IS CONVENTIONAL TREATMENT STILL THE FIRST CHOICE IN PEDIATRIC PATIENTS WITH *PHEX* MUTATIONS IN AN ERA OF MONOCLONAL FGF-23 ANTIBODY?

A ALIKASIFOGLU[1], Y UNSAL[1], E N GONC[1], Z A OZON[1], N KANDEMİR[1], M ALIKASIFOGLU[2]

1. Hacettepe University Faculty of Medicine, Department of Pediatrics, Division of Pediatric Endocrinology, Ankara, Turkey.
2. Hacettepe University Faculty of Medicine, Department of Medical Genetics, Ankara, Turkey.

ESPE 2021
The 59th Annual Meeting Online
22-26 September 2021

INTRODUCTION

- Hereditary hypophosphatemic rickets (HR) is a rare renal phosphate wasting disorder.
- HR causes burden on pediatric patients despite conventional treatment of phosphate and calcitriol.

AIM

1. To explore genotype and phenotypic spectrum of HR
2. To analyze short-term, long-term and pubertal impact of conventional treatment on XLHR

METHOD

Genetic analysis

Sanger sequencing MLPA

- 1- *PHEX*
- 2- *FGF23*
- 3- *CLCN5*

Genotype-phenotype analysis

Retrospective analysis

- Clinical caracteristics
- Response to conventional treatment

RESULTS

Figure 1: The distribution of genetic defects

33 subjects from 12 unrelated families
- 16 patients with HR
- 17 first-degree relatives

- ***PHEX* mutation in 18 subjects/ 9 families**
  - **-13 index cases (13/16; 81%)**
  - **-5 first-degree relatives**
  - **9 different mutations**
    - **-5 previously defined**
    - **-4 novel**
    - **- 4 truncating**
    - **- 5 non-truncating**
- **Novel *FGF23* mutation**
  - **-1 index (6.25%)**
  - **-1 first-degree relative**
- **No defect**
  - **2 index cases (12.5%)**

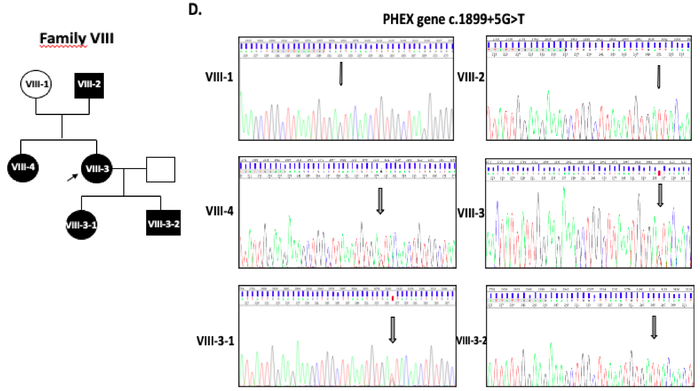
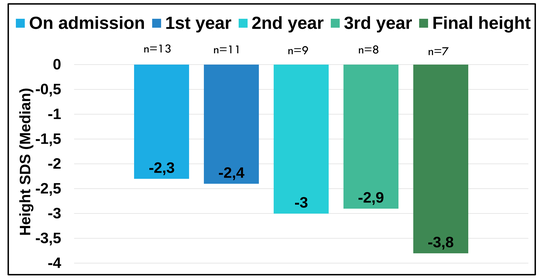


Figure 2: Novel heterozygous splice-site mutation (c.1899+5G>T) of the *PHEX* gene from family VIII. Black symbols indicate affected individuals, and white symbols indicate unaffected individuals. The arrow indicate the proband.

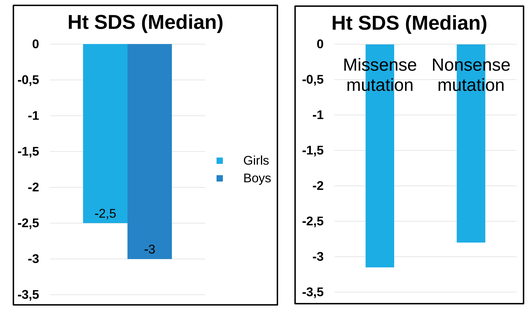
CLINICAL CARACTERISTICS AND RESPONSE TO CONVENTIONAL TREATMENT (Tx)

Figure 3: Change in height (Ht) SDS



	Compliant (n=4)	Non-compliant (n=9)	p
On admission			
Height SDS	-1.70	-2.25	0.386
Phosphate (mg/dl)	3.10	2.70	0.608
ALP (U/L)	512	700	0.044
PTH (pg/ml)	68.2	47.50	0.562
Last Clinic Visit			
Height SDS	-2.62	-3.66	0.045*
Phosphate (mg/dl)	2.23	2.32	0.811
ALP (U/L)	365	560	0.677
PTH (pg/ml)	66	65	0.370

Figure 4,5: Ht SDS for gender and severity of mutation



- **Median phosphate and pubertal ht SDS was lower during puberty (p=0.014 ; 0.09).**
- **Pubertal growth spurt was not observed.**

Follow-up longer than 5 years (n=5)
- Nephrocalcinosis (n=3)
- Hyperparathyroidism (n=2)
- Correction osteotomy (n=4)

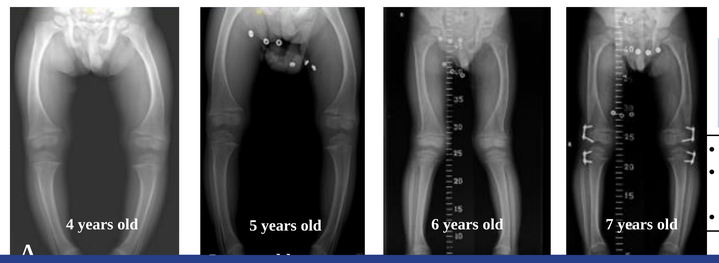


Figure 6: A; The change in lower extremities of subject VI-2 (good compliance) (height SDS when he was 4, 5, 6 and 7 years old were -1.7, -2.19, -1.87, -2.18, respectively).

- All patients had radiologically confirmed rickets.
- 6/10 patients had radiologic recovery at the last clinical visit
- All patients had bowing deformity

CONCLUSIONS

- **Complete metabolic, clinical and radiographic recovery is unlikely during conventional treatment.**
- **Puberty is a period of detorioration in metabolic control and growth during treatment of XLHR.**
- **These findings question the recommendation of conventional treatment as first-line in patients with XLHR.**

CONTACT INFORMATION

Yagmur Unsal, MD
Department of Pediatrics
Division of Pediatric Endocrinology
Hacettepe University Faculty of Medicine, Ankara, 06230, TURKEY
Phone: +905367950760
Email: yagmurunsal@yahoo.com