IS CONVENTIONAL TREATMENT STILL THE FIRST CHOICE IN PEDIATRIC PATIENTS WITH

PHEX MUTATIONS IN AN ERA OF MONOCOLONAL FGF-23 ANTIBODY?

A ALIKASIFOGLU, Y UNSAL¹, E N GONÇ¹, Z A OZON², N KANDEMİR¹, M ALIKASIFOGLU²
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.

METHOD

Genetic analysis

Genotype-phenotype analysis

Retrospective analysis

Clinical characteristics

Response to conventional treatment

Sanger sequencing

MLPA

1. PHEX

2. FGF23

3. CLCN5

CONCLUSIONS

• Complete metabolic, clinical and radiographic recovery is unlikely during conventional treatment.
• Puberty is a period of deterioraion 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

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

RESULTS

Figure 1: The distribution of genetic defects

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

PHEX mutation
- 16 subjects/9 families
- 9 index cases (13/16; 81%)
- 5 first-degree relatives

Novel FGF23 mutation
- 1 index (6.25%)
- 1 first-degree relative

No defect
- 2 index cases (12.5%)

4 truncating
- 4 previously defined
- 4 novel

-5 non-truncating

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

On admission 1st year 2nd year 3rd year Final height

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

CONCLUSIONS

• Complete metabolic, clinical and radiographic recovery is unlikely during conventional treatment.
• Puberty is a period of deterioraion 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

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, 2.18, 2.19, respectively).

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