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LETTER

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What is the value of the 60-minute cortisol measurement in the short synacthen test (SST)? Evidence for the defence

Letter to the editor

Adrenocortical insufficiency is caused by failure of the adrenal glands to produce physiological amounts of cortisol and sometimes aldosterone (Addison's Disease). This can be a consequence of pituitary/adrenal failure or suppression of endogenous cortisol production as a result of taking exogenous steroids for a prolonged period of time.

The short synacthen test (SST) is the most commonly performed investigation to assess adrenal function[1,2] as it is more practical than the 'gold standard' insulin tolerance test (ITT).[3] In some centres, a 60-minute serum cortisol post-synacthen is still checked as part of the STT protocol while in other centres it is not deemed necessary to do this.

In the light of these differences in practice, we investigated whether the 60-minute serum cortisol adds value in to interpretation of the SST. All patients attended a single-centre, Salford Royal Foundation Trust (SRFT) for their tests. Data from 207 consecutive SSTs were obtained from the Hospital Electronic Patient Record (EPR). All tests were performed before midday. We looked at a period of 12 months from mid-June 2017 to mid-June 2018. Where a patient had more than 1 SST, the first of the SSTs was analysed.

Serum cortisol was measured by immunoassay on the Siemens Centaur XP analyser (Erlangen, Germany). The analytical range of this assay is 13.8-2069 nmol/L.

Whenever possible, an individual on oral corticosteroids was changed to oral hydrocortisone for 48 hours prior to the SST being performed (if they were not already on this) with omission of hydrocortisone on the evening before and the morning of the test or omission on the morning of the test if on daily prednisolone/dexamethasone. A 30-60-minute cortisol concentration of ≥450 nmol/L defined a pass; 350-449 nmol/L defined borderline.

Our findings were that in relation to the post-synacthen cortisol pass cut-off of ≥450 nmol/L, in 16/207 (7.2%) of cases the 60-minute cortisol was ≥450 nmol/L (adequate adrenocortical function) but the 30-minute cortisol was below this. In all cases where the 30-minute cortisol did indicate a pass (ie, was ≥450 nmol/L), the 60-minute cortisol was also ≥450 nmol/L. Thus, the 60-minute cortisol measurement resulted in 7.2% of patients being deemed to have adequate adrenocortical function when the 30-minute cortisol would not have done so.

The 60-minute cortisol therefore retains utility in ruling out adrenocortical insufficiency. Determination of the 60-minute cortisol is done in some endocrine centres and was reported by Chitale et al[4] The authors of that paper stated that individuals passing the SST only at 60 minutes tend to exhibit a 'delayed response' to exogenous adrenocorticotrophic hormone (ACTH) but in essence have normally functioning adrenal glands.

As part of this evaluation, we undertook a telephone survey covering all hospitals in the NW of England on 14 April 2021. Of the 23 hospital laboratories surveyed, 11 do not measure both a 30- and a 60-minute cortisol (1 of the 11 laboratories measures a 60-minute but not 30-minute cortisol).

Thus although the evidence base is in support of the value of the 60-minute cortisol,[5-7] this measurement is far from routine at many laboratories. Furthermore, if patient management was to be based solely on the 30-minutes sample, they would at least have to undergo further tests or be commenced on unnecessary, long-term steroid replacement therapy. This conclusion was supported in a recent paper by Butt et al[8] who looked at 849 people undergoing SSTs and reported that 9.5% of patients had a suboptimal response at 30 minutes, but reached the threshold value at 60 minutes. There is also the possibility that the 60-minute serum cortisol level may actually be more representative of physiological adrenocortical function than the 30-minute serum cortisol.[9]

To conclude, the 60-minute cortisol retains utility as part of the SST. Reliance on a 60-minute cortisol level can identify all normal and abnormal responses, while relying on 30-minute cortisol level alone may falsely ascribe individuals to having adrenocortical insufficiency. It would surely be sensible to work towards a consensus in relation to inclusion of the 60-minute cortisol in all SST protocols, while taking into account the known variation in cortisol assay performance.

ROLE OF THE SPONSOR

There was no research sponsor for this study.

TRANSPARENCY STATEMENT

Dr Heald as corresponding author affirms that this is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

ETHICS STATEMENT

As this project was deemed by our local Research and Development Committee as a quality improvement (QI) project, no individual

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patient was contacted in the course of the evaluation and data were fully anonymised prior to analysis, it was not felt that formal ethics permission was required.

DISSEMINATION OF STUDY RESULTS TO PARTICIPANTS

Dissemination to interested patient groups both locally and nationally will be done once the analysis has been finalised.

PATIENT CONSENT

This was not deemed necessary as no individual patient was contacted or asked to do anything beyond their usual clinical care.

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DISCLOSURE

No author has anything to disclose in relation to conflict of interest.

AUTHOR CONTRIBUTIONS

AHH and AR conceived the study. MM and LM collected the data. MM, AAF and GY conducted the data analysis. CJD, ML and AAF provided perspective from the laboratory. AN assisted with the literature review. MM, LM, GY, ML, SD, AR, AN, AAF, CJD, AHA, PT and AHH all contributed to writing of the paper. AAF, AHA and PT provided an overview of the manuscript.

DATA AVAILABILITY STATEMENT

We used patient level data which were fully anonymised prior to analysis. Any requests for access to these data should be made to the corresponding author, Dr Adrian Heald.

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