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Title: Hypothalamic-pituitary-adrenal axis suppression in children at Cape Town allergy units – Prevalence and predictive factors

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Body: Background: Hypothalamic-pituitary-adrenal axis suppression (HPAS) is generally thought to be rare in children treated with corticosteroids (CS), since HPAS may be partially masked by recovering HPA function. Objective: To determine the prevalence & predictive factors for HPAS in children treated with CS at the allergy clinics in Cape Town. Methods: 143 asthmatic children, 5-18 years old, on inhaled CS (ICS) with additional CS were recruited. Clinical features compatible with HPAS were documented. Daily and cumulative CS dose, adherence, asthma score and lung functions were recorded. A metyrapone test was performed if the 08:00 hr cortisol (C) was >83nmol/l. Spearman correlation coefficients (r) were calculated between the post-metyrapone (PMTP) ACTH, 11-deoxycortisol (11DOC), 11DOC+C, and each variable. A multiple linear regression model of $\sqrt{\text{ACTH}}$ & a logistic regression model for HPAS were developed. Results: Prevalence: All HPAS 65.1(56.5-72.9)%; low (PMTP 11DOC, 11DOC+cortisol)32.3(23.7-40.9)%; low (PMTP ACTH, 11DOC, 11DOC+cortisol)16.3(9.3-23.3)%; hypocortisolaemia 6.1(1.8-10.5)%. GIT symptoms in hypocortisolaemic children were associated with HPAS in 2/8 (p=0.016). Log daily NS/m² was associated with HPAS [OR=3.7(1.1-13.6)]. Daily ICS+nasal steroid dose (NS)/m² correlated with ACTH (r=-0.29, p<0.001). BMI (p=0.048), poor adherence to ICS (p<0.001) and NS (p=0.002) were predictive to $\sqrt{\text{ACTH}}$. Conclusions: About 2/3 of asthmatic children on CS may have a degree of HPAS. In one third the adrenals may still be suppressed while hypothalamic-pituitary function may have recovered. Predictive factors for HPAS are concomitant NS use, BMI, adherence to ICS and NS.