

# Outcomes of vitamin D analogues and phosphate supplements in patients with hereditary hypophosphatemic rickets (HHR), comparison with non-treated patients.

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## BACKGROUND

→ treatment with vitamin D analogues (VDA) and phosphate supplements (“conventional treatment”)

- The evidence of the so-called “conventional treatment” is based on few reports and reviews of cohorts of patients with HHR.
- Despite the current “conventional treatment”, complications include short stature, pseudofractures, due to severe osteomalacia, bone pain, muscle weakness, fatigue, hyperparathyroidism, nephrocalcinosis and entesopathies.
- Our objective was to compare the adults who received the “conventional treatment” during their childhood with adults who did not, and appraise the burden of the disease in adulthood.

## METHODS

- We retrospectively studied 108 adults currently followed or symptomatic first-degree relatives of patients followed at Bicêtre Hospital (Le Kremlin-Bicêtre, France) and Queen Fabiola Hospital (Brussels, Belgium)

Group 1 - 50 patients who received VDA and phosphate supplements during childhood

- Group 2 - 58 patients who did not receive VDA :
- 27 out of 58 received phosphate supplements
  - 31 out of 58 never had any treatment

- Last available data were recorded from patients' medical files.

- The diagnosis of HHR was made on biochemical criteria:

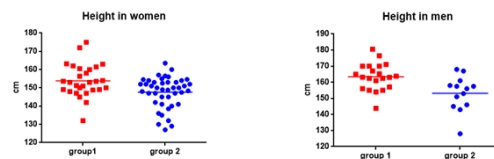
- 1- low serum phosphate and
- 2- low TRP
- and/or
- 3- elevated FGF23.

Adults outcomes	Group 1 (VDA+P) N=50	Group 2 N= 58	P
M:F ratio	1:1.38	1:3.45	
PHEX	29	34	
Age (years)	25.17 (23.24-27.10)	41.69 (37.85-45.53)	<0.0001
<b>1. Growth</b>			
Adult height (SD)	-1.70 (-2.16- -1.25)	-2.91 (-3.31- -2.51)	0.0001
BMI (kg/m <sup>2</sup> )	25.13 (23.43-26.82)	26.44 (25.00-27.88)	0.2333
<b>2. Bone disease</b>			
Leg bowing	14/39 (35.89%)	25/28 (89.28%)	<0.0001
Bone pain	20/28 (71.42%)	28/32 (87.5%)	0.2190
Fractures	2/39 (5.12%)	12/42 (28.57%)	0.0019
Corrective leg surgery	14 (28.00%)	40 (68.96%)	0.0001
<b>Bone mineral density</b>			
Spine L1-L4: g/cm <sup>2</sup>	1.46 (1.15-1.76)	1.18 (0.95-1.42)	0.0918
Spine L1-L4: Z-score	2.29 (1.22-3.35)	0.81 (0.68-0.94)	0.0764
Femoral neck: g/cm <sup>2</sup>	1.17 (0.98-1.37)	0.82 (0.72-0.92)	0.0053
Femoral neck: Z score	1.77 (0.30-3.25)	-0.54 (-1.09-0.01)	0.0005
<b>3. Teeth</b>			
Decayed Missing Filled Teeth index	3.4	19.3	<0.0001
<b>4. Neuroauditive diseases</b>			
Reported hearing impairment	0/50 (0.00%)	5/58 (8.62%)	0.0956
Chiari 1 malformation in MRI	2/50 (4.00%)	1/58 (1.72%)	0.8962
<b>5. Mineral metabolism</b>			
Hyperparathyroidism	5 (10.00%)	4 (6.89%)	0.8156
Nephrocalcinosis on renal ultrasound	5/29 (17.24%)	3/43 (6.97%)	0.3286
<b>6. Metabolism</b>			
Systolic blood pressure (mmHg)	117.33 (110.51-124.15)	120.32 (113.81-126.83)	0.5161
Diastolic blood pressure (mmHg)	72.47 (66.89-78.05)	73.4 (67.88-78.91)	0.8096
Cholesterol (mmol/l)	4.78 (4.20-5.36)	4.88 (4.13-5.64)	0.8423
Tryglicerides (mmol/l)	1.01 (0.78-1.24)	1.12 (0.86-1.39)	0.5450
Fasting glycemia (mmol/l)	4.81 (4.50-5.11)	4.94 (4.78-5.09)	0.3706
Fasting insulin (pmol/l)	14.8 (3.78-25.81)	6.13 (3.70-8.55)	0.0112

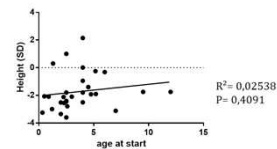
## RESULTS

➢ Group 1 patients vs group 2 patients:

- were taller
- had better correction of leg bowing
- had less leg corrective surgeries
- had better dental health.
- VDA treatment was associated with a higher femoral neck T score and lower fracture incidence in adulthood.
- Complications such as nephrocalcinosis and hyperparathyroidism were similar between groups.



➢ No correlations between age at treatment start and final adult height



## CONCLUSIONS

- The current “conventional” treatment improves height, leg bowing and cortical bone density.
- Corrective surgery is less frequent in patients who received “conventional” treatment during infancy.
- Our results in a large cohort of HHR patients confirm that the use of vitamin D analogues is safe and associated with better long-term outcomes.
- Several features of the disease are not cured and require new therapies