REVIEW OF LOW DOSE SHORT SYNACTHEN TESTS (LDSST) IN A LARGE COHORT OF CHILDREN

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INTRODUCTION

Short Synacthen tests (SST) are used widely for the diagnosis of adrenal insufficiency (AI) in children.

LDSST are more sensitive but less specific than the SDSST[1-4].

Concerns regarding accuracy of dosing and reproducibility of the LDSST have been raised, leading to concerns of over diagnosis and treatment.

AIM

To report:

1. Prevalence of AI, defined as suboptimal or abnormal responses to the LDSST, according to indication for testing
2. Effect of age and gender on baseline and peak cortisol measurement

METHOD

Retrospective study of children tested between 2008-2020

Test protocol:

500ng/1.73m^2 Synacthen as IV bolus. Sampling at 0, 15, 25 and 35 minutes

Only the first LDSST were analysed if child tested more than once

Serum cortisol measured using Siemens Immunlite 2000XPi immunoassay system.

Classification of test results:

Pass: Peak cortisol ≥ 450nmol/L

Suboptimal: Peak cortisol 350-449 nmol/L

Hydrocortisone during stress periods only

Abnormal: Baseline cortisol <100nmol/L ± Peak cortisol <350nmol/L

Prescribed daily hydrocortisone

RESULTS

Table 1: Age and sex of children undergoing the LDSST by diagnostic category.

Indication for test (N)	Percentage of all tests	Age (years) Mean ±1SD	Male, N (%)
All patients(481)	-	9.5 ± 5.2	295 (61)
Inhaled steroids (ICS) (106)	22	10.5 ± 3.6	66 (62)
Iatrogenic not ICS (40)	8	9.7 ± 5.8	20 (50)
Structural brain abnormality (136)	28	9.4 ± 1.0	77 (57)
Poor cortisol response to GH stimulation test (29)	6	8.2 ± 4.5	19 (66)
GHD* (27)	6	10.6 ± 3.5	21 (78)
Infants (35)	7	0.3 ± 0.3	24 (69)
Fatigue (37)	8	11.7 ± 4.5	19 (51)
Autoimmune (13)	3	15.1 ± 1.9	6 (46)
Miscellaneous (58)	12	9.5 ± 5.4	43 (74)

*GHD: Growth hormone deficiency confirmed on stimulation testing

Table 2: Baseline and stimulated cortisol responses to the LDSST, and percentage of children with normal, suboptimal and abnormal results by diagnostic category

Indication for test (N)	Baseline cortisol (nmol/L	Peak cortisol (nmol/L)	Normal (%)	Suboptimal (%)	Abnormal (%)
All patients (481)	221 ± 120	510 ± 166	336 (70)	78 (16)	67 (14)
Inhaled steroids (106)	192 ± 94	431 ± 123	59 (56)	26 (24)	21 (20)
Iatrogenic not ICS (40)	197 ± 91	410 ± 150	20 (50)	8 (20)	12 (30)
Structural brain abnormality (136)	241 ± 125	553 ± 125	108 (79)	15 (11)	13 (10)
Poor cortisol response to GH stimulation test (29)	236 ± 86	649 ± 88	26 (90)	3 (10)	0 (0)
GHD (27)	241 ± 85	639 ± 137	22 (81)	4 (15)	1 (4)
Infants (35)	183 ± 188	465 ± 249	13 (37)	9 (26)	13 (37)
Fatigue (37)	236 ± 117	583 ± 85	36 (97)	1 (3)	0 (0)
Autoimmune (13)	305 ± 185	609 ± 185	10 (77)	3 (23)	0 (0)
Miscellaneous (58)	214 ± 109	525 ± 170	42 (72)	9 (16)	7 (12)

Baseline cortisol

Age: Cortisol increased by 2.7% (95% CI: 1.8%, 3.7%) / 1 year increase in age

Sex: Cortisol measurements 11.5% higher in girls than boys (p = 0.030, 95% CI: 1.1%, 23.1%) after adjusting for diagnostic group and age

Cortisol concentrations were highest in patients with isolated GHD and autoimmune disease and lowest in those with structural brain abnormalities (F-test p = 0.006)

Differences between diagnostic groups persisted after adjusting for age and gender

Peak cortisol

Age: No relationship between age and peak cortisol

Sex: Cortisol 60nmol/L (95% CI: 31.4, 88.6, p<0.001) higher in girls than in boys after adjusting for diagnostic group and age

Coritsol concentrations were lowest in children treated with pharmacological doses of steroids, structural brain abnormalities and infants (F-test p<0.0001), who were most likely to be prescribed hydrocortisone

Differences between diagnostic groups persisted after adjusting for age, gender and using baseline cortisol as a predictor

CONCLUSIONS

The relatively small number of children treated with daily hydrocortisone and the clustering of children with an abnormal result in diagnostic groups we consider to be at greatest risk of AI, suggest that overdiagnosis and treatment of AI is unlikely to be very common.

While a statistically significant effect of age and sex was seen on baseline cortisol, and an effect of sex on peak cortisol, these differences are modest and we suggest do not justify the complexity of introducing age and sex related reference ranges.

REFERENCES

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