Original article

EARLY NEURODEVELOPMENT OF INFANTS BORN TO HIV-SEROPOSITIVE MOTHERS

Orawan Louthrenoo, M.D., Thanyawee Puthanakit, M.D., Nongyow Wongnum, P.N., Virat Sirisanthana, M.D.

Department of Pediatrics, Faculty of Medicine, Chiang Mai University

Abstract

Objective To examine neurodevelopment during the first 12 months of life in infants born to HIV infected mothers.

Methods Infants born to HIV infected mothers, who were receiving prenatal zidovudine monotherapy, were followed up at the Infectious Disease Clinic, Chiang Mai University Hospital and enrolled in this study. Neurodevelopmental assessment was administered at the age of 12 months by using Bayley Scales of Infant Development (BSID). Confirmed HIV infection status was performed at 18 months of age.

Results Thirty-nine infants, 10 infected and 29 uninfected, were studied. Demographic and perinatal characteristics including birth weight, length, head circumference, prematurity, maternal age, and maternal education were no different between the 2 groups. At 12 months, growth parameters of HIV infected and non-infected groups were not different, but Mental Developmental Index (MDI) and Psychomotor Developmental Index (PDI) were significantly lower in the HIV-infected group than in the non-infected group (MDI=90 vs. 99, \( p = 0.001 \); PDI=83 vs. 96, \( p < 0.001 \), respectively). In the HIV infected group, infants with symptomatic HIV infection had lower MDI and PDI scores than asymptomatic ones.

Conclusion HIV infected infants showed early lower developmental scores. Neurodevelopment may be one of the early markers of disease progression within the first 12 months in infants with HIV infection. Chiang Mai Med Bull 2004;43(1):1-7.

Keywords: neurodevelopment, infants, HIV infection

HIV infection often causes impairment of growth and development in children. Numerous observational data describe neurological involvement and developmental delay in pediatric HIV infection. (1-6) Neurological abnormalities are related
to a primary HIV infection or may be from HIV-related morbidity. The most common neurological findings in children with HIV infection include progressive encephalopathy, nonprogressive developmental delay, and motor dysfunction.\(^{1,7}\) Failure to gain weight could also be a direct consequence of HIV infection, secondary to HIV-related illness, or it could be associated with an adverse social environment and may occur later. Immunological markers were identified as associated with disease progression. Neurological involvement and impaired developmental milestones are often early markers of HIV infected infants and may precede other signs of disease progression.\(^{8,9}\) Therefore, the purpose of this study was to examine neurodevelopment in mental and motor functioning during the first 12 months of life in infants born to HIV infected mothers.

**Methods**

**Study population**

From January 2001 to December 2002, infants born to HIV infected mothers, who were followed up in the Infectious Disease Clinic, Chiang Mai University Hospital, were enrolled. Oral informed consent was obtained from their parents. At the time of this study, zidovudine monotherapy was included in standard perinatal care,\(^{10-11}\) so all of the mothers received prenatal zidovudine.

**Measurement**

Demographic characteristics and perinatal history were obtained by interviewing mothers and from medical records.

Growth and neurodevelopmental assessments were performed at 12 months of age using the Bayley Scales of Infant Development (BSID).\(^{12}\) The BSID consists of mental and psychomotor scales. It is widely used to evaluate sensory-perceptual acuity, discrimination and response ability, problem solving ability, verbal communication, and motor coordination skills for infants from 0-42 months of age. The neurodevelopmental assessment was performed by the developmental pediatrician (O.L.). Prematurity was adjusted as per instructions for calculating developmental scores. Results are described as Mental Developmental Index (MDI) and Psychomotor Developmental Index (PDI), which have an average of 100 and a standard deviation of 15. An MDI or a PDI score of less than 85 is considered below average.

The HIV infection status of infants in our study was documented and confirmed at 18 months of age. Because HIV status was not certain in infants at 12 months of age, there was a natural blinding of the examiner during this time.

The study was approved by the Research Ethics Committee of the Faculty of Medicine.

**Statistical analysis**

Data were analyzed by using the SPSS 10.0 program (SPSS Inc, Chicago, IL). A Chi square for proportions and a Student t test for continuous variables were used to compare the two groups. A p value of less than 0.05 was considered statistically significant.
Results

Between January 2001 and December 2002, 40 pairs of infants and caregivers enrolled in the study. Because 1 mother refused her child’s blood test to confirm HIV status at the age of 18 months, 39 infants were studied, including 10 infected cases. Perinatal characteristics including birth weight were no different between HIV infected and non-infected infants (Table 1). More male than female infants were found in the infected group, but there was no statistically different. Infected and uninfected infants were from similar social backgrounds and the mother’s age and education were not significantly different between the two groups. All of the mothers received zidovudine monotherapy prenatally except for one in the non-infected group.

At 12 months of age there was no significant difference in growth parameters between HIV infected and non-infected groups (Table 2). Mean MDI and PDI were significantly lower in HIV-infected infants. Abnormal MDI or PDI was found only in the HIV infected group. Among 10 infected cases, 5 had non-specific HIV symptoms and lower MDI and PDI scores than asymptomatic infected and non-infected infants (Table 3).

Discussion

Of the 39 infants, 10 were found to be infected at the age of 18 months, confirmed by HIV antibodies. There was no difference in characteristic background including gender, growth parameters at birth, or prematurity. In

| Table 1. Demographic and perinatal characteristics of HIV infected and non-infected infants. |
|---------------------------------|-----------------|-----------------|-----------------|
| Gender: male                    | HIV-infected (n=10) | HIV-negative (n=29) | p value |
|                                 | Male 5/10 (50%)    | Male 8/29 (28%)   | 0.25       |
| Prematurity                     | Prematurity 2/10 (20%) | 5/29 (17%)     | 0.59 |
| Birthweight (gm)                | Birthweight 2,679 ± 576 | 2,648 ± 420 | 0.86 |
| Length (cm)                     | Length 47.4 ± 3.2 | 46.9 ± 2.6 | 0.64 |
| Head circumference (cm)         | Head circumference 32.4 ± 1.6 | 32.1 ± 2.4 | 0.75 |
| Maternal age (yr)               | Maternal age 26.5 ± 5.0 | 28.1 ± 4.9 | 0.39 |
| Maternal education (yr)         | Maternal education 9.5 ± 4.7 | 9.5 ± 3.1 | 0.97 |

| Table 2. Growth parameters and developmental indices at 12 months of age of HIV infected and non-infected infants. |
|---------------------------------|-----------------|-----------------|-----------------|
| Age (mo)                        | HIV-infected (n=10) | HIV-negative (n=29) | p value |
|                                 | Age 12.3 ± 0.8 | Age 12.2 ± 0.2 | 0.21 |
| Weight (gm)                     | Weight 9,194 ± 1683 | 9,305 ± 1177 | 0.82 |
| Length (cm)                     | Length 72.4 ± 4.3 | 73.3 ± 2.8 | 0.44 |
| Head circumference (cm)         | Head circumference 45.4 ± 1.6 | 44.8 ± 1.4 | 0.32 |
| Mean mental developmental index | Mean mental developmental index 90.0 ± 9.6 | 99.2 ± 6.4 | 0.001 |
| Mean psychomotor developmental index | Mean psychomotor developmental index 83.3 ± 9.8 | 96.0 ± 7.9 | < 0.001 |
| Abnormal MDI or PDI score       | Abnormal MDI or PDI score 5/10 (50%) | 0/29 (0%) | < 0.001 |
previous studies,\(^{(13-14)}\) birth weight was not associated with the HIV infection status of infants born to HIV-infected women, which was consistent with this study. Maternal age and education were similar between infected and uninfected infants. All but one mother in the uninfected group received prenatal zidovudine. All pregnancies were normal labor without a complication of chorioamnionitis, which has been reported as a risk factor for perinatal transmission of HIV.\(^{(15)}\)

At 12 months of age, when HIV status was not yet definite, growth parameters were no different between infected and non-infected groups. The slower growth of infected infants can occur from HIV-related symptoms, so asymptomatic cases may not show growth failure. However, neurodevelopment quotients in terms of MDI and PDI were found to be significantly lower in infected infants than infants who were HIV exposed but uninfected. The rate of development was reported to be slower in infected infants at 3 months of age, which was much slower over time.\(^{(3)}\) On the contrary, it was also reported that the difference in development was not found until 12 months of age.\(^{(16)}\) The relationship of head circumference and neurodevelopment was not found in this study. Growth impairment might occur later than neurological involvement. A small difference in the growth of infected and non-infected infants was found as early as 3-4 months of age before the time of prenatal zidovudine monotherapy.\(^{(17-19)}\) Below average MDI or PDI score or developmental delay was found only in the infected group.

### Table 3. Mental and Psychomotor Developmental Indices of symptomatic and asymptomatic HIV infected and non-infected infants.

<table>
<thead>
<tr>
<th></th>
<th>HIV-infected Symptomatic (n=5)</th>
<th>HIV-infected Asymptomatic (n=5)</th>
<th>HIV-negative (n=29)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean MDI</td>
<td>88.0 ± 13.3</td>
<td>92.0 ± 4.3</td>
<td>99.2 ± 6.4</td>
<td>0.005</td>
</tr>
<tr>
<td>Mean PDI</td>
<td>79.2 ± 12.7</td>
<td>87.4 ± 3.6</td>
<td>96.0 ± 7.9</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Figure 1. Mental and Psychomotor Developmental Indices in infants of mothers with HIV infection.
In symptomatic cases, MDI and PDI scores were significantly lower than in infected infants who had no symptoms. More severe neurological involvement was described in infants with the clinical manifestations of symptomatic HIV infection.\(^{(20)}\) The study sample was too small to evaluate the effects of HIV status and other variables, such as prematurity and maternal education of less than 9 completed years, which may be associated with low developmental score.\(^{(8)}\)

There were some limitations in this study. The small sample size may affect the statistical result of the study. The study population was not randomized and only some of the demographic data were obtained to compare between infected and non-infected infants.

In summary, our findings documented early abnormal neurodevelopmental outcome in pediatric HIV, infection which were similar to previous studies conducted prior to the time of prenatal zidovudine.\(^{(3-5,16,21-22)}\) Larger sampling and long-term follow up would give more information. Careful monitoring of developmental growth is a necessary component of comprehensive medical care in infants with HIV infection.

References
พัฒนาการระยะแรกของเด็กทารกที่เกิดจากแม่ติดเชื้อเอชไอวี

ฮารุน เลาหเรณู, พ.บ., ธันยวี ภูธนกิจ, พ.บ.,
นงเยาววงศ์นุ, ประกาศนียบัตรผู้ช่วยพยาบาล, วิวัช ศิริสันธะ, พ.บ.

ภาควิชาการวิชาศาสตร คณะแพทยศาสตร มหาวิทยาลัยเชียงใหม

บทคัดย่อ
วัตถุประสงค เพื่อตรวจประเมินพัฒนาการในช่วง 12 เดือนแรกในเด็กทารกที่เกิดจากแม่ติดเชื้อเอชไอวี

วิธีการ ได้ทำการตรวจประเมินพัฒนาการในเด็กทารกที่เกิดจากแม่ติดเชื้อเอชไอวีซึ่งได้รับยา zidovudine ป้องกันขณะตั้งครรภ ที่ได้รับการติดตามในหน่วยโรคติดเชื้อ ศิริราช โรงพยาบาลจุฬาลงกรณ์ ฯ ในเด็กที่มีอายุ 12 เดือนโดยใช้ Bayley Scales of Infant Development (BSID) และทำการตรวจยืนยันสถานะการติดเชื้อเอชไอวีของเด็กเมื่ออายุ 18 เดือน

ผลการศึกษา เด็กจำนวน 39 คน ติดเชื้อ 10 คน และไม่ติดเชื้อ 29 คน ไม่พบความแตกต่างของลักษณะทางสังคมและภาวะระหว่างการคลอด ซึ่งรวมถึงน้ำหนัก ความยาว และส่วนรอบศีรษะเมื่อเทียบกับเด็กที่ไม่ติดเชื้อ ที่อายุ 12 เดือนจากการเจริญเติบโตไม่มีความแตกต่างแต่ค่าดัชนีของพัฒนาการเริ่มจัดอยู่ที่ Mental Developmental Index (MDI) และ Psychomotor Developmental Index (PDI) ที่ต่ำกว่า 90, P= 0.001; PDI=83 และ 96, P<0.001 ตามลำดับ ในกลุ่มเด็กที่ติดเชื้อ เด็กที่แสดงอาการของโรคเอชไอวีมีค่าดัชนีของพัฒนาการต่ำกว่าเด็กที่ไม่มีอาการ

สรุปผลการศึกษา เด็กที่ติดเชื้อเอชไอวีมีผลกระทบต่อพัฒนาการที่แตกต่างจากเด็กที่ไม่ติดเชื้อ เด็กที่แสดงอาการของโรคเอชไอวีมีค่าดัชนีของพัฒนาการต่ำกว่าเด็กที่ไม่มีอาการ

ค่าสำคัญ พัฒนาการ เด็กทารก การติดเชื้อเอชไอวี