

Total and Free Cortisol Levels During 1 µg, 25 µg and 250 µg Cosyntropin Stimulation Tests Compared to Insulin Tolerance Test: Results of a Randomized, Prospective, Pilot Study

Background

- The insulin tolerance test (ITT) is the standard test for diagnosis of secondary adrenal insufficiency (SAI); however, the test is difficult to conduct and potentially harmful.¹
- The cosyntropin stimulation test (CST), which measures cortisol levels in response to the introduction of cosyntropin, has been shown to be a useful alternative for diagnosing SAI. However, the appropriate dose of cosyntropin to use for CST is unclear.^{1,2}
- **Objective:** In this pilot study, the investigators evaluated the diagnostic utility of the CST at 3 different doses, comparing results to those of the ITT.

Methods

- The study included 10 patients with SAI and 12 healthy volunteers.
- Three doses of cosyntropin were tested for the CST: 1 µg (low), 25 µg (medium), and 250 µg (high).
- Total and free cortisol levels were measured for the 3 CST doses and for ITT. Total and free cortisol levels were measured by liquid chromatography and mass spectrometry.
- The performance of ITT and CST (at each insulin dose) for discriminating between SAI patients and control subjects was assessed using receiver operator characteristics (ROC) analysis. ROC analysis uses sensitivity and specificity of an assay to determine optimal cut-offs.

Results

- Total and free cortisol levels obtained with the CSTs at all 3 cosyntropin doses correlated well with those obtained with ITT.
- The optimal free cortisol cut-off for SAI with the ITT was 1 µg/dL. (The accepted cut-off for total cortisol is 18 µg/dL.)
- The optimal cortisol cut-offs for SAI with the CST are shown below; sensitivity and specificity refer to total cortisol:
 - Low dose (30 minutes): 14.6 µg/dL total; 0.9 µg/dL free
 - Sensitivity for SAI: 100%; specificity: 100%
 - Medium dose (30 minutes): 18.7 µg/dL total; 0.9 µg/dL free
 - Sensitivity for SAI: 100%; specificity: 88%
 - High dose (30 minutes): 16.1 µg/dL total; 0.9 µg/dL free
 - Sensitivity for SAI: 100%; specificity: 100%
 - High dose (60 minutes): 19.5 µg/dL total; 1.3 µg/dL free
 - Sensitivity for SAI: 100%; specificity: 100%

Conclusions

- This pilot study demonstrated that all CST doses performed well compared to ITT, if appropriate cut-offs were used.
- The data suggest that a free cortisol cut-off of 1 µg/dL can be used for low, medium, and high (30 minutes) CST doses, as well as ITT.
- A larger study should be conducted to confirm this cut-off.

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