FGF-23 Levels before and after Renal transplantation

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Abstract

Background: Fibroblast growth factor 23 (FGF23), a novel bone-derived hormone that inhibits phosphate reabsorption and calcitriol production by the kidney, has uncovered primary regulatory pathways and new systems biology governing bone mineralization, vitamin D metabolism, parathyroid gland function and renal phosphate handling.

Objectives: Our study investigated FGF-23 levels in patients with end-stage renal disease before and after a successful renal transplantation and their probable association with markers of bone and mineral metabolism.

Methods: 40 patients were studied for 6 months and divided into two groups (hemodialysis vs renal transplantat patients).The estimations of serum FGE23 ,calcium, phosphorus, intact parathyroid hormone were performed in both groups . We compared the changes in serum FGF23 ,calcium, phosphorus, and intact parathyroid hormone in renal transplant patients 3 and 6 months after successful renal transplantation.

Results: The serum FGF23 decreased significantly after renal transplantation. i PTH and P levels also decrease significantly after renal transplantation, while Ca increase.

Conclusion: FGF23 are markedly increased in patients with end stage renal disease associated with increase in phosphorous and i PTH levels . FGF-23 levels decrease dramatically after successful renal transplantation and remain within normal limits when graft function is good.

i PTH and P levels also decrease significantly after renal transplantation, while Ca increase.

Key words: FGF-23 , CKD, CRF, Renal transplantation .

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LIST OF ABBREVIATIONS

1,25(OH)2D	**1,25dihydroxy vitamin D**
25 (OH)D	**25dihydroxy vitamin D**
ACEI	**Angiotensin converting enzyme inhibitor**
ADHR	**Autosomal dominant hypophosphatemic rickets**
ADMA	**Asymmetrical diethylarginine**
ADYN	**Adynamic bone disease**
ANP	**Atrial naturietic peptide**
ARF	**Acute renal failure**
ARHR	**Autosomal recessive hypophosphatemic rickets**
ASARM	**Acidic, serine and aspartate rich motif**
AKI	**Acute kidney injury**
ARHR1and 2	**Autosomal recessive hypophosphatemic rickets,type 1and 2**
BMP	**Bone morphogenetic protein**
BMD	**Bone mineral denisty**
CAR12	**Carbonic anhydrase 12**
CaCO3	**Calcium carbonate**
CaXPO4	**Calciumxphosphate**
CKD	**Chronic Kidney disease**
CKD-MBD	**Chronic kidney disease:Mineral and bone disorder**
CrCl	**Creatinine clearance**
CRF	**Chronic renal failure**
CRP	**C-reactive protein**

CSF	**Cerebrospinal fluid**
CSR	**Calcium-sensing receptor**
CV	**Cardiovascular**
CaSR	**Calcium-sensing receptor**
cKL	**Shedded full-length Klotho**
CYP24A1	**1,25dihydroxyvitamin D 24-hydroxylase**
CYP27B1	**25-dihydroxyvitamin D 1-alpha-hydroxylase**
DM	**Diabetes mellitus**
DMP1	**Dentin matrix protein 1**
ECF	**Extracellular fluid**
ENPPI	**Ectonucleotide pyrophosphate/phosphdiesterase**
ESRD	**End stage renal disease**
FDA	**Food and drug administration**
FGF23	**Fibroblast growth factor 23**
FSGS	**Focal and segmental glomerulosclerosis**
FGF	**Fibroblast growth factor**
Fgf23-/-	**Fibroblast growth factor 23 knockout mice**
FGFR	**Fibroblast growth factor receptor**
FD	**Fibrous dysplasia**
GALNT3	**Polypeptide N-acetylgalactosaminyltransferase 3**
GFR	**Glomerular filtration rate**
GPCR	**G-protein coupled receptor**
HD	**Hemodialysis**
HFTC	**Hyperphosphatemic familial tumoral calcinosis**

HPTH	**Hyperparathyroidism**
HPT	**High turnover osetodystropy**
HRH	**Hyperparathyroidism**
IL	**Interleukin**
Klotho-/-	**Klotho knockout mice**
Ksp -KL-/-	**Distal tubule-specific Klotho knockout mice**
KDIGO	**Kidney Disease Improving Global Outcomes**
LAV	**Left atrial volume**
LDL	**Low density lipoprotein**
LTOM	**Low turnover osteomalacia**
LVH	**Left ventricular hypertrophy**
LVMI	**Left ventricular mass index**
MEPE	**Matrix extracellular phosphoglycoprotein**
MGP	**Matrix G1a protein**
MUO	**Mixed uremic osteodystropy**
NaPi- II	**Sodium phosphate cotransporters**
NKF	**National kidney foundation**
NO	**Nitric oxide**
NPT2a	**Sodium phosphate cotransporters**
OGD	**Osteoglophonic dysplasia**
OPN	**Osteopontin**
PHEX	**Phosphate-regulating endopeptidase homolg,X-linked**
PHPT	**Primary hyperparathyroidism**
PRMT	**Protein methyltransferase**

PTG	**Parathyroid gland**
PTH	**Parathyroid hormone**
PTHrP	**Parathyroid hormone-related peptide**
PTH-KL-/-	**Parathyroid-specific Klotho knockout mice**
PTH1R	**Parathyroid hormone 1 receptor**
RAAS	**Renin-Angiotensin-Aldosterone system**
RCT	**Randomized controlled study**
RGD	**Arginine glycine aspartate**
RVR	**Renal vascular resistance**
sFRP4	**Secreted frizzled-related protein 4**
SIBLING	**Small integrin binding ligand N-linked glycoprotein**
sHPT	**Secondary hyperparathyroidism**
TGF-B	**Transforming growth factor -3**
TIO	**Tumor induced osteomalacia**
TNF	**Tumor necrosis factor**
US	**United states**
USRDS	**The united states Renal Data System**
VC	**Vascular calcification**
VDR	**Vitamin D receptor**
VDRE	**Vitamin D receptor element**
VSMC	**Vascular smooth muscle cell**
XLHR	**X linked hypophosphatemic rickets**

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Introduction and aim of the work

- Our understanding of the dramatic changes in bone and mineral metabolism that occur in patients with chronic kidney disease (CKD) has increased with the discovery of the bone-derived hormone fibroblast growth factor 23 (FGF-23) .

(Silver J et al,2013)

-The discovery of fibroblast growth factor 23 (FGF23), a novel bone-derived hormone that inhibits phosphate reabsorption and calcitriol production by the kidney, has uncovered primary regulatory pathways and new systems biology governing bone mineralization, vitamin D metabolism, parathyroid gland function and renal phosphate handling. ***(Evenepoel P et al,2007)***

-As our knowledge expands regarding the regulation and functions of FGF23, the assessment of FGF23 will become an important diagnostic marker as well as a therapeutic target for management of disordered mineral metabolism in a variety of acquired and hereditary disorders. ***(Stubbs J et al ,2007)***

-Disordered phosphate homeostasis with elevated circulating levels of fibroblast

growth factor 23 (FGF23) is an early and pervasive complication of CKD. CKD is

likely the most common cause of chronically elevated FGF23 levels, and the

clinical condition in which levels are most markedly elevated.***(Wolf M,2012)***

-Recently, FGF-23 has been suggested to be responsible for the hypophosphatemia and inappropriately low calcitriol levels observed after renal transplantation .

(Evenepoel P et al,2007)

Aim of work

The aim of the present prospective study was therefore to investigate FGF-23 levels in patients with end-stage renal disease before and after a successful renal transplantation and their probable association with markers of bone and mineral metabolism.

Chapter One

Bone and Mineral Metabolism in Chronic Kidney Disease

Bone and Mineral Metabolism in Chronic Kidney Disease

The chronic kidney disease-bone and mineral disorders (CKD-MBD) represents a dynamic area of research. Recently, new factors such as FGF-23 have been added to the classic list of regulators of bone metabolism, which include calcium, phosphorus, PTH and calcitriol. ***(Mejía N et al,2011)***

Vascular calcification, one of the most important complications of CKD-MBD is regulated by a complex variety of promoters and inhibitors. The relationship between vascular calcification, bone loss and mortality, together with the existence of likely common signaling pathways are subject of interesting investigations. ***(Mejía N et al,2011)***

In healthy individuals kidneys regulate calcium and phosphorus homeostasis through tubular reabsorption mechanisms. Patients with chronic kidney disease have seriously compromised homeostatic mechanisms, giving rise to different adaptive changes in calcium (Ca), phosphorus (P), parathyroid hormone (PTH), vitamin D and fibroblastic growth factor (FGF-23) levels. ***(Torregrosa JV et al ,2011)***

There are various clinical signs, although secondary hyperparathyroidism (SHPT), fractures, bone pain, vascular calcification and cardiovascular events are highlighted as causing lower quality of life with a high morbidity and mortality.***(KBS,2005) (Mejía N et al,2011)***