Intact whole bioactive parathormone: problems arising from comparing different methods

**Background.** Parathyroid hormone (PTH) has important applications in the nephrological clinical practice. Because assays of Intact PTH (I-PTH) are liable to interferences by N-truncated fragments, a novel method for whole-(1-84) PTH has been proposed. This study is aimed at comparing the latter with some of the previous I-PTH assays. For each method the results are referred to pertinent markers of mineral metabolism.

**Methods.** We enrolled 171 subjects, including 56 healthy controls (C), 65 calcium stone-formers (CaSF), 40 haemodialyzed patients (HD), and 10 primary hyperparathyroidism (PHP). On blood samples were assayed: I-PTH with 4 methods (N-Tact, Advantage, Elecsys, Scantibodies), PTH intero definite CAP (Cyclase Activating PTH), calcium total and ionized, phosphorus, vitamin D, osteocalcin and crosslaps. The difference between I-PTH Scantibodies and CAP is defined CIP (Cyclase Inhibiting PTH).

**Results.** There was notable dispersion of values of PTH among methods, although all were correlated with r > 0.97. For all, the values of reference for PTH were different from those provided by the manufacturers. Applying these corrected ranges resulted that 10 NL had values over range not always associated with other anomalies of mineral metabolism. One of the patients with PHP had I-PTH normal with 2/4 methods. Among HD the dispersion of values was also greater, there were correlations inversely with ionized calcium (p<0.05) and directly with osteocalcin and crosslaps (p<0.001). The ratio CAP/CIP was lower in HD with low turnover, but with a wide overlap between the two subgroups.

**Conclusions.** From the study emerges the persistence of problems of reliability in the dosage of I-PTH, and among the 4 methods tested does not appear to be the best. The dosage of CAP improves but does not resolve the diagnostic efficiency, while the ratio CAP/CIP does not have an acceptable discriminant capacity in HD. It is therefore consiliable that each Center establishes reference values internally. The dosage of PTH should always be accompanied by the dosage of other markers of mineral metabolism and by a renal functional evaluation.

**PAROLE CHIAVE:** Paratormone, Metabolismo minerale, Nefrolitiasi, Ipiperiparatiroidismo primitivo, Uremia, Metodi immunometrici
sis patients (HD), 10 with primary hyperparathyroidism (PHP). On blood samples we measured: I-PTH by four methods (N-Tact, Advantage, Elecsys, Scantibodies), whole-(1-84) PTH, defined as CAP (Cyclase Activating PTH), total and ionised calcium, phosphate, vitamin D, osteocalcin and Crosslaps. The difference between I-PTH and CAP Scantibodies is defined as CIP (Cyclase Inhibiting PTH).

**Results.** Despite relating to each other ($r>0.97$) PTH values varied remarkably among methods. For all methods, the reference intervals differed from those provided by the producer. Assuming these new ranges, 10 CaSF had over-range values not always associated with abnormalities of mineral metabolism. One of the PHP patients was normal for I-PTH with 2/4 methods. In HD the differences among methods were even greater, there were inverse ($p<0.05$) and direct ($p<0.001$) relationships with ionised calcium and osteocalcin-crosslaps, respectively. The CAP/CIP ratio was lower in low bone turnover patients, but the two subgroups widely overlapped.

**Conclusions.** This study indicates that the reliability of I-PTH assays is still unsatisfactory, and none of the four methods emerged as the best. Assay for CAP only improves diagnostic efficiency, whereas the CAP/CIP ratio does not exhibit powerful discriminating capacity. Our suggestion is that each Centre should establish its own reference ranges. PTH assay should always be coupled with measurements of other markers of mineral metabolism as well as renal function. (G Ital Nefrol 2002; 19: 467-75)

**KEY WORDS:** Parathormone, Mineral metabolism, Nephrolithiasis, Primary hyperparathyroidism, Uremia, Immunometric methods