Dokkyo Journal of Medical Sciences
30(1) : 9～11, 2003

Originals

Influence of Acyclovir on Antibody Production of Antibody to Chickenpox

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SUMMARY

Titers of immunoglobulin (Ig) G and IgM antibody to varicella zoster virus (VZV) were measured in 20 pediatric patients with chickenpox during treatment with acyclovir, an antiviral agent. Acyclovir doses, each 80 mg/kg/day, were administered for 5 days, beginning within 4 days after the onset of the rash. All patients displayed positive IgG and/or IgM anti-VZV antibodies. No significant difference was noted in the IgG ($p = 0.417$) or IgM titer ($p = 0.846$) between patients treated within 24 hours of the onset of the rash and those treated one or more days after onset. No significant differences was noted in the IgG ($p = 0.212$) or IgM titer ($p = 0.570$) between patients tested within 10 days after the onset of the rash and those tested more than 10 days after. We conclude that administration of acyclovir does not affect anti-VZV antibody production in patients with chickenpox.

Key Words : antibody production, chickenpox, acyclovir

INTRODUCTION

Acyclovir, an anti-varicella zoster virus (VZV) agent, was developed in 1980. This drug is apparently effective for resolving the clinical symptoms of chickenpox, but whether the drug affects the production and maintenance of anti-VZV antibodies, when administered within 24 hours after the onset of the chickenpox rash, remains unclear[1, 2]. This study was conducted to measure antibody titers and evaluate antibody production in pediatric patients with chickenpox treated with acyclovir within 24 hours after the onset of the rash.

SUBJECTS AND METHODS

We studied the cases of 20 pediatric patients with severe chickenpox, as diagnosed on the basis of history and physical findings between 1997 and 1999. After the parents of patients provided informed consent, patients received acyclovir therapy and the anti-VZV IgG and IgM antibody titers were measured. Patient ages ranged between 3 months and 12 years 9 months, with a mean age of 4 years 5 months.

The presence or absence of antibody production was examined in the 20 patients after acyclovir therapy. Anti-VZV IgG and IgM antibody titers in the two groups were compared : those who received treatment within 24 hours after onset of the rash (early treatment group, n = 12) ; and those who received treatment after the first 24 hours after onset of the rash (late treatment group, n = 8). Anti-VZV IgG and IgM antibody titers in another two groups were also compared : those who received treatment within 10 days after onset of the rash (early phase group, n = 10), and those who received treatment more than 10 days after onset of the rash (late phase group, n = 10).

Acyclovir was administered orally at a dose of 80 mg/kg/day for 5 days. Anti-VZV IgG and IgM antibody

Received September 20, 2002 ; accepted December 6, 2002
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Table 1 Frequency of IgG and IgM antibody positivity after acyclovir therapy

Anti-VZV IgG antibody	Anti-VZV IgM antibody	Number of patients
+	+	10
+	−	7
−	+	1
−	−	0
+	±	1
±	+	1

Table 2 Anti-VZVIgG and anti-IgM titers

	Anti-VZV IgG antibody titers	Anti-VZV IgM antibody titers
Group 1 (n = 12)	33.22 ± 8.6 *	2.54 ± 0.67 **
Group 2 (n = 8)	29.80 ± 13.18	2.93 ± 0.99

Data are the mean ± SE.
Group 1 : Acyclovir therapy within the first 24 hours after the rash
Group 2 : Acyclovir therapy more than 24 hours after the rash
* : P = 0.417, not significant compared with Group 2
** : P = 0.846, not significant compared with Group 2

titers were measured by enzyme immunoassay (EIA), a serological diagnostic method. Titers of IgG antibody to VZV ≧ 4.0 were considered positive, those between 2.0 and 4.0 intermediate, and those ≦ 2.0 negative. Titers of IgM antibody to VZV ≧ 1.2 were considered positive, those between 0.8 and 1.2 intermediate, and those ≦ 0.8 negative. Wilcoxon's rank sum test was utilized for statistical analysis.

RESULTS

When we measured patient titers of IgG and IgM antibodies to VZV, we found the results shown in Table 1. Ten patients displayed positive titers for both IgG and IgM antibodies. Seven patients had positive titers for IgG antibody and negative titers for IgM antibody. One patient had a negative titer for IgG antibody and a positive titer for IgM antibody. One patient had a positive titer for IgG antibody and an intermediate titer for IgM antibody. One patient had an intermediate titer for IgG antibody and a positive titer for IgM antibody.

As shown in Table 2, the early treatment group had a mean (± SE) anti-VZV IgG antibody titer of 33.22 ± 8.62 and a range of 5.0-109.0. The late treatment group had a mean (± SE) anti-VZV IgG antibody titer of 29.80 ± 13.18 and a range of 2.0-117.0. No significant difference was observed between the two groups (p = 0.417) in IgG antibody titers. As shown in Table 2, the early treatment group had a mean (± SE) anti-VZV IgM antibody titer of 2.54 ± 0.67 and a range of 0.60-6.53. The late treatment group had a mean (± SE) anti-VZV IgM antibody titer of 2.93 ± 0.99 and a range of 0.40-7.93. The difference between the two groups in IgM antibody titers was not significant (p = 0.846). Differences between the early and late phase groups in IgG and IgM antibody titers were likewise not significant (p = 0.212, p = 0.570, respectively).

DISCUSSION

Chickenpox is a viral disease characterized by fever, severe itching, and bulbous skin eruptions. The disease may be complicated by pneumonia, encephalitis, or arthritis. Acyclovir, an antiviral agent, has been commonly administered for the treatment of chickenpox since 1994. Acyclovir produces an anti-VZV effect after the activation of VZV thymidine kinase. Acyclovir should be administered in the early phase of chickenpox. Recent studies have focused on improvements to clinical symptoms [3, 4] and immune responses [1] in patients with chickenpox after receiving acyclovir therapy. The results of this study suggest that the production of anti-VZV IgG and IgM antibodies and titers throughout the clinical course of chickenpox is unaffected by acyclovir treatment.

The varicella zoster virus enters the body via the respiratory tract, proliferates in the regional lymph nodes, and causes primary viremia within 4 to 6 days after infection. Disseminated virus particles further proliferate in reticulum cells in the liver and spleen, resulting in secondary viremia. Skin eruptions are produced about 14 days after infection[5].

Aspects of the immune responses of a VZV-infected host have been clarified. Some studies[6, 7] have reported that most of the anti-VZV IgG and IgM antibodies are produced during the first 6 days after the onset of chickenpox rash. Conversely, a positive antibody titer was found in 84% of patients who received acyclovir during secondary viremia[1].

Our results suggest that antibody production begins during primary or secondary viremia and is completed by the time skin eruptions appear. The humoral immune response to VZV is therefore complete by the time a clinical diagnosis is typically established. We conclude that the administration of acyclovir for the resolution of clinical symptoms does not affect VZV antibody production in patients with chickenpox.

Acknowledgment. This study was supported in part by a 1998 Urawa Medical Foundation Grant. This article is dedicated to the memory of my beloved wife, Fumiko Tsuji, who devoted her life to supporting my research efforts.

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