Dexamethasone Therapy in Chronic Lung Disease

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Abstract. Steroids have been used in the treatment of infants with chronic lung disease (CLD) for over a decade. Some studies have reported beneficial effects from long, tapering 42-day course of dexamethasone. Short term regimens have also shown beneficial effects on ventilator dependent infants with CLD. Although steroid therapy has been successful in infants with established CLD, more recently, dexamethasone therapy is being initiated in infants with RDS considered to be at risk for developing CLD. Some of the initial studies reported higher rates of infection, but more recent prospective data have not shown an increased incidence of sepsis in patients treated with steroids. Presently, early steroid therapy appears to be beneficial to minimize lung injury in infants treated with surfactant (Indian J Pediatr 1996; 63: 61-64)

Key words: Dexamethasone, Steroids, Chronic lung disease, Low birth weight infants.

Corticosteroid treatment of infants with chronic lung disease (CLD) was introduced in 1978 by Kramer and Hultzen. Since then, a diverse number of clinical studies have applied corticosteroids (dexamethasone) to preterm infants with or at risk for CLD. Except for one study of aerosolized dexamethasone, all other clinical trials have used either parenteral or enteral treatment. Although steroids have a number of potential beneficial effects, the precise mechanism of action of corticosteroids in infants with CLD still remains a topic of speculation. Several mechanisms such as stabilization of cell and lysosomal membranes, increase in surfactant synthesis, stimulation of anti-oxidant enzyme activity, inhibition of prostaglandin and leukotriene synthesis, enhanced β adrenergic activity and reduction in pulmonary edema have been suggested for the improvement in ventilator dependent infants. It is unclear which potential mechanism of action plays a greater role in the improvement of lung function in these infants, thereby making treatment decisions difficult.

Apparent beneficial outcomes have been noted with both short-term and long-term regimens of steroid therapy. However, the ideal dose of dexamethasone and the duration of treatment to minimize lung injury with minimal side effect are unknown.

LONG-TERM REGIMEN VERSUS SHORT-TERM REGIMEN OF STEROID THERAPY

For the last several years many investigators have looked at the effect of steroids on ventilator dependent infants with CLD. These studies have employed long-term and short-term treatment regimens, and...
have administered steroids to a variety of patient populations. Cummings and co-workers reported a beneficial effect only from a long, tapering, 42-day course of dexamethasone. Despite the effectiveness of the long-term regimen, many centers use short-term steroid treatment regimens because one of the major concerns about long-term therapy has been infection. In the study by Mammel et al, 83% rate of infection was noted in infants treated with dexamethasone therapy for one to four months. Although studies have differed somewhat in detail, most studies using short-term regimens have shown a reduced need for mechanical ventilation and oxygen support and have been associated with earlier extubation. In our recent publication, we have demonstrated that a 1-week course of early dexamethasone improved pulmonary compliance and increased survival without CLD in very low birth weight infants.

**Early Versus Late Postnatal Steroid Therapy in Preterm Infants with Severe Respiratory Distress Syndrome (RDS)**

Initial clinical trials with dexamethasone therapy were concentrated on infants with well established CLD. Yoder et al demonstrated that 72 hours of dexamethasone in infants with established CLD significantly improved compliance and reduced ventilatory support. More recent studies have examined the role of dexamethasone therapy in infants with RDS felt to be at risk for developing CLD. Pathologic changes consistent with early CLD are seen by 7 to 11 days of age in premature baboons and probably earlier in premature human neonates. Yeh et al have demonstrated improved pulmonary compliance and decreased need for mechanical ventilation when dexamethasone treatment was initiated as early as < 12 hours of age. In our study we used dexamethasone as early as 7-14 days of age and demonstrated a significant increase in respiratory compliance, a reduction in the duration of mechanical ventilation, and a decrease in CLD in a population of very low birth weight infants largely treated with surfactant. Early postnatal dexamethasone treatment seems logical, in that bronchial inflammation already present could be modulated to minimize chronic lung injury.

**Adverse Effects of Steroid Therapy**

*Short-term adverse effects*

Safety of corticosteroid therapy in infants with CLD has always been a concern. Initial studies reported high rates of infection in preterm infants treated with steroids. However, subsequent prospective studies involving larger number of patients have not shown an increase in incidence of sepsis in patients treated with steroids when compared to control infants. The potential adverse effects of a short course of steroid therapy on the hypothalamic-pituitary-adrenal axis have been studied. Most of the reports have shown that these effects are transient. Brundage et al in their study using 0.5 mg/kg/day of dexamethasone for 7 days reported no adrenal suppression.

Dexamethasone may increase blood pressure and blood glucose, but neither of the effect poses a serious risk. Werner et al from their trial concluded that transient myocardial hypertrophy can occur with prolonged courses of dexamethasone therapy. Reports on the effects of dexamethasone on retinopathy of prema-