after the second vaccine dose using VIDAS Varicella-Zoster IgG ELFA technique. All patients have been receiving combined antiretroviral treatment (cART). The analyzed factors included: age at HIV diagnosis, age when receiving the first vaccine dose, Centers for Disease Control and Prevention (CDC) classification at diagnosis, at time of vaccination and at evaluation.
Results: Post-vaccination VZV antibodies were present in 52% of patients. HIV infection was diagnosed at the mean age of 13 months (range 1 month to 4.5 years). Prior to evaluation 11/21 children had experienced moderate to severe HIV symptoms. Six children experienced severe immunodeficiency, 6 were moderate immunodeficient in the past, 46% of them responded to vaccination. At time of vaccination all the children were immunocompetent. At the time of the antibodies evaluation 20 children were classified N1/A1, one received C1 classification due to HIV encephalopathy. The subjects who had VZV protective antibody titers had shorter time since vaccination and were less likely to have prior immunodeficiency. No children developed varicella during the mean 3.5 years of follow-up.
Conclusion: Serological immune response to varicella vaccination in HIV-infected children was insufficient.

1. Introduction

Varicella is a common pediatric disease with the incidence of 540 per 100 000 in Poland and the substantial hospitalization rate [1,2]. Widespread varicella vaccination in such countries like USA and Germany has led to decrease in factors as related ambulatory care, number of hospitalizations and mortality [3,4]. HIV-infected children are at increased risk of developing unusually severe and progressive course of varicella infection. They have also suffered from herpes zoster more often than their uninfected peers, especially before combined antiretroviral treatment (cART) era.

The introduction of cART has transformed vertically acquired HIV infection into a chronic treatable disease, but HIV-infected children still remain at a greater risk of vaccine-preventable infections when compared to not-infected children. Vaccination recommendations in HIV-infected children without severe immunodeficiency include two doses of VZV vaccine [5–7]. In other settings of immunocompromise, such as leukemia during chemotherapy maintenance phase the benefit of live vaccine is considered to outweigh the potential risk [8].

Because of impaired function of cellular and humoral immunity, HIV-infected children may not produce sufficient immunologic response after vaccination (poor primary response, impaired ability to generate memory responses and/or loss of acquired immunity).

Life attenuated VZV vaccines appear to be safe in HIV-infected children who are not severely immunosuppressed. In polish national health program the vaccine is included in the high risk groups and their close contacts as a mandatory vaccination.

* Corresponding author at: 02-201 Warszawa, ul. Wolska 37, Poland. Tel.: +48 22 33 55 250.
E-mail address: a-oldakowska@wp.pl (A. Ołdakowska).

http://dx.doi.org/10.1016/j.hivar.2015.03.004
1730-1270/

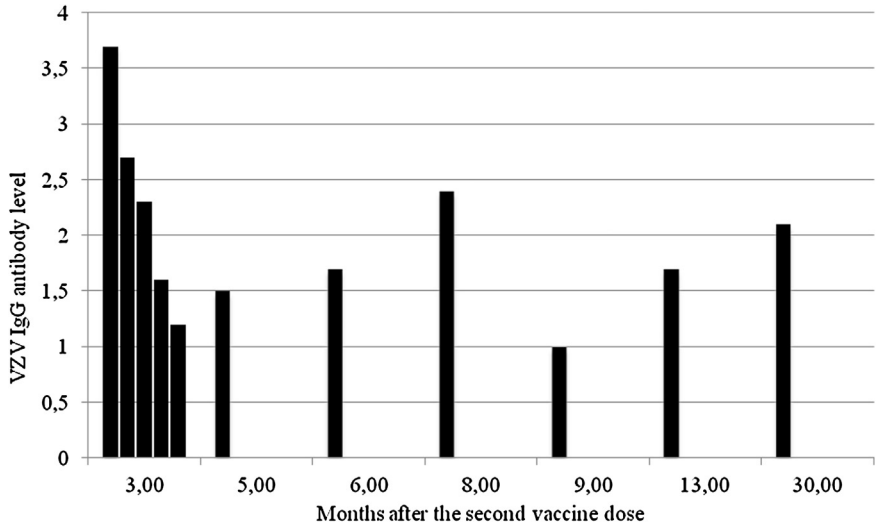

Fig. 1. VZV IgG antibodies level according to the time since the last vaccine dose.

The aim of the study was to assess the immunogenicity of varicella vaccination in HIV-infected children receiving cART and to establish factors which influence vaccination effectiveness.

2. Materials and methods

8/21 children were tested for VZV IgG antibodies before receiving the varicella vaccine. Post-vaccination anti-VZV antibody level after administering two doses of vaccine was determined in 21 children (8 males) aged from 2.5 to 14 years (mean 5 years), vertically infected with HIV. Children had no prior history of varicella. Twenty were Caucasian, one Asian.

All participants received 2 doses of live attenuated varicella vaccine subcutaneously (Varilrix, GlaxoSmithKline Biologicals S.A.), each 0.5 ml contained at least 2000 PFU (plaque forming unit) of OKA virus. Vaccination schedule consisted of two doses given at least 12 weeks apart. VZV antibody was measured from 3 to 36 months (at the mean of 10 months) after vaccination. The VZV IgG titers were analyzed by using VIDAS Varicella-Zoster IgG enzyme linked fluorescent assay (ELFA) technique consistent with the manufacturer's recommendations. In the study antibody level greater than 0.9 was regarded as positive, results <0.6 negative, 0.6–0.9 equivocal (equivocal results were consider as negative). Children were observed for up to 4.5 years.

Medical history, including CDC clinical category, CD4 lymphocyte count and percentage, HIV RNA (viral load (VL)), history of antiretroviral therapy was collected from the medical records. The analyzed factors included: age at HIV diagnosis, age at the first and the second vaccine dose administration, CDC classification at diagnosis, at the time of vaccination and at evaluation. All the children have been receiving cART throughout the course of the study. VL was quantified using Real Time PCR, HIV-1 Abbott (lower limit of quantitation was 40 copies/ml), lymphocyte subsets were determined using flow cytometry.

Written informed consent was obtained from each tested child's parent or legal guardian according to "Medical care of HIV-infected children program. KB/1/A/2014".

3. Results

All patients tested before vaccination were seronegative for VZV antibody at baseline. 11/21 (52%) children developed post-vaccination VZV IgG antibodies after two doses of varicella vaccine. The antibodies level ranged from 1 to 3.7 (mean 2.0). VZV IgG antibodies level is shown in Fig. 1. The percentage of responders differ in those tested within the first 6 months after receiving the second vaccine dose and those tested past 6 months being 63% (7/11) to 40% (4/10) respectively.

The baseline study characteristic is shown in Table 1. At the time of diagnosis 11/21 (52%) children had experienced moderate-to-severe HIV symptoms: CDC clinical category B ($n = 6$) and C ($n = 5$) respectively. CD4% ranged from 11.7 to 76% (mean 36%). 5/21 (24%) children had moderate and 6/21 (28%) had severe immunodeficiency at diagnosis. cART was started at the age from 1 month to 5.5 years (mean 15 months), 14/21 (67%) of children had started treatment during the first 12 months of life. Age at HIV diagnosis was different in children with positive post-vaccination antibodies comparing to those without detectable antibodies, being 16 months (range 1–59 months) and 9 months (range 1–40 months), respectively.

At the time of vaccination all the children were immunocompetent. 4/21 had detectable VL, 3 of them were responders.

At the time of antibodies evaluation 20 children were CDC classified N1/A1, one as C1 due to HIV encephalopathy – cerebral palsy (she had protective antibody level). CD4 count ranged from 519 to 2998 (mean 1440). CD4 count did not differ in responders and non-responders. Prior to evaluation 12/21 children had experienced immunodeficiency (6 children – severe, 6 – moderate). All the children were receiving antiretroviral therapy with the median treatment duration of 4 years (range 6 months to 13 years) and had undetectable HIV RNA (<40 copies/ml) at evaluation.

Characteristic of HIV-infected children stratified by antibody response is shown in Table 2.

Among 8 children who were seronegative at baseline, VZV antibody was detected in 6 after the second dose of varicella vaccine.

Table 1
Baseline study group characteristic ($n = 21$).

Age at HIV diagnosis (months)	12.81
Mean (range)	(0–59)
Age at the first vaccine dose (months)	47.19
Mean (range)	(10–57)
Age at evaluation (months)	63.24
Mean (range)	(28–167)
CD4% nadir	36.06
Mean (range)	(11.7–76)
CD4% within last 3 months before evaluation	50.33
Mean (range)	(35–67)