Salivary Cortisol and Cortisone after Low-dose Corticotropin Stimulation in the Diagnosis of Adrenal Insufficiency.
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Introduction
An accurate diagnosis of adrenal insufficiency is important because it is potentially life-threatening if missed; while over-diagnosis may lead to unnecessary replacement of glucocorticoids, leading to decreased quality of life and increased mortality. The short synacthen tests (SSTs) are most widely employed, owing to its convenience, safety and reasonably good correlation with the insulin tolerance test. However, the reference cut-off values for post-SST serum cortisol ranged from 418-574 nmol/L in the literature, likely due to the variations in study methodologies, serum cortisol assays and serum binding protein levels. Salivary cortisol and cortisone may serve as better alternatives, as salivary test is non-invasive and reflects the level of serum free cortisol. Yet, little is known about the optimal cut-offs and performance characteristics of these tests.

Objectives
To derive the cut-off values and study the performance characteristics of salivary cortisol and salivary cortisone in the diagnosis of adrenal insufficiency.

Methodology
Prospective study in a regional hospital in Hong Kong from January 2014 to September 2015 including 56 Chinese healthy volunteers and 171 patients suspected of having adrenal insufficiency. All participants underwent low-dose SST (LDSST) with intravenous injection of 1 microgram Synacthen 1-24. Serum cortisol, salivary cortisol and cortisone levels were measured at baseline, 30 and 60 minutes after.

Result
Using the reference cut-off (mean–2SD of post-LDSST peak serum cortisol) derived from healthy volunteers as the gold standard, ROC analysis of patients’ data revealed
both post-LDSST peak salivary cortisol and cortisone performed well and better than basal tests. The most optimal cut-off values for serum cortisol as measured by immunoassay (Abbott ARCHITECT i2000SR, USA), and salivary cortisol and cortisone as measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS) were 376, 8.6 and 33.5 nmol/L respectively for the post-LDSST peak values, and 170, 1.7 and 12.5 nmol/L respectively for the basal values. The correlation coefficients (r) between peak salivary cortisol and cortisone with the peak serum total cortisol levels were 0.779 and 0.852 respectively. Salivary cortisone had a better and more linear correlation with serum total cortisol, while salivary cortisol rose exponentially after serum cortisol level reached 400-600 nmol/L. Their measurements by LC-MS/MS can alleviate problems associated with serum cortisol immunoassays, as LC-MS/MS enables accurate measurement of specific steroids, results are less specific-assay-dependent and more comparable among laboratories.