Method-specific serum cortisol responses to the adrenocorticotropic test: comparison of two generations of Roche automated immunoassays using \textit{monoclonal} versus \textit{polyclonal} antibodies

\textbf{OBJECTIVES}

The plasma cortisol response to the adrenocorticotropic (ACTH) test is known to vary significantly by assays. An automated cortisol immunoassays with increased specificity due to the shift from polyclonal to monoclonal antibodies, and standardized against mass spectrometry was recently introduced, with an expected decrease in cortisol concentrations by 20%. Cut-offs used in clinical practice for patient evaluation will thus have to be adjusted.

We aimed to assess the normal cortisol response to ACTH stimulation measured by Elecsys®Cortisol II.

\textbf{METHODS}

An ACTH test (250 μg iv ACTH, 0–24) was undertaken in 100 healthy volunteers (age, 18–70 years; 50 women) and 13 women on oral contraceptives.\textsuperscript{1}

Plasma cortisol was measured by two commercially available immunoassays: Elecsys®Cortisol (polyclonal Ab) and Elecsys®Cortisol II (monoclonal Ab)(Roche).

The estimated lower reference limit for the 30 min plasma cortisol response to ACTH was derived from the adjusted 2.5th percentile, defined as: 2.5th percentile-1.96*SE.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|}
\hline
                & Elecsys®Cortisol & Elecsys®Cortisol II \\
\hline
Min             & 534              & 399              \\
STDEV           & 94               & 79               \\
SE              & 9.44             & 7.69             \\
5th percentile  & 602              & 450              \\
2.5th percentile & 590              & 434              \\
Adj. 2.5th percentile & 572           & 420              \\
1.96*SE         & 1.96*SE          & 1.96*SE          \\
\hline
\end{tabular}
\caption{30 min-p-cortisol in response to the 250 microg ACTH test}
\end{table}

\textbf{RESULTS}

Cortisol concentrations measured by Elecsys®Cortisol II were approximately 20% lower relative to Elecsys®Cortisol. The 30 min cortisol response was normally distributed in males but not in females, with no significant gender difference at baseline nor post-ACTH (p = 0.1). The cortisol concentrations including the lower reference limit for the 30 min cortisol response was method-specific (Table 1); Elecsys®Cortisol (range: 534–1013; adj. 2.5th percentile: 572 nmol/L) and Elecsys®Cortisol II (range: 399–817; adj. 2.5th percentile: 420 nmol/L), and remained significantly elevated by both methods in women on oral contraceptives.

\textbf{CONCLUSIONS}

The cutoff defining a normal 30 min. cortisol response to the ACTH test is influenced significantly by assay employed as well as oestrogen treatment. New cutoffs should be introduced with the introduction of new generation immunoassays with higher specificity.

Elecsys®Cortisol II derived a cutoff of 420 nmol/L, which is significantly lower than the commonly recommended cutoff of 500 nmol/L, but similar to the cutoff previously suggested for mass spectrometry.\textsuperscript{2}

\textbf{References}

\textsuperscript{1}Klose M et al. J Clin Endocrinol Metab, 2007; 92(4):1326
Factors influencing the adrenocorticotropic test: role of contemporary cortisol assays, body composition, and oral contraceptive agents.

\textsuperscript{2}El-Farhan N et al, Clin Endocrinol (Oxf), 2013; 78(5):673
Method-specific serum cortisol responses to the adrenocorticotropic test; comparison of gas chromatography-mass spectrometry and five automated immunoassays.