Lowest effective dose of dexamethasone in the respiratory care of very preterm infants

Title

1. Journal: Early Human Development

2. Category: Letter to the Editor

3. Title: Lowest effective dose of dexamethasone in the respiratory care of very preterm infants

4. Authors: Hirokazu Tsukahara MD/PhD, Mitsufumi Mayumi MD/PhD
Department of Pediatrics, Faculty of Medical Sciences, University of Fukui, Fukui 910-1193, Japan

6. Correspondence: Hirokazu Tsukahara MD/PhD
Department of Pediatrics, Faculty of Medical Sciences, University of Fukui, Fukui 910-1193, Japan (TEL: +81-776-61-3111; FAX: +81-776-61-8129; E-mail: htsuka@fmsrsa.fukui-med.ac.jp)

To the Editor:

Recently, we had the opportunity to read the article by Doyle et al [1]. Prior studies of the 1980s used considerably large cumulative doses of dexamethasone (DEX) for preterm infants (usually > 3 mg/kg over 1–6 weeks, started after 2 weeks of age). Newer studies in the 1990s applied DEX to preterm infants with respiratory distress deemed to be at risk for developing BPD. Early postnatal administration of DEX (started before 2 weeks of age) has been based on this contention. The cumulative DEX doses in the *early* protocols were considerably lower (usually < 3 mg/kg) than in the *delayed* protocols. It is noteworthy that the very preterm infants studied by Doyle et al. received lower end of the range of doses used for any reported trials (0.89 mg/kg over 10 days, started at 0.15 mg/kg per day). In 1999, we reported that early (4–7 days of age) low-dose DEX therapy (0.125 mg/kg, every 12 h, for 6 doses) facilitated extubation and improved the clinical outcome in preterm infants with respiratory distress [2]. Infants in our study were somewhat mature at birth than were those in the study by Doyle et al. (mean gestational age: 28 weeks vs. 25 weeks). Absence of significant steroid adverse effects is probably explained by the low doses of DEX treatments in both studies.

Jobe [3] stated that the “standard” initial dose of 0.5 mg/kg per day DEX (equivalent to 12 mg of cortisol) is extremely high relative to the 24-h basal production rate of about 0.5 mg cortisol for a preterm infant weighing 1 kg and a stress production rate of about 1.5 mg per day. The initial dose of 0.1–0.2 mg/kg per day DEX should be sufficient and might be too high for preterm infants. The dose and duration of DEX therapy should be limited to the minimum necessary to achieve the desired effects. Recently, we conducted an observational study in which we used an even lower dose of DEX (0.06 mg/kg, once or twice per day) for an even shorter interval (1–2 days) [4]. Short-term beneficial clinical effects were readily apparent. For that reason, it can be recommended that a low dose (0.06 mg/kg, once or twice per day) of DEX be administered to very preterm infants at risk for BPD as a short-term (1–2 days) pulse – with administration started at 4–7 days of age and repeated periodically (e.g. once per week) if necessary – to provide treatment benefits while attenuating the risk of possible adverse effects.

Preterm infants with BPD are now much less mature than originally described over 30 years ago. In addition to its changing epidemiology, the nature of BPD has also evolved, such that pathological signs of severe chronic lung injury with striking fibrosis and cellular proliferation are less common. Disruption of the normal sequence of lung development, engendering alveolar simplification and dysmorphic vascular growth, is the hallmark of *new BPD*. We hope that new

strategies for maturing very preterm lung (e.g., using angiogenic factors or tissue survival factors) can yield treatment alternatives and minimize the cumulative DEX doses in the respiratory care of very preterm infants.

References

[1] Doyle LW, Davis PG, Morley CJ, McPhee A, Carlin JB; DART Study Investigators. Low-dose dexamethasone facilitates extubation among chronically ventilator-dependent infants: a multicenter, international, randomized, controlled trial. Pediatrics. 2006; 117: 75-83.

[2] Tsukahara H, Watanabe Y, Yasutomi M, Kobata R, Tamura S, Kimura K, Hiraoka M, Mayumi M. Early (4–7 days of age) dexamethasone therapy for prevention of chronic lung disease in preterm infants. Biol Neonate. 1999; 76: 283-290.

[3] Jobe AH. Glucocorticoids in perinatal medicine: misguided rockets? J Pediatr. 2000; 137: 1-3.

[4] Tsukahara H. Early postnatal steroid therapy for preventing chronic lung disease in preterm infants. Perinat Med 2002; 32: 777-784 (in Japanese).