Clinical and Biological parameters Associated to the Severity of X-linked Hypophosphatemia in Children

A.Salcion-Picaud[1], A.Rothenbuhler[2], A.Etcheto[1], A.Molto[1], K.Briot[1], A.Linglart[2]
[1]Department of Rheumatology, Cochin Hospital, APHP 75014 Paris, France
[2] Department of Pediatric Endocrinology and Diabetes, Bicêtre Hospital, Paris Sud University, APHP, 94275 Le Kremlin Bicêtre, France.

Background

X-linked hypophosphatemia or XLH is a rare genetic disease, often revealed in children by rickets, growth failure, delayed walking, and leg bowing. Clinically the severity is reflected by leg deformities. The aim of our study was to assess the clinical and biochemical parameters correlated to the severity of XLH at the end of growth.

Patients and Methods

Monocentric retrospective study of patients treated with phosphate supplements and vitamin D analogs followed (between 1965 and 2017) from diagnosis of XLH to their final height with data available all along follow-up. Patients treated with recombinant human growth hormone or who had orthopedic surgery before the end of growth were excluded. Data concerning final height, family history of XLH, age at diagnosis, adherence to treatment (range from 0 to 5), history of tooth abscesses, alkaline phosphatase (ALK) level at diagnosis, ALK levels outside the therapeutic target during follow-up were collected.
Severity was defined by leg deformities (intermalleolar distance > 0 cm and intercondylar distance ≥ 6 cm) at end of growth.

Straight legs at near final height
neat final height

Leg bowing at

Results

Among the 234 patients screened, 101 were still growing, 17 had surgery before the end of growth, 27 received recombinant human growth hormone treatment and 58 had missing data. Finally, 31 patients were included of which 22 women with a mean age of 27.3 years. 14 patients had straight legs at the end of growth and 17 had leg deformities. On univariate analysis, only age (31.3 vs 22.5 OR=1.06 [1.00-1.15] p=0.078) familial history of XLH (7 vs 10 OR=0.39 [0.11-1.55] p=0.068), treatment adherence (2.5 vs 3.8 OR=0.03 [0.01-0.02] p=0.0041) and ALK level outside the therapeutic target (106vs54 OR=1.01 [0.99-1.03] p=0.086) were significantly different between the two groups.
On multivariate analysis only treatment adherence appears to be significantly associated to the severity of the disease (OR=0.02 [0.00-0.022] p=0.007).

	Leg bowing N=17	Straight legs N=14
Age (years)	31.3 +/-14.4	22.5 +/- 9.9
Sexe (female)	12 (70%)	10 (71%)
Familial XLH	7 (41%)	10 (71%)
Age at treatement initiation (years)	3.79 +/- 3.9	2.29 +/- 1.24
Treatement initiation < 2 years	8 (47%)	9 (64%)
Adherence score (0 to 5)	2.53 +/-1.12	3.81 +/- 0.48
History of dental abcesses	9 (53%)	7 (50%)
Alkaline Phospatase at diagnosis (IU/L)	738 +/- 432	938 +/- 479
Final height (cm)	154.6 +/-4.9	158.9 +/- 8.5
Final height (SDS)	-1.35	-1.03

Conclusions
This retrospective study suggests that non-adherence to treatment is a major factor associated to severe disease at the end of growth, emphasizing the importance of therapeutic education of patients and their caregivers.

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Bone, growth plate and mineral metabolism
A Rothenbuhler
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