Eur J Pediatr (1996) 155:573–575

K. Smets
P. Vanhaesebrouck

Dexamethasone associated systemic hypertension in low birth weight babies with chronic lung disease

Received: 4 July 1995
Accepted: 17 October 1995

K. Smets (✉) · P. Vanhaesebrouck
University Children's Hospital 'C. Hooft',
Neonatal Intensive Care Unit,
De Pintelaan 185, B-9000 Ghent, Belgium
Fax: 00 32 9 240 38 29

Abstract To assess the role of dexamethasone treatment as a cause of systemic hypertension and associated complications, blood pressure was registered prospectively before, during and after a 4-week dexamethasone course in 22 neonates with chronic lung disease. In all patients systolic blood pressure rose significantly during treatment (median rise 34 mm Hg, range 4→59 mm Hg), without complications attributable to hypertension. In all but one patient blood pressure returned to pretreatment values within 2 weeks after stopping dexamethasone treatment.

Conclusion Dexamethasone induced hypertension is transient, even after a 4-week course, and is not associated with hypertensive complications, so treatment is not necessary. When hypertension persists after dexamethasone withdrawal other causes should be considered.

Key words Hypertension · Dexamethasone · Chronic lung disease

Introduction

Bronchopulmonary dysplasia is frequently complicated by systemic hypertension and dexamethasone treatment is one of the contributing factors [1, 11–13]. Some reports suggest dexamethasone induced hypertension is transient [12, 13]. Several complications attributed to hypertension are reported in the literature and raise the question of indications for treatment [1, 5, 7, 9]. We anticipated that dexamethasone induced hypertension is indeed transient and well tolerated and does not need to be treated immediately. We therefore prospectively registered blood pressure before, during and after a 4-week dexamethasone course in babies with chronic lung disease and looked for complications that might be associated with dexamethasone induced hypertension.

Patients and methods

Twenty-two patients (11 males, 11 females) were included in the study. Their median birth weight was 1087 g (714–1920 g) and gestational age 30 weeks (25–36 weeks). Steroid treatment was started at the median age of 25 days (8–56 days). Chlorothiazide and spironolactone were given to all patients as part of the overall management of infants with chronic lung disease. No patient was treated with theophylline.

Infants were selected for steroid treatment when they remained oxygen dependent beyond the 1st week of life and showed no improvement in oxygen dependency during the previous 3–5 days, after exclusion of treatable conditions, such as patent ductus arteriosus, idiopathic persistent pulmonary hypertension, congenital heart disease and sepsis or pneumonia. In all patients dexamethasone was administered during a 4-week course: 0.6 mg/kg per day for 3 days, then 0.3 mg/kg per day for 3 days with subsequent tapering of the dose over a 3-week period.

Blood pressure was measured by a noninvasive oscillometric method. At least 30 measurements per 24 h were available, from which the mean value of the systolic pressure was calculated for follow up. Registration continued for 3 weeks after the end of dexamethasone treatment.

During the observation period the neurological status was assessed by clinical examination and brain ultrasound. When high systolic blood pressure was noted an electrocardiogram was performed looking for left and/or right ventricular hypertrophy. From the 40th postnatal day, an examination of the retina was done repeatedly as a routine screening for retinopathy of prematurity.

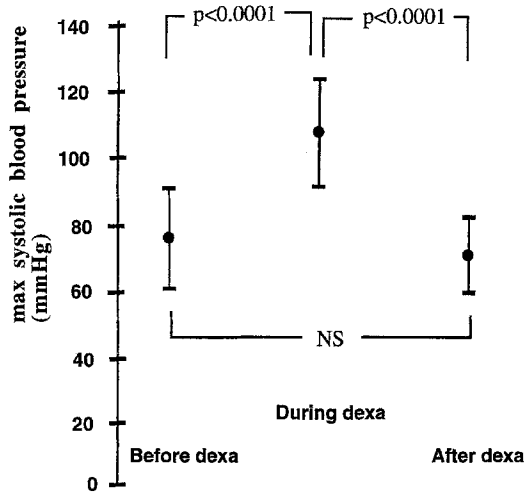

Fig 1 Maximal systolic blood pressure (mean ± SD) before, during and 2 weeks after dexamethasone (*dexa*) treatment in 22 patients with chronic lung disease. *NS* not significant ($P = 0.19$)

Table 1 Numerical data

Patient number	Systolic blood pressure before treatment	Systolic blood pressure during treatment	Systolic blood pressure after treatment
1	82	116	68
2	86	113	100
3	82	117	59
4	66	101	85
5	79	124	71
6	75	116	79
7	88	121	75
8	47	95	57
9	58	109	73
10	62	121	80
11	99	115	77
12	87	145	75
13	62	96	54
14	97	101	80
15	93	123	82
16	75	96	75
17	66	107	60
18	93	108	69
19	48	66	64
20	69	94	54
21	70	88	68
22	92	103	61

According to DeSwiet et al. [4] we defined systemic hypertension as a systolic blood pressure repeatedly above 113 mm Hg (P95); antihypertensive treatment, however, was considered only if associated complications were documented.

Results

Mean systolic blood pressure rose significantly ($P < 0.0001$) during dexamethasone treatment (Fig. 1, Table 1). In nine patients systolic pressure rose above 113 mm Hg. In one of them treatment with hydralazine was started because of a systolic blood pressure above 140 mm Hg. The median rise in systolic blood pressure was 34 mm Hg (range 4→59), with a maximum blood pressure after a median of 8 days (range 2→24) of dexamethasone treatment. In all but one patient systolic blood pressure was < 95 mm Hg 2 weeks after the end of steroid treatment ($P < 0.0001$). There was no significant difference in systolic blood pressure before starting and 2 weeks after the end of the dexamethasone treatment ($P = 0.19$). Hypertension was not complicated by left heart failure or signs of left ventricular hypertrophy on electrocardiogram. On routine ophthalmological examination, no signs of hypertensive vascular changes were noted.

Discussion

To evaluate the causal role of dexamethasone in systemic hypertension in infants with chronic lung disease we deliberately did not choose a placebo-controlled trial. Although it has not been established that long-term pulmonary or neurodevelopmental outcome is improved, the acute short-term improvement in pulmonary function with earlier weaning from mechanical ventilation makes it rather unacceptable to give placebo to infants in whom dexamethasone treatment is clinically indicated. Concern about the potential adverse effects of dexamethasone precludes the treatment of infants in the absence of a clear indication. The study of the adverse effects of dexamethasone therefore cannot be realised without the confounding influence of the underlying disease. By using our pretreatment blood pressure as control data for each patient individually, the influence of the numerous other factors contributing to systemic hypertension in chronic lung disease was probably eliminated.

The definition of hypertension is controversial and not easy in newborns since blood pressure is related to postnatal age [5]. Anand gives values for severe hypertension related to birth weight in preterm neonates: < 1000 g = RR_s > 70 mm Hg; 1000–1500 g = RR_s > 80 mm Hg; 1501–2500 g = RR_s > 90 mm Hg [2]. DeSwiet et al. [4] defined hypertension as a systolic blood pressure greater than 113 mm Hg, being the 95th percentile for blood pressure in infants studied between 6 weeks and 1 year of age, who were awake at the moment of investigation. Harkavy et al. [8] considers as hypertension a systolic blood pressure above 100 mm Hg. Abman et al. [1] defined arterial hypertension as three times a RR_s > 115 mm Hg in patients with oxygen therapy at home during the 1st year of life. According to DeSwiet et al. [4] we defined hypertension as a systolic blood pressure greater than 113 mm Hg.

Hypertension as a complication of dexamethasone treatment is repeatedly reported in literature [12, 13]. In some patients there is a significant rise in blood pressure, both systolic and diastolic, without development of hyper-

tension [5, 7]. Fauser et al. [6] showed that blood pressure rose and diuresis increased after administration of a single dose of dexamethasone (0.25 mg/kg) in hypotensive extreme low birth weight babies who were treated with vasopressors and catecholamines without succes. Emery and Greenough [5] showed that both early and late treatment with dexamethasone can raise systolic pressure significantly in premature babies independent of their postnatal and postconceptional age. Brozanski et al. [3] evaluated the effect and side-effects of pulse dexamethasone therapy started at 7 days postnatal age in very low birth weight infants at high risk of having chronic lung disease. Mean arterial pressure increased in a transient way in the pulse therapy group during each administration of study drug, but no infant could be classified as hypertensive. In the studies of Yeh et al. [13] and Werner et al. [12] there was no significant difference in blood pressure between dexamethasone treated babies and controls 2 and 4 weeks after treatment had ceased. Their findings suggest that dexamethasone induced hypertension is not chronic and that persisting hypertension must be explained by other factors.

In our patients there was a significant rise in systolic blood pressure during dexamethasone treatment, occurring mostly within the first 2 weeks of treatment. In only 9/22 did systolic pressure exceed 113 mm Hg and hypertension did not persist after stopping treatment. No complications attributable to arterial hypertension were present. The rather low occurrence of very high blood pressures and the lack of complications may be explained by the systematic administration of diuretics as part of the respiratory management of chronic lung disease, but this was not proven since all our patients were equally treated. Hydrochlorothiazide blocks chloride and sodium retention in the kidney and spironolactone acts by an aldosterone inhibiting effect. Sodium retention and hyperaldosteronism are factors contributing both to the genesis of hypertension in bronchopulmonary dysplasia. The association with diuretics may have given a more gradual increase in blood pressure (maximum increase in our patients occurred on day 8 versus day 4 in the study of Greenough et al. [7]), perhaps allowing adaptation to the hypertension. Perlman and Volpe [10] showed that chronic hypertension altered adaptive responses in both cerebral and renal blood flow so that it is well tolerated and that acute decreases in systolic blood pressure to normal values by captopril were accompanied by oliguria and neurologic abnormalities (seizures). It is possible that the time period in which systolic blood pressure raises is more important in causing complications than the maximum value of systolic blood pressure in itself.

Our data confirm previous reports that dexamethasone raises blood pressure in babies with chronic lung disease in a transient way. Complications related to hypertension do not occur even with a systolic pressure up to 113 mm Hg, so treatment is not necessary. Close monitoring without antihypertensive treatment may avoid the addition of more drugs to the already complicated drug combination frequently administered to neonates with chronic lung disease. Association of diuretics does not prevent the rise in blood pressure, induced by dexamethasone, but may probably temper its degree. When hypertension persists for more than 2 weeks after stopping dexamethasone treatment other causes should be considered.

References

1. Abman SH, Warady BA, Lum GM, Koops BL (1984) Systemic hypertension in infants with bronchopulmonary dysplasia. J Pediatr 104: 928–931
2. Anand SK (1991) Hypertension. In: Taeusch HW, Ballard RA, Avery ME (eds) Diseases of the newborn. Saunders, London, p 906
3. Brozanski BS, Jones JG, Gilmour CH, Balsan MJ, Vazquez RL, Israel BA, Newman B, Mimouni FB, Guthrie RD (1995) Effect of pulse dexamethasone therapy on the incidence and severity of chronic lung disease in the very low birth weight infant. J Pediatr 126: 769–776
4. DeSwiet M, Fayers P, Shinebourne EA (1980) Systolic blood pressure in a population of infants in the first year of life: the Brompton study. Pediatrics 65: 1028–1035
5. Emery EF, Greenough A (1992) Effect of dexamethasone on blood pressure – relationship to postnatal age. Eur J Pediatr 151: 364–366
6. Fauser A, Pohlandt F, Bartmann P, Gortner L (1993) Rapid increase of blood pressure in extremely low birth weight infants after a single dose of dexamethasone. Eur J Pediatr 152: 354–356
7. Greenough A, Emery EF, Gamsu HR (1992) Dexamethasone and hypertension in preterm infants. Eur J Pediatr 151: 134–135
8. Harkavy KL, Scanlon JW, Chowdkry PK, Grylack LJ (1989) Dexamethasone therapy for chronic lung disease in ventilator- and oxygen-dependent infants: a controlled trial. J Pediatr Der 115: 979–983
9. Hawkins KC, Watson AR, Rutter N (1995) Neonatal hypertension and cardiac failure. Eur J Pediatr 154: 148–149
10. Perlman JM, Volpe JJ (1989) Neurologic complications of captopril treatment of neonatal hypertension. Pediatrics 83: 47–52
11. Perlman JM, Moore V, Siegel MJ, Dawson J (1986) Is chloride depletion an important contributing cause of death in infants with bronchopulmonary dysplasia? Pediatrics 77: 212–216
12. Werner JC, Sicard RE, Hansen WR, Solomon E, Cowett RM, Oh W (1992) Hypertrophic cardiomyopathy associated with dexamethasone therapy for bronchopulmonary dysplasia. J Pediatr 120: 286–291
13. Yeh TF, Torre JA, Rastogi A, Anyebuno MA, Pildes RS (1990) Early postnatal dexamethasone therapy in premature infants with severe respiratory distress syndrome: a double-blind controlled trial. J Pediatr 117: 273–282