Recombinant Human Growth Hormone In Paediatric Inflammatory Bowel Disease: Short Term Effects On Bone Biomarkers and Long Term Effects On Bone And Lean Mass

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Background

Abnormalities in skeletal health and body composition have been reported in children with IBD. The use of rhGH may lead to improvement in linear growth in children with IBD. Given the anabolic effects of GH, it is possible that rhGH therapy may lead to improvement in bone mass and body composition in these children. However, the effect of rhGH on bone biomarkers as well as bone density in children with IBD remains unclear.

Objectives

To investigate the effects of rhGH on bone and lean mass in paediatric IBD from bone biomarkers and DXA bone mineral density and .

Methods

Bone biomarkers and inflammatory cytokines were evaluated in 12 children,11 crohn's disease (CD) (10M), median age 14.4yr (8.9,16.2); median disease duration 3.7yr (0.6,10.1)who received rhGH (0.067 mg/kg/day). Eight received rhGH for 24 months and had DXA evaluation. Results were reported as median (range) at baseline (T+0), six months (T+6), twelve months (T+12) and 24 months (T+24).

Results

Table 1: Change in Therapy, Anthropometric and Puberty

	T+0 (n,12)	T+6 (n,12)	T+12 (n,8)	T+24 (n,8)
Prednisolone	4/12	1/12	1/8	1/8
Anti TNF therapy	1/12	2/12	2/8	2/8
Surgery	1/12	0/12	1/8	0/8
Enteral nutrition	4/12	1/12	1/8	0/8
BMI SDS	-0.4 (-1.9,0.3)	-0.6 (-1.6,0.4)	-0.3 (-2.3,0.7)	-0.8 (-1.7,1.5)
Ht SDS	-2.3 (-3.3,-1.2)	-1.8 (-3.0,-1.1)*	-1.4 (-2.9,-0.8)*	-0.9 (-2.4,-0.2)*
Tanner stage 1	2/12	2/12	2/8	1/8
Tanner stage 2-3	7/12	5/12	1/8	1/8
Tanner stage 4-5	3/12	5/12	5/8	6/8

Short Term Effects On Bone Biomarkers- 6 Months

Figure 1: Markers of Osteoblastic Function

rhGH for 6 months

↑ Procollagen type I N-terminal propeptide (PINP) and receptor activator of nuclear factor-Kb ligand (RANKL)

↔ Osteoprogeterin (OPG) and bone alkaline phophatase (Data not shown)

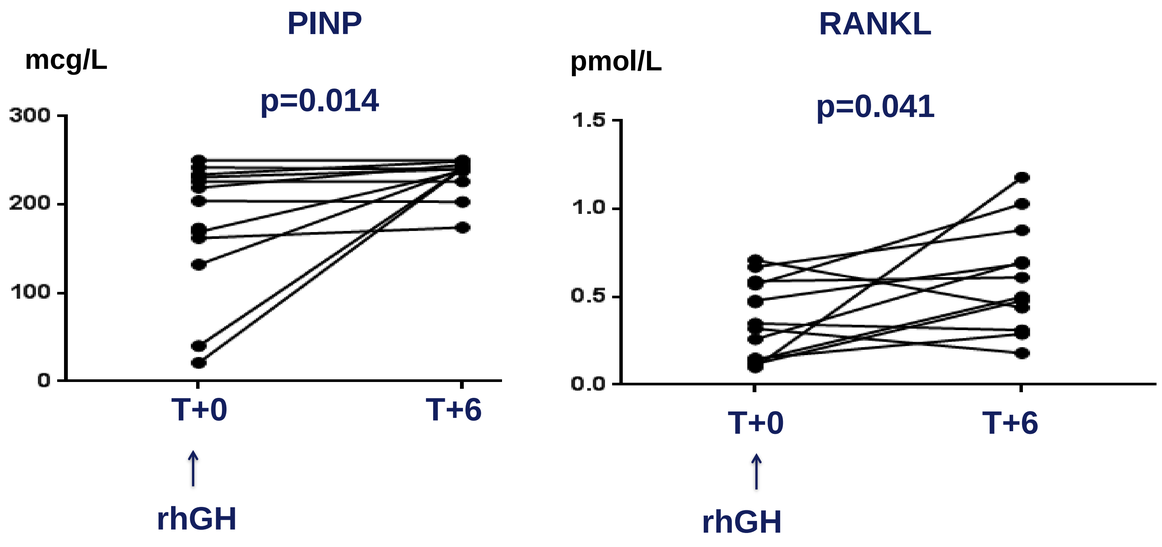
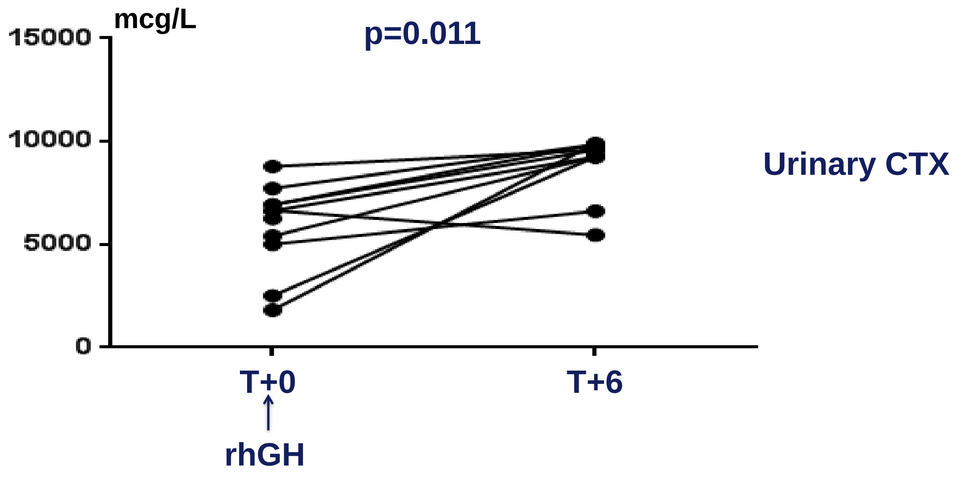


Figure 2:Markers of Osteoclastic Function

rhGH for 6 months

↑ collagen type 1 cross linked c-telopeptide (CTX)



Results contd

Table 2: Disease Biomarkers and Inflammatory Cytokines

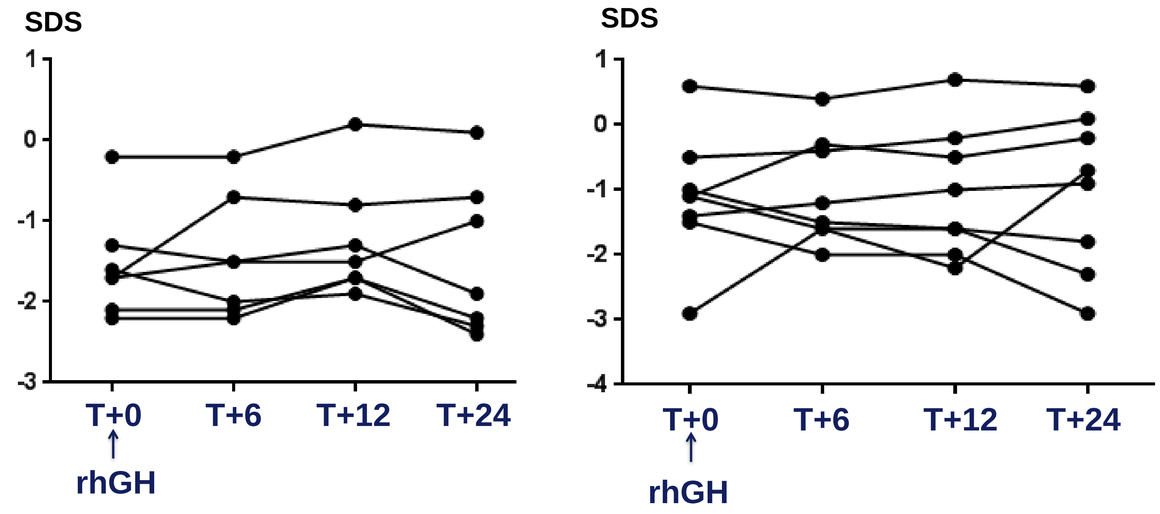
	T+0 (n,12)	T+6 (n,12)	T+12 (n,8)	T+24 (n,8)
ESR (mm/hr)	21.0 (1.0,51)	22.0 (4,50)	22.0 (3,30)	17 (5,48)
CRP (mg/l)	7.0 (7.0,42)	7.0 (7.0,38)	7 (7,26)	9 (3,35)
ALB (g/l)	35.5 (20,40)	36.0 (25,41)	37 (19,41)	37 (30,39)
Platelets (10/l)	398 (272,748)	357 (248,507)	377 (225,504)	375 (200,453)
TNFα (pg/ml)	3.0 (2.8,100.6)	3.4 (3.1,5.3)	NA	NA
IL6 (pg/ml)	3.0 (3,17.5)	3.0 (3.0,28.6)	NA	NA
IL1β (pg/ml)	11.7 (3,796.7)	9.95 (1.3,476)	NA	NA
IFNα (IU/ml)	97.5 (25.1,575.4)	98.5 (25.9,116.3)	NA	NA
IFNγ (pg/ml)	26.9 (20,894.6)	24.9 (4.7,76.4)	NA	NA

Long Term Effects On Bone Density And Lean Mass- 24 Months

Figure 3: DXA LS BMD SDS

rhGH for 24 months

↔ in LS BMD SDS adjusted for bone age or height.



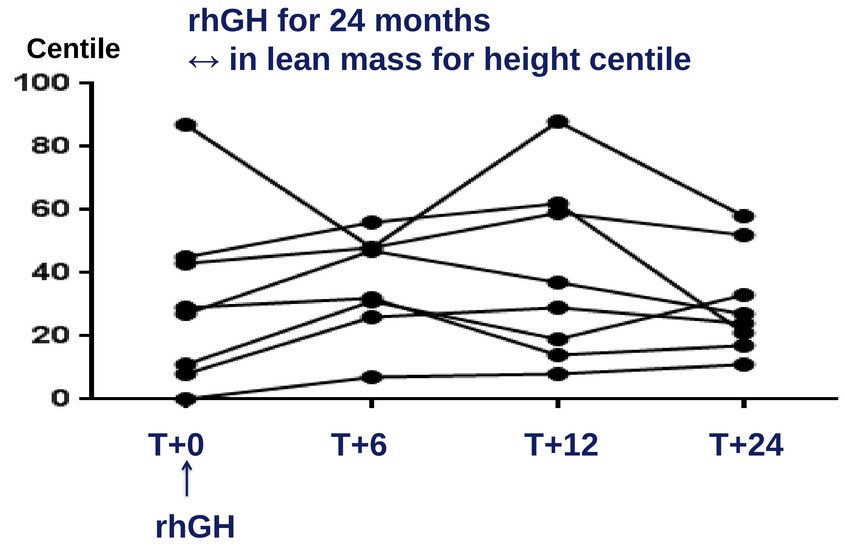
rhGH for 24 months

↔ total body (TB) BMD SDS adjusted for bone age or height and TB bone area adjusted for height centile (Data not shown).

Figure 4: DXA Lean mass(LM) for height centile

rhGH for 24 months

↔ in lean mass for height centile



Conclusion

In this preliminary study, short term treatment with rhGH in paediatric IBD was associated with increase in bone turnover but longer term treatment did not lead to improvement in bone density and lean mass.

rhGH therapy should not be used primarily to improve bone mass in paediatric IBD until results of further studies are available.

Future studies of rhGH should include assessments of bone geometry and microarchitecture in these children.