Prospective evaluation of bone mineralization, PTH regulation and metabolic profile in adult patients with hereditary hypophosphatemic rickets (HHR).

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INTRODUCTION

- Hereditary hypophosphatemic rickets (HHR) is a rare genetic disease characterized by renal phosphate wasting, caused by elevated circulating FGF23.
- Despite the current available treatment complications include short stature, hyperparathyroidism, pseudofractures, bone pain, bone demineralization and osteoporosis, nephrocalcinosis and enthesopathies.
- Elevated circulating FGF23 was recently involved in glucose and lipid metabolism and cardiovascular function.

OBJECTIVES

Our objective was
- to prospectively evaluate complications of the disease and patients' metabolism.
- to compare outcomes between patients who received vitamine D analogues (VDA) during infancy with those who did not.

METHODS

We prospectively studied 28 patients with HHR followed at Kremlin Bicêtre endocrinology department.
-19 patients received VDA during childhood
-9 patients did not received
We analyzed anthropometric measurements, mineral metabolism (calcemia, phopphatemia, urine sample, bone densitometry, presence of hyperparathyroidism or nephrocalcinosis), lipid profile (serum lipides and body composition by x-ray dual absorptiometry), glucose metabolism

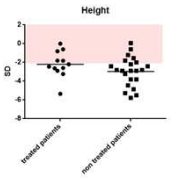
RESULTS

	All patients	Treated	Non treated	p
Age (years)	39.0 (34.8-43.1)	27.6 (21.8-31.6)	43.4 (39.9-46.9)	0.0060
Height (DS)	-2.7 (-3.3- -2.2)	-2.3 (-3.5- -1.2)	-2.9 (-3.7- -2.2)	0.3567
Body mass Index (kg/m²)	28.2 (25.9-30.5)	29.1 (22.9-35.4)	27.8 (25.5-30.1)	0.6086
SBP (mmHg)	118 (111-125)	111 (99-123)	122 (113-131)	0.1273
DBP (mmHg)	72 (66-77)	67 (59-76)	74 (67-81)	0.2370
Mineral metabolism				
24 h urinary calcium excretion (mg/kg/day)	2.3 (1.7-2.9)	1.2 (0.3-2.2) [b]	2.7 (1.6-3.3)	0.0290
PTH (pg/ml)	37.0 (31-.0-53.0)*	37.1 (22.8-51.4)	37.9 (32.0-52.0)*	0.3297
Bone densitometry				
L1 -L4 T score	2.4 (1.8-3.1)	2.7 (1.3-4.2)	2.3 (1.5-3.1)	0.4980
Femural neck T score	-0.2 (-0.6-0.2)	0.73 (-0.4-1.9)	-0.5 (-0.9- -0.1)	0.0174
Lipid profile				
Total cholesterol (mmol/l)	5.3 (5.0-5.7)	5.2 (4.6-5.7)	5.4 (4.9-5.8)	0.5314
LDL cholesterol (mmol/l)	3.3 (2.9-3.6)	3.3 (2.7-3.8)	3.3 (2.8-3.7)	0.9458
HDL cholesterol (mmol/l)	1.6 (1.4-1.7)	1.5 (1.1-1.8)	1.6 (1.4-1.8)	0.3684
Tryglycerides (mmol/l)	1.1 (0.9-1.3)	1.0 (0.7-1.2)	1.2 (0.9-1.5)	0.3356
Total body fat mass (%)	39.40 (34.40-44.40)	46.7 (21.6-53.0)[b]	36.8 (30.9-47.8)	0.5480
Android fat mass (%)	46.25 (27.05-51.93)*	52.7 (22.2-61.0) [b]	40.1 (26.8-48.2)*	0.2731
Gynoid fat mas (%)	47.90 (43.43-51.94)	49.7 (31.4-57.5) [b]	47.7 (42.7-52.6)	0.9786
Glucose metabolism				
Fasting glycaemia (mmol/l)	4.9 (4.7-5.0)	4.9 (4.6-5.2)	4.9 (4.8-5.0)	0.9888
120 min glycaemia (mmol/l)	6.4 (5.9-7.0)	6.3 (5.5-7.1)	6.5 (5.7-7.3)	0.7478
Fasting insulin (pmol/l)	7.0 (4.0-10.0)*	13.2 (5.3-21.1)	6.0 (4.0-8.0)	0.0051
120 min insulin (pmol/l)	35.0 (25.0-67.7)*	67.0 (43.0-132.0)	29.5 (21.0-65.0)*	0.1815
HOMA	1.3 (0.8-2.1)*	3.0 (0.9-5.0)[b]	1.3 (0.9-1.7)	0.0057

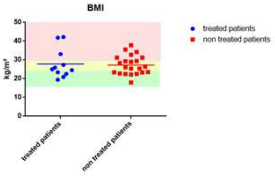
*median (95%CI),), [b] few values

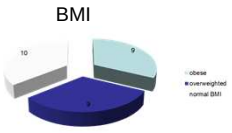
Mineral metabolism
•2 patients (7.1%) presented lithiasis, none had nephrocalcinosis
•1 patient (3.6%) already had a parathyroidectomy, 1 patient (3.6%) had a newly diagnosed parathyroid adenoma

We studied 28 patients:
•89.3% (25) had a PHEX mutation
•M:F ratio 1:3.6
•mean age 39 years (19.4-69.3)
•mean height for males was 160.6 cm and for female 147.0 cm



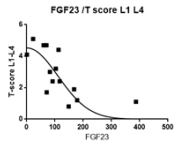
Metabolic profile
•Nine (32.1%), nine (32.1%) and ten (35.8%) patients were obese, overweighted and had a normal body mass index (BMI), respectively





•2 patients (7.1%) had glucose intolerance, none had diabetes
•6 patients (21,4 %) presented dyslipidemia
•No correlations between FGF23 and lipides, body mass composition or glucose metabolism.

Bone mineralisation
•The spinal T score correlated with FGF23 values
R² 0.561



CONCLUSIONS

1. Overweight and obesity is frequent in HHR patients.
2. Vitamin D analogues treatment improves height and cortical bone mineral density.
3. Complications like nephrocalcinosis and hyperparathyroidism are rare.