

Assessment of Circulating Hypocalcemic PTH Fragment Level and 1-84 PTH in Patients with Primary and Secondary Hyperparathyroidism Pre-and Post-Parathyroidectomy

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N-truncated PTH fragment(s) are secreted directly by the parathyroid gland and are in normal subject circulation being under direct control of serum Ca. 7-84 PTH exhibits strong hypocalcemic action in vivo and inhibits osteoclast formation in vitro.

A novel DUO PTH IRMA was validated to accurately measure circulating levels of this fragment(s). The method uses 2 immunoassays with common reagents: one specifically measures the sum of 1-84 PTH plus fragment; the other measures 1-84 PTH exclusively. Subtraction of the 1-84 PTH level from the sum yields the fragment level. The only difference between assays is the specific tracer antibody (tAb) which, for the 1-84 PTH assay, binds only 1-84 PTH, not 2,3,4,5,7-84 PTH. The tAb for the sum PTH assay binds 1,2,3,4,5,7-84 PTH. Specificities were validated with fractions from HPLC resolved ESRD patient plasma. Both assays measured synthetic 1-84 PTH in an equal molar manner with a linear measurement up to 2100 pg/mL PTH and sensitivities of 1–2 pg/mL. The inter assay CV was <7.76%; intra assay CV was <4.94%. EDTA-plasma from 82 normals, 36 1° HPT and 157 ESRD subjects were studied. The level of the hypocalcemic fragment was ($X \pm SE$) 10.56 ± 0.73 pg/mL in normals with a fragment/1-84 PTH ratio (ratio) of 0.46 ± 0.02 . In 1° HPT the fragment level before PTX was 65.26 ± 16.97 pg/mL with a ratio of 0.57 ± 0.10 . Following PTX the fragment level remained consistently higher with respect to 1-84 PTH level and persisted at 1.49 ± 0.53 , 3.15 ± 1.70 and 2.43 ± 0.61 at 5 min, 10 min and 15 min respectively, which indicates a relatively longer circulating half-life of this fragment compared to 1-84 PTH. In ESRD pts, the fragment level was 197.00 ± 26.76 pg/mL with a ratio of 0.96 ± 0.05 ($p < 0.001$ to normal group). This method is suitable to study the hypocalcemic fragment. Both the relatively high level of this PTH fragment, and its longer half-life may impact calcium and bone metabolism.

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