
Surgical treatment of patients with ACTH-dependent Cushing syndrome would be enhanced by the availability of a rapid ACTH assay (1–3). This would allow the intraoperative documentation of a decrease in ACTH during the removal of putative ACTH-secreting tumors (4). The immunoradiometric assay (IRMA) for parathyroid hormone (PTH) has been modified for intraoperative measurement (5). Now, an immunochemiluminescence assay (ICMA) for ACTH has also been developed, with even greater sensitivity than the IRMA for ACTH and the potential for modification to a rapid assay.

We used the ICMA for ACTH generously supplied by the Nichols Institute (San Juan Capistrano, CA). Rather than incubating samples for 22 h at room temperature, we incubated them for 15 min in a standard shaker water bath set at 37°C and 60 cycles/min. Otherwise, the assay was performed and results quantified according to the manufacturer’s instructions.

We analyzed 28 human plasma samples with a wide range of ACTH concentrations (by IRMA) to correlate the rapid (15-min) assay with the standard 22-h incubation. Plasma samples from eight patients were pooled for determination of the intrasay CV. Confidentiality of patient information was maintained in accordance with the Helsinki Declaration of 1975, as revised in 1983. Interassay CVs were determined by assaying the two controls (low and high ACTH concentration) supplied by the Nichols Institute.

Figure 1 shows the correlation of the results obtained with the standard incubation time (22 h) at room temperature vs the results after the 15-min incubation at 37°C. The correlation was highly significant (r = 19.4; 26 df; P < 0.005). The slope (1.2 ± 0.3) and y-intercept (0.5 ± 6.9 pmol/L) were not significantly different from 1.0 and 0.0, respectively; and the SEE was 5.0 pmol/L. There was no loss of sensitivity of the rapid assay down to an ACTH concentration of 2 pmol/L (Fig. 1 insert: slope = 1.1 ± 0.4; y-intercept = 1.4 ± 4.1 pmol/L; SEE 2.1 pmol/L; n = 21).

The intrasay CV for the rapid assay was 8% (8.8 ± 0.7 pmol/L; n = 9), compared with <4% for the 22-h incubation. The interassay CVs were 13% (8.4 ± 1.1 pmol/L; n = 6) and 8% (71.3 ± 5.5 pmol/L; n = 6), compared with 5% and 7%, respectively, for the longer assay. The 50% binding point of the standard curve (ED50) was 129.1 ± 7.0 pmol/L (mean of six standard curves; intrasay curve CV = 5%).

The intrasay CV was well within the limits of our specification for intraoperative application, given that ACTH decreases by >50% within 15 min of tumor removal (1, 6) consistent with the half-life of ACTH(1–39) of <15 min (7). However, intra- and interassay CVs at low ACTH concentrations were greater than those of the standard ICMA or IRMA for ACTH.

This rapid assay has several potential clinical applications. Bronchial carcinoid tumors may be occult, even with modern imaging techniques (4). A rapid assay would be useful during open-chest pulmonary vein sampling to establish a significant gradient in the pulmonary vein of the affected lobe (6) and to document successful removal of an ACTH-secreting bronchial carcinoid tumor (6). Finally, the most important use of the assay may be to document the complete removal of a pituitary microadenoma during transphenoidal surgery.

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References