ABSTRACT. Objectives. To study the outcome at 2-year corrected age of infants who participated in a double-blind controlled trial of early (<12 hours) dexamethasone therapy for the prevention of chronic lung disease (CLD).

Methods and Materials. A total of 133 children (70 in the control group, 63 in the dexamethasone-treated group) who survived the initial study period and lived to 2 years of age were studied. All infants had birth weights of 500 to 1999 g and had severe respiratory distress syndrome requiring mechanical ventilation within 6 hours after birth. For infants in the treatment group, dexamethasone was started at a mean age of 8.1 hours and given 0.25 mg/kg every 12 hours for 1 week then tapered off gradually over a 3-week period. The following variables were evaluated: interim medical history, socioeconomic background, physical growth, neurologic examinations, mental and psychomotor development index score (MDI and PDI), pulmonary function, electroencephalogram, and auditory and visual evoked potential.

Results. Infants in the control group tended to have a higher incidence of upper respiratory infection and rehospitalization than did the dexamethasone-treated group because of respiratory problems. Although there was no difference between the groups in somatic growth in girls, the dexamethasone-treated boys had significantly lower body weight and shorter height than the control boys (10.7 ± 3.0 vs 11.9 ± 2.0 kg: 84.9 ± 5.7 vs 87.5 ± 4.8 cm). The dexamethasone-treated group had a significantly higher incidence of neuromotor dysfunction (25/63 vs 12/70) than did the control group. The dexamethasone-treated infants also had a lower PDI score (79 ± 26) than the control group (87 ± 23), but the difference was not statistically significant. Both groups were comparable in MDI, incidence of vision impairment, and auditory and visual evoked potential. Significant handicap, defined as severe neurologic defect and/or intellectual defect (MDI and/or PDI ≤ 69), was seen in 22 children (31.4%) in the control group and 26 (41.2%) in the dexamethasone-treated group.

Conclusions. Although early postnatal dexamethasone therapy for 4 weeks significantly reduces the incidence of CLD, this therapeutic regimen cannot be recommended at present because of its adverse effects on neuromotor function and somatic growth in male infants, detected at 2 years of age. A longer follow-up is needed.

If early dexamethasone therapy is to be used for the prevention of CLD, the therapeutic regimen should be modified. The proper route of administration, the critical time to initiate the therapy, and the dosage and duration of therapy remain to be defined further. Pediatrics 1998; 101/5. URL: http://www.pediatrics.org/cgi/content/full/101/5/67; preterm infant, early dexamethasone therapy, follow-up study.

ABBREVIATIONS. CLD, chronic lung disease; RDS, respiratory distress syndrome; EEG, electroencephalogram; VEP, visual evoked potential; BAEP, brainstem auditory evoked potential; BSID, Bayley Scale of Infant Development; BP, blood pressure; PDI, psychomotor development index; MDI, mental development index.

Early postnatal dexamethasone therapy has been used recently for the possible prevention of chronic lung disease (CLD) in preterm infants with respiratory distress syndrome (RDS). However, very few long-term outcome studies have been performed on these infants. In most of the previous follow-up studies, dexamethasone had been given to infants ≥2 weeks of age. Moreover, the study cases were not randomized, used historic control, or had small sample sizes. None of these studies has shown a clear difference in the growth and development between the dexamethasone-treated and control infants.

We have recently conducted a multicenter double-blind trial of early postnatal (<12 hours) dexamethasone therapy for the prevention of CLD. In this study, we have shown that the early dexamethasone therapy was associated with a significant decrease in the incidence of CLD. However, the dexamethasone-treated infants also experienced various transient but significant side effects, including infection and sepsis, hyperglycemia, hypertension, cardiac hypertrophy, hyperparathyroidism, and a delay in weight gain. The present report summarizes the follow-up findings at about 2 years’ postnatal age.

SUBJECTS AND METHODS

All infants born between October 1992 and April 1995 in the six participating hospitals (National Cheng Kung University Hospital, Chang Gung Children’s Hospital, Mackay Memorial Hospital, China Medical College Hospital, Chang Shan Medical College Hospital, and Kuang Tien Hospital) whose birth weights ranged from 500 to 1999 g were eligible for inclusion in the original double-blind multicenter clinical trial. The criteria of selection for the study included 1) severe radiographic RDS, requiring mechanical ventilation within 6 hours of birth, and 2) the absence of prenatal infection, complex congenital anomalies, or lethal cardiopulmonary status. Each infant received either dexamethasone or saline placebo intravenously; the first dose was given within 12 hours.
hours after birth. In the infants who received dexamethasone, the following schedule of dexamethasone sodium phosphate was administered: 0.25 mg/kg/dose bid from day 1 to day 7, 0.12 mg/kg/dose bid from day 8 to day 14, 0.05 mg/kg/dose bid from day 15 to day 21, and 0.02 mg/kg/dose bid from day 22 to day 28. A standard protocol for the management of infants with RDS was followed by the participating hospitals.12 The diagnosis of CLD was made if the infant had 1) respiratory distress requiring supplemental oxygen therapy for ≥28 days and 2) an abnormal chest radiograph. All infants were also observed for possible side effects during the study.

A total of 262 infants were included in the initial study; 130 received saline placebo and 132 received dexamethasone. The result of the study was reported previously.12 In summary, early dexamethasone therapy significantly reduced the incidence of CLD determined either at the 28th postnatal day (21/132 in the dexamethasone-treated group vs 40/130 in the control group) or at the 36th postconceptional week (20/132 in the dexamethasone-treated group vs 37/130 in the control group). The mortality rate was comparable between the two groups (44/132 in the treated group vs 39/130 in the control group). Significantly more infants in the dexamethasone-treated group had bacteremia and/or clinical sepsis (43/132 vs 27/130). Dexamethasone-treated infants had transient hyperglycemia, hypertension, cardiac hypertrophy, hyperparathyroidism, and a transient delay in the rate of weight gain. By postnatal day 28, there was no significant difference between the groups in any of these variables.

Follow-up Study

The follow-up study was performed at about 2 years' postnatal age. Of the 262 infants included in the initial study, 39 in the control group and 44 in the dexamethasone-treated group died during the initial study period. Of the 179 initial survivors, 9 infants in the control group and 13 in the dexamethasone-treated group could not be located. The total number of infants located was 157 (87.7%). However, the follow-up study could not be completed in 3 infants in the control group and 6 infants in the dexamethasone-treated group because of either absence of parental consent or lack of cooperation from the children. In addition, 9 infants in the control group (all had CLD) and 6 in the dexamethasone-treated group (5 had CLD) died during the first 2 years of age. Most of these infants died of respiratory problems. Because none of these infants underwent autopsy, the cause of death could not be well defined. The total number of children included for data analyses was 133 (81% of the survivors who lived to 2 years of age and who could be located); of these, 70 were in the control group and 63 in the dexamethasone-treated group.

The follow-up study was performed at the central participating hospital (National Cheng Kung University Hospital). At each visit, an interim medical history was obtained and a physical examination was performed. Weight, occipitofrontal head circumference, and supine crown–heel length measurements were recorded. Each medical examination was accompanied by a neurologic assessment of mental status, motor development (including coordination, general reflex, muscle tone), and cranial nerves by a pediatric neurologist (C.C.H.). The neuromotor dysfunction was classified as mild, moderate, or severe, based on the mobility of the child, as described by Costello et al.13 Motor dysfunction not severe enough to interfere with the mobility was defined as mild. Dysfunction was defined as moderate if the child was independently mobile when provided hand-holding, and severe if the child was not independently mobile even with hand-holding. A standard 12-lead monopolar and bipolar electroencephalogram (EEG) also was performed and included visual stimulation (visual evoked potential [VEP]) and auditory stimulation (brain stem auditory evoked potential [BAEP]) at 30 and 70 dB by a pediatric neurologist (Y.C.C.). Psychometric evaluations were performed using the Bayley Scale of Infant Development (BSID) by a pediatric psychologist (Y.J.L.). Data were obtained on mental and motor development. The cardiopulmonary status of the infant also was evaluated at each visit. A clinical RDS score of Downes et al.,13 which evaluated the respiratory rate, degree of retraction, color, and level of quiet and active respiratory distress, was used. Arterialized capillary samples were obtained for blood gas and acid-base analysis. Pulmonary function test (BI Core Monitoring System, Inc, Irvine, CA) was performed to measure tidal volume, respiratory rate, and total dynamic lung compliance and resistance.

All tests were performed in the presence of the infant’s mother or guardian, with the examiners completely blinded to group assignment. For analysis of physical growth and developmental performance, the infant’s postnatal age was corrected by the degree of prematurity before term (40 weeks).

Infants were from one ethnic group of Chinese descendants. Data on family background and socioeconomic status were obtained from parents or, occasionally, from a guardian. Maternal education level was classified into four categories: below high school graduation (compulsory 9-year education), high school graduate (12 years), some college education (12 to 16 years), and college graduate (>16 years). The average annual income per capita in Taiwan is about US $14,000. Family income was probably underreported because this information was obtained only through verbal communication. The father’s occupation was evaluated using a scoring system modified from Hollingshead and Redlich,14,15

Statistics

Analysis of variance and, where appropriate, the t test were used to make group comparisons for continuous variables. The χ2 test was used to compare groups with respect to categoric variables. The simple two-variable regression analysis was used to compare the values of a selective continuous variable with the corresponding values of other selective continuous variables. Multiple correlations were performed to evaluate the outcome at 2 years' postnatal age in relation to perinatal and neonatal factors. Except where indicated otherwise, values are specified as mean ± SD.

RESULTS

Perinatal Period

The clinical and biochemical characteristics in the perinatal period of the follow-up study infants are shown in Table 1. All variables showed no significant differences between the control and dexamethasone-treated groups. There also was no significant difference between the groups with respect to inborn or outborn status (14/70 vs 13/63) and proportion of prenatal glucocorticoid therapy (21/70 vs 21/63). None of the mothers were drug abusers. The initial cardiopulmonary status on admission to the neonatal intensive care unit also was comparable between the groups. The mean postnatal age at the time of the first dose of dexamethasone was 8.1 ± 2.8 hours.

| TABLE 1. The Clinical and Biochemical Characteristics in the Perinatal Period |
|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
|                        | Control Infants (n = 70) | Dexamethasone-treated Infants (n = 63) |
| Gestational age (wk)   | 29.4 ± 2.4              | 30.3 ± 2.2              |
| Birth weight (g)       | 1364 ± 353             | 1420 ± 305             |
| Head circumference (cm)| 27.3 ± 2.4              | 27.7 ± 1.9              |
| Length (cm)            | 39.5 ± 4.0             | 39.3 ± 4.4             |
| Sex (M/F)              | 36/34                  | 33/30                  |
| AGA/SGA                | 56/14                  | 47/16                  |
| Mode of delivery       |                        |                        |
| C-section              | 33                     | 35                     |
| Vaginal                | 37                     | 28                     |
| Appgar score           |                        |                        |
| 1 Min ≤3               | 18                     | 16                     |
| 4–6                    | 31                     | 29                     |
| >6                     | 21                     | 18                     |
| 5 Min ≤3               | 4                      | 2                      |
| 4–6                    | 22                     | 14                     |
| >6                     | 44                     | 47                     |
| Prenatal steroid therapy | 21                   | 21                     |
| Age of study (h)       | 7.8 ± 3.5              | 8.1 ± 2.8              |
| mean ± SD              |                        |                        |
Initial Hospital Course

Clinical features during the initial hospital course that may affect the long-term prognoses are shown in Table 2. More infants in the control group than in the dexamethasone-treated group had CLD (26/70 vs 13/63) but the difference was not statistically significant. Infants in the dexamethasone-treated group had a significantly lower incidence of clinical patent ductus arteriosus and required a shorter duration of high O₂ therapy (FiO₂ > 0.4) than did the control infants. There was no significant difference between the groups in the incidence of intraventricular hemorrhage (≥Gr II), retinopathy of prematurity, and duration of mechanical ventilation, total supplemental O₂ therapy, and hospitalization. Eight infants in the control group and 5 in the dexamethasone-treated group who had severe CLD required the open steroid therapy after completion of the initial study. The open steroid therapy (0.25 mg/kg/q 12 hours) was given only to infants who were respirator-dependent. The duration of therapy usually lasted for 4 to 7 days. The purpose of steroid therapy in these infants was primarily for facilitating weaning from intermittent mechanical ventilation. Steroid therapy was usually discontinued after a maximum of 7 days. Because of the small number of infants receiving the open steroid therapy and the relatively short duration of therapy, these infants were not excluded from the follow-up study. Of the 8 infants in the control group who received open steroid therapy, 5 had neuromotor dysfunction (1 severe, 2 moderate, and 2 mild). Of the 5 infants in the dexamethasone-treated group who received open steroid, 3 had neuromotor dysfunction (2 severe, 1 moderate).

Social History

The socioeconomic status of the family is shown in Table 3. Both groups were comparable with respect to the maternal age, maternal education levels, father’s occupation, and family income. Most of the children came from middle class families. Sixty-eight parents in the control group and 62 in the dexamethasone-treated group had middle class families. Sixty-eight parents in the control group and 62 in the dexamethasone-treated group lived together. Two parents in the control group and one in the dexamethasone-treated group were widowed, separated, or divorced from their spouse and living alone. Sixty-seven children in the control group and 61 in the dexamethasone-treated group were living with their natural parent. Three children in the control group and 2 in the dexamethasone-treated group were living with grandparents or guardians.

General Health

The mean postnatal age at the time of follow-up was 27.4 ± 5.4 months for the control group and 26.7 ± 4.6 months for the dexamethasone-treated group. The corrected age was 25.4 ± 5.4 months for the control group and 24.3 ± 4.4 months for the dexamethasone-treated group. Three infants in the control group, who had CLD, still had mild respiratory distress at the time of follow up; two of three required supplemental oxygen therapy. One infant in the dexamethasone-treated group had clinical respiratory distress but did not require supplemental O₂ therapy. Nineteen infants (17 with CLD) in the control group and 12 (9 with CLD) infants in the dexamethasone-treated group required rehospitalization; this difference was not statistically significant. There was no difference between the groups in the incidence of frequent upper respiratory infection (32/70 vs 23/63), defined as >10 upper respiratory infections per year. Blood pressure (BP) was comparable between the control and dexamethasone-treated infants at the time of follow-up (systolic BP, 98 ± 15 vs 96 ± 20 mm Hg; diastolic BP, 44 ± 12 vs 46 ± 18).

Twenty-one infants in the control group and 17 in the dexamethasone-treated group had eye problems. Strabismus was seen in 12 control and 8 dexamethasone-treated infants, nystagmus in 6 control and 4 dexamethasone-treated infants, and significant vision impairment in 3 control and 5 dexamethasone-treated infants.

Physical Growth

The body weight, height, and head circumference of the individual male and female child are plotted, based on their corrected age, on the growth chart for Chinese children (Figs 1 and 2). In the girls, there was

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**TABLE 2.** The Initial Outcome and Hospital Course of Infants Included for the Follow-up Study

<table>
<thead>
<tr>
<th></th>
<th>Controls (n = 70)</th>
<th>Dexamethasone-treated (n = 63)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLD</td>
<td>26</td>
<td>13</td>
<td>—</td>
</tr>
<tr>
<td>Intraventricular hemorrhage (≥Gr II)</td>
<td>21</td>
<td>22</td>
<td>—</td>
</tr>
<tr>
<td>Sepsis</td>
<td>11</td>
<td>15</td>
<td>—</td>
</tr>
<tr>
<td>Patent ductus arteriosus</td>
<td>23</td>
<td>8</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Retinopathy of prematurity</td>
<td>9</td>
<td>9</td>
<td>—</td>
</tr>
<tr>
<td>Duration of intermittent mechanical ventilation (d)</td>
<td>9.3 ± 10.1</td>
<td>8.4 ± 8.2</td>
<td>—</td>
</tr>
<tr>
<td>Duration of supplemental O₂ therapy (d)</td>
<td>24.3 ± 11.4</td>
<td>23.4 ± 11.6</td>
<td>—</td>
</tr>
<tr>
<td>Duration of supplemental O₂ (FiO₂ &gt; 0.4) therapy (d)</td>
<td>11.6 ± 4.1</td>
<td>7.1 ± 6.5</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Duration of hospitalization (d) mean ± SD</td>
<td>59 ± 21</td>
<td>56 ± 11</td>
<td>—</td>
</tr>
</tbody>
</table>

**TABLE 3.** Socioeconomic Status of the Study Infants

<table>
<thead>
<tr>
<th></th>
<th>Control Infants (n = 70)</th>
<th>Dexamethasone-treated Infants (n = 63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (y)</td>
<td>26.7 ± 4.3</td>
<td>27.1 ± 6.4</td>
</tr>
<tr>
<td>Maternal education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not high school graduate</td>
<td>26</td>
<td>19</td>
</tr>
<tr>
<td>High school graduate</td>
<td>37</td>
<td>33</td>
</tr>
<tr>
<td>Some college</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>College graduate</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Family income (US dollars/y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;7500</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>7501–15 000</td>
<td>40</td>
<td>30</td>
</tr>
<tr>
<td>15 000–30 000</td>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td>30 000–45 000</td>
<td>35</td>
<td>1</td>
</tr>
<tr>
<td>&gt;45 000</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Occupation score (mean ± SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Father</td>
<td>4.9 ± 1.1</td>
<td>5.0 ± 1.4</td>
</tr>
<tr>
<td>Mother</td>
<td>6.8 ± 1.9</td>
<td>6.4 ± 2.1</td>
</tr>
<tr>
<td>mean ± SD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
no significant difference between the control and dexamethasone-treated groups with respect to mean body weight (10.8 ± 2.1 vs 10.6 ± 1.8 kg), height (84.2 ± 5.8 vs 83.8 ± 6.0 cm), and head circumference (46.2 ± 1.9 vs 46.1 ± 2.1 cm). There also was no significant difference between the groups with respect to distribution of weight, height, and head circumference on the growth chart. Five infants in the dexamethasone-treated group and eight infants in the control group had body weight below the third percentile. None in the dexamethasone-treated group and one in the control group had height below the third percentile.

In the boys, there was no significant difference between the control and dexamethasone-treated groups in head circumference (47.2 ± 1.8 vs 47.1 ± 2.0 cm). However, the body weight was significantly lower ($P < .05$) and height significantly shorter ($P < .05$) in the dexamethasone-treated group than in the control group (10.7 ± 3.0 vs 11.9 ± 2.0 kg and 84.9 ± 5.7 vs 87.5 ± 4.8 cm, respectively). Five infants in the dexamethasone-treated group and one in the control group had height below the third percentile.

![Graph](image-url)
group had body weight below the third percentile. Three infants in the dexamethasone-treated group and none in the control group had height below the third percentile.

Neurologic Assessment

Six children in the control group and seven in the dexamethasone-treated group had a history of clinical seizure. Table 4 summarizes the neurologic diagnosis. A greater proportion of infants in the dexamethasone-treated group (25/63) than in the control (12/70) group had abnormal neurologic examination ($P < .01$). More infants in the dexamethasone-treated group than in the control group were likely to have diplegia and hypotonia. Classifying the severity of neuromotor dysfunction as defined in “Subjects and Methods,” more infants in the dexamethasone-treated group (13/63) than in the control group (4/
with neuromotor dysfunction. Paroxysmal dis-
fast activity was reported to be seen often in infants
found over the area past the frontal region. Excessive
per second occurred during wakefulness and were
defined if there was a considerable amount of fast
activity with frequencies of predominantly 20 to 26
spike activity was seen in 2 infants in the control
spike activity was seen in 2 infants in the control
combined paroxysmal and nonparoxysmal abnor-
activity was seen in 2 infants in the control group.
nonparoxysmal discharge with local slow
spike activity was seen in 2 infants in the control
group and in 2 infants in the dexamethasone-treated
group. Nonparoxysmal discharge with local slow
activity was seen in 2 infants in the control group
and 2 infants in the dexamethasone-treated
group. Combined paroxysmal and nonparoxysmal abnor-
malities were seen in 1 infant in the control group
and in 1 infant in the dexamethasone-treated group.
No significant correlation could be shown between
the abnormal EEG patterns and neurologic outcome.
There was no significant difference between the
groups either in proportion of abnormal BAEP (with
30 dB, 4/70 vs 4/63; with 70 dB, 3/70 vs 4/63) or in
the mean values of amplitude and interval of BAEP
and VEP.

 Intellectual Development (Table 5)
The mean mental development index score (MDI)
was 78 ± 20 for the control group and 74 ± 21 for the
dexamethasone-treated group. This difference in
MDI between the groups was not statistically
significant. The mean psychomotor developmental
index score (PDI) for the dexamethasone-treated

group was 79 ± 26 and for the control group was 87 ± 23.
This difference also was not statistically significant.
Sixteen infants in the control group (23%) and 25 in
the dexamethasone-treated group (39%) had PDI
scores of ≤69. This difference in proportion of infants
with PDI ≤69 between the groups was not statistically
significant. The proportion of infants with PDI
<85 also was comparable between the groups (28/70
vs 36/63). Both PDI and MDI were <69 for the 2
children in the control group and the 5 in the dexam-
ethasone-treated group who had severe neurologic
defects.

 Significant Handicap With Severe Neurologic and/or
Intellectual Defects
The total number of children with significant
handicap, either from severe neurologic defects as
defined in “Subjects and Methods” or from signifi-
cant intellectual defects (PDI and/or MDI ≤69), was
seen in 22 (31.4%) children in the control group
and 26 (41.2%) in the dexamethasone-treated group.
This difference in proportion of infants with significant
handicap between the groups was not statistically
significant.

 Correlation of Significant Handicap With Perinatal
Events and Neonatal Course
Comparison of infants with significant handicap
and those without handicap within the control group
showed no significant difference in perinatal charac-
teristics and neonatal course. Similarly, comparison
of infants with significant handicap and those with-
out handicap within the dexamethasone-treated
group showed no significant difference in perinatal
characteristics and neonatal course. However, when
comparison of infants with handicap and those with-
out handicap of all infants studied was performed,
more infants in the handicapped group were likely to
have been born by vaginal delivery (30/48 [63%] vs
35/85 [41%]) and to have required intubation imme-
diately after birth (26/48 [54%] vs 31/85 [36%]), sug-
 resting that they were probably more sick at birth.
There was no significant difference between the
handicapped and nonhandicapped children in inci-
dence of prenatal steroid therapy or in Apgar score
at birth (26/48 [54%] vs 31/85 [36%]), suggesting that
they were probably more sick at birth.

 The incidence of severe neurologic dysfunction was
comparable between the groups (2/70 vs 5/63).

 EEG, BAEP, and VEP
Fifteen infants in the control group (21.4%) and 15
infants in the dexamethasone-treated group (23.8%)
had abnormal EEG findings. More infants in the
dexamethasone-treated group than in the control
group were likely to have excessive fast activity
(8/63 vs 2/70; P > .05). Excessive fast activity was
defined if there was a considerable amount of fast
activity with frequencies of predominantly 20 to 26
per second occurred during wakefulness and were
found over the area past the frontal region. Excessive
fast activity was reported to be seen often in infants
with neuromotor dysfunction. Paroxysmal dis-
charge with focal spike/sharp wave activity was seen
in 9 infants in the control group and in 6 infants
in the dexamethasone-treated group, and multiple
spike activity was seen in 2 infants in the control
group and in 2 infants in the dexamethasone-treated
group. Nonparoxysmal discharge with local slow
activity was seen in 2 infants in the control group
and 2 infants in the dexamethasone-treated group.

### Table 4. Neurologic Assessment at ~2 Years of Age

<table>
<thead>
<tr>
<th>Severity</th>
<th>Normal</th>
<th>Borderline</th>
<th>Abnormal</th>
<th>Tetraparesis</th>
<th>Hemiparesis</th>
<th>Diplegia</th>
<th>Hypotonia</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>55</td>
<td>3</td>
<td>12</td>
<td>2</td>
<td>3</td>
<td>6</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Dexamethasone-treated</td>
<td>37</td>
<td>1</td>
<td>25</td>
<td>4</td>
<td>4</td>
<td>12</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

P < .05.

### Table 5. Developmental Assessment (BSID II) (MDI, PDI)

<table>
<thead>
<tr>
<th>Events and Neonatal Course</th>
<th>Control Infants (n = 70)</th>
<th>Dexamethasone-treated Infants (n = 63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDI</td>
<td>78 ± 20</td>
<td>74 ± 21</td>
</tr>
<tr>
<td>85–114</td>
<td>24</td>
<td>22</td>
</tr>
<tr>
<td>70–84</td>
<td>21</td>
<td>13</td>
</tr>
<tr>
<td>≤69</td>
<td>22</td>
<td>26</td>
</tr>
<tr>
<td>PDI</td>
<td>87 ± 23</td>
<td>79 ± 26</td>
</tr>
<tr>
<td>85–114</td>
<td>37</td>
<td>20</td>
</tr>
<tr>
<td>70–84</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>≤69</td>
<td>16</td>
<td>25</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

60 of 8 FOLLOW-UP STUDY ON EARLY DEXAMETHASONE THERAPY

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Glucocorticoids have been used for years in infants with bronchopulmonary dysplasia. The use of steroid was often associated with short-term benefits of improving lung compliance and facilitating the early removal of the endotracheal tube. Glucocorticoids recently have been given early in postnatal life for possible prevention of CLD. The results of these studies were mixed, and some were conflicting. It is difficult to interpret these results because each of these studies was designed differently with respect to the time of initiating therapy, dosage and duration of therapy, and the sample size. In our multicenter double-blind trial, we have demonstrated a significant decrease in incidence of CLD associated with early dexamethasone therapy. However, the mortality rate was not decreased, possibly because more infants died of infection and sepsis. Side effects associated with dexamethasone therapy were transient, including hyperglycemia, hypertension, cardiac hypertrophy, hyperparathyroidism, and a delay in weight gain.

The long-term side effects of early dexamethasone therapy have not been well studied, although this concern has been emphasized by various investigators. Mammal et al followed eight ventilator-dependent infants with bronchopulmonary dysplasia who were treated with dexamethasone (0.5 mg/kg/day) for 7 days and then tapered over 2 weeks. The authors could not find any significant long-term sequelae at 1 year of age in these infants compared with eight similar ventilator-dependent infants. In this study, the first dose of dexamethasone was given at 2 weeks' postnatal age. Cummings et al conducted a double-blind trial on 36 preterm infants who were dependent on oxygen and mechanical ventilation at 2 weeks of age. The authors concluded that dexamethasone therapy for 42 days improved pulmonary and neurodevelopmental outcome when followed at 6 and 15 months of age. 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We conclude that although early postnatal dexamethasone therapy significantly reduced the incidence of CLD in preterm infants with RDS, this therapeutic regimen cannot be recommended at present because of its adverse effects on neuromotor function and somatic growth detected at 2 years of age. A longer follow-up is needed. The results of our study also raise a serious caution about glucocorticoid therapy that was commonly used in infants with established CLD. We strongly suggest that if dexamethasone is to be used for early prevention of CLD, a modification of the therapeutic regimen is needed. The proper route of administration, the time of starting the therapy, and the dosage and duration of therapy remain to be studied further.

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