New Insights into Low Dose Dexamethasone Suppression Test in Paediatric Cushing's Syndrome (CS)

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Introduction:

The Low dose dexamethasone suppression test (LDDST) is an important investigation for suspected Cushing's Syndrome (CS). The traditional definition of normal suppression of serum cortisol to ≤50 nmol/L during the LDDST (0.5 mg 6 hrly x 48 hrs) comes from a time when biochemical autoanalysers did not routinely detect very low values. Previous studies reported 5.1-8.3% of patients with Cushing's Disease (CD) suppressed to <50nmol/L at 48 hrs during LDDST. Many clinicians experienced in the assessment of suspected CS consider that 'normal' individuals should suppress to ≤20 nmol/L during a LDDST and that LDDST values of 20-50 nmol/L represent a range of uncertainty. Current sensitivity and specificity is reported as 90% and 100% for a cut off of ≤50 nmol/L.

Methods:

We reviewed a retrospective cohort of paediatric patients referred to our centre with suspected CS between 1982 and 2018.

Results:

Of 84 suspected CS patients, 50 had Cushing's Disease (CD), 8 had Primary Pigmented Nodular Adrenocortical Disease (PPNAD) and 26 'control' subjects, in whom the diagnosis of CS was excluded following detailed biochemical evaluation and prolonged clinical/auxological follow-up. The patient characteristics are summarised in table 1.

Table 1. Patient characteristics in the different diagnostic groups

Patient Group	CD	PPNAD	Controls	Total for all groups
Patients, n	50	8	26	82
Males	29	4	5	38
Mean age, years	12.4	12.9	12.3	12.3
Standard Deviation	3.4	2.2	4.3	3.6
Range	5.6-17.8	10.5-16.9	4.3-17	4.3-17.8

The serum cortisol remained >50 nmol/l in 44/50 (88%) CD patients (29 males, median age 13.31 years) during LDDST. In contrast, cortisol during LDDST was >20 nmol/l in 49/50 (98%) CD patients. One patient with cortisol ≤20 nmol/L during LDDST had a high clinical suspicion of CD and investigations including bilateral simultaneous inferior petrosal sinus sampling confirmed this.

Figure 1 summarises the mean cortisol values at the start of the LDDST, whereas figure 2 summarises the mean cortisol values post LDDST in each of the groups. The sensitivity and specificity of a LDDST cut off value of ≤20 nmol/l is 98% (95% confidence interval 89.4-100%) and 96% (80.4-99.9%). None of the 8 PPNAD patients (4 male, median age 12.5 years, range 10.5-16.9) had cortisol levels of ≤50 nmol/l during LDDST. Cortisol levels in 25/26 controls (5 males, median age 14 years, range 4.3-17.0) suppressed to ≤20 nmol/l during LDDST. In one other patient with a diagnosis of mosaic turners syndrome, high androgens, hypertension and obesity, the cortisol suppressed to 22 nmol/l.

Figure 1. Pre LDDST mean cortisol levels (nmol/l) in each group

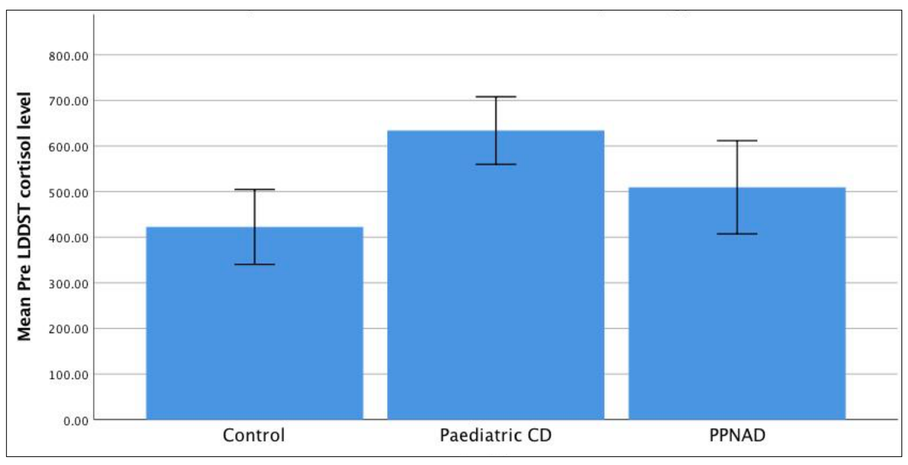
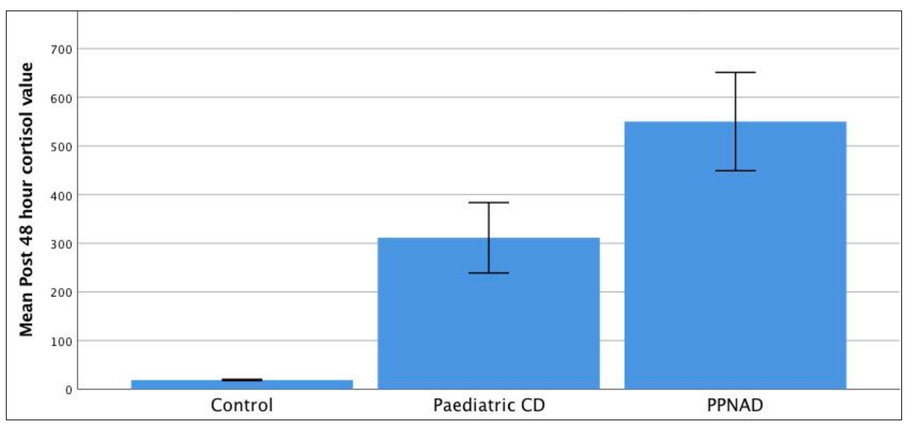


Figure 2. Post LDDST mean cortisol levels (nmol/l) in each group



Conclusion:

Whilst the numbers are small, changing the LDDST cut off from ≤50 nmol/L to ≤20 nmol/L improves the sensitivity of the test from 85.71% to 97.96% in our paediatric CD patients. This does not adversely affect the specificity which remains 100%. We therefore suggest using serum cortisol of ≤20 nmol/l as a new diagnostic cut off value.

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57ESPE 15--P1
Adrenals and HPA Axis
Ingrid Wilkinson
Poster presented at: 57th ESPE 2018 Meeting ATHENS GREECE 27-29 September 2018
PosterSessionOnline.com