

ASSESSMENT OF THE HYPOTHALAMUS-PITUITARY-ADRENAL AXIS WITH DIFFERENT CORTICOTROPIN TESTS IN ADULTS PATIENTS WITH PRADER-WILLI SYNDROME

G Grugni, A Corrias, A Sartorio, L Beccaria, S Bocchini, S Di Candia, D Fintini, L Iughetti, A Mussa, L Ragusa, L Gargantini, A Salvatoni, M Delvecchio, G Chiumello, A Crinò

on behalf of the Genetic Obesity Study Group of the Italian Society of Pediatric Endocrinology and Diabetology - ITALY



Background

Hypothalamic-pituitary anomalies are well proven in Prader-Willi syndrome (PWS), consistent with deficiency of many pituitary hormones. In this context, we have previously demonstrated that central adrenal insufficiency (CAI) may be part of the PWS phenotype. However, the diagnostics of CAI insufficiency is a critical issue, due to the variety of the diagnostic stimulations available, to the lack of flawless and fully reliable tests, and to the difficulties in their interpretation. The hypothalamus-pituitary-adrenal (HPA) axis response to insulin hypoglycemia (ITT) is still considered the gold standard in the evaluation of suspected CAI, even though its validity has been recently questioned. Several studies have looked at the clinical usefulness of the low dose (1 µg) short synacthen test (LDSST) compared to the conventional dose (250 µg) test (SDSST) in patients with pituitary disease. Actually, the dose used in the conventional SDSST is considered supraphysiological and might produce a deceptively adequate cortisol (F) response. Nevertheless, other reports suggested no difference between the LDSST and SDSST in patients with multiple pituitary hormone deficiency.

Aim

The objective of our study was to compare the F response to both LDSST and SDSST in a large group of adult patients with PWS.

Patients and Methods

The characteristics of the study group are reported in Table 1. At the time of the study, no PWS patient had had glucocorticoid replacement, whereas 13 (9 males) had been on treatment with recombinant human GH for at least 6 months. Thirteen patients had previously undergone GH treatment, which had been withdrawn in all cases at least 12 months before enrolment in this study (6 males). Three females and one male suffered from hypothyroidism and were biochemically euthyroid. None of the patients in the cohort reported any signs or symptoms suggestive of adrenal insufficiency, neither had ever been admitted for CAI, a critical illness, health conditions requiring intensive care or abnormal/complicated courses of common infections. All patients underwent both LDSST and SDSST, in random order and at least 7 days apart. In each test the subjects were evaluated in the morning, after a 12-hour overnight fast, 30 min after an indwelling catheter had been placed in an antecubital vein. Blood samples for F determination were taken at -15, 0 and 30 min. According to current literature, we have taken into consideration a cortisol peak response to LDSST <math>< 18.1 \mu\text{g/dl}</math> (=500 nmol/L) for diagnosing CAI.



Patients

Number	46
Sex (m:f)	23:23
Age (yrs) range	28.5±6.7 18-41
Karyotype	34 del15 12 UPD15

Data are expressed as mean±SD

Table 1

Results

No adverse effects were noticed during or after testing in any of the subjects studied. The mean peaks of F after LDSST and SDSST were similar ($p=0.8$) (Figure 1), whereas the average increase of F from baseline was significantly lower after LDSST in respect to SDSST (Figure 2). The LDSST and SDSST produced 32 normal and 2 abnormal concordant results. Seven patients who passed the SDSST failed the LDSST, while 5 subjects failed the SDSST but passed the LDSST.

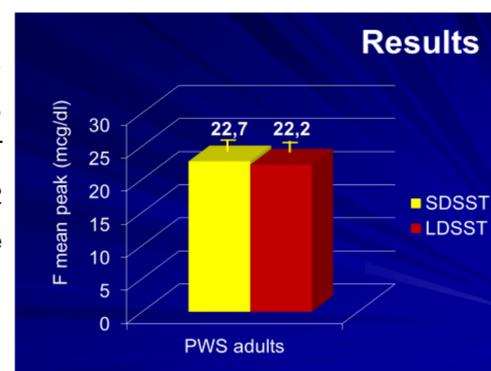


Fig. 1

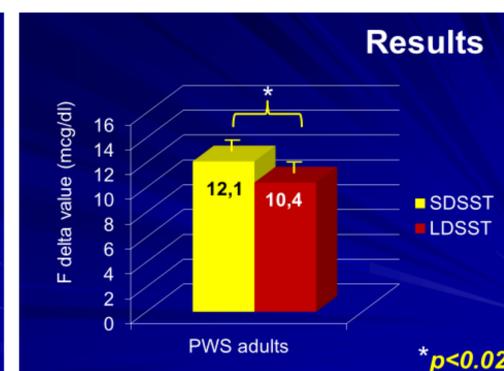


Fig. 2

Conclusions

- Our results support the view that CAI may be part of the PWS, but its frequency is largely lesser than that previously estimated.
- Differently from non-PWS patients with hypothalamic-pituitary diseases, our group of PWS showed a significantly higher F delta value after SDSST in comparison to LDSST.
- F responses to different SST tests were discordant in 26.1% of cases.
- More research is needed to define what is the more reliable test for diagnosing CAI in these patients - for example, an ITT or overnight metyrapone test on those who had abnormal response to LDSST or SDSST in order to confirm the presence of CAI.



References

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