PATRICK C. D'HAESE, PHD
AND
MARC DE BROE, MD, PHD, FRCP

BOTH OF
EDEGEM, ANTWERPEN BELGIUM

TOPIC: EVALUATION OF RENAL OSTEODYSTROPHY

Patrick C. D'Haese & Marc E De Broe
Laboratory of Nephrology-Hypertension, University of Antwerp, Belgium

Abstract

During the last 15 years various bone biopsy-based world-wide epidemiological studies, investigating the spectrum of and renal osteodystrophy in dialysis patients, CAPD patients and end-stage renal failure patients not yet in dialysis have been set up in our laboratory. Data of these studies revealed an evolution and a distinctly different pattern of the various types of renal osteodystrophy within the various study groups. Using the histomorphometric analysis of a bone biopsy as the golden standard, various bone markers have been evaluated for the non-invasive diagnosis of renal osteodystrophy. In both the dialysis and CAPD populations we found the electrophoretic measurement of bone alkaline phosphatase to be superior to both iPTH and osteocalcin to differentiate between high and low bone turn-over. In end-stage renal failure patients not yet in dialysis, osteocalcin was found to hold a substantial diagnostic performance also. In our lab the recent introduction of the proteomics technique in combination with the use of primary osteoblast cultures, might be useful in the search for new markers.

In a recent study, the histomorphometric analysis of duplicate bone biopsies taken at the start of dialysis treatment and after a 1-year follow-up period was used to evaluate the effect of lanthanum carbonate on the evolution of renal osteodystrophy.

Aside from the histomorphometric analysis, methods have been developed for the measurement (atomic absorption, inductively coupled plasma emission mass spectrometry) and ultrastructural localisation (histochemical staining, electron probe X-ray micro analysis, synchrotron-based X-ray fluorescence) of various metals (e.g. aluminium, lanthanum, strontium …) as well as to study the effect of these or other substances on bone quality (X-Ray diffraction). The relevance of these measurements in the development of particular types of renal bone disease was studied.

Aside from clinical studies the remnant kidney Wistar rat has been characterized and its value as a model for human renal osteodystrophy was evaluated. This model has repeatedly been applied for dose-finding studies of therapeutic compounds (lanthanum, strontium, …), temporal evolution/reversal of renal bone disease etc … .

As for human studies, in these experimental investigations also, we have repeatedly been confronted with the lack of reliable reference values.

During the last years cell culture models of primary osteoblasts derived from rat calvaria or rat bone marrow cells have been developed. In combination with techniques such as proteomics and real-time PCR, these models allow us to study the pathophysiological mechanisms interfering with osteoblast function and mineralization and identify proteins and genes involved in these processes.