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The authors have nothing to disclose

Analysis of CD133⁺CD45⁺ hematopoietic progenitor/stem cells and CD133⁺/CD45⁻ very small embryonic-like stem cells in children with growth hormone deficiency subjected to growth hormone (GH) therapy.

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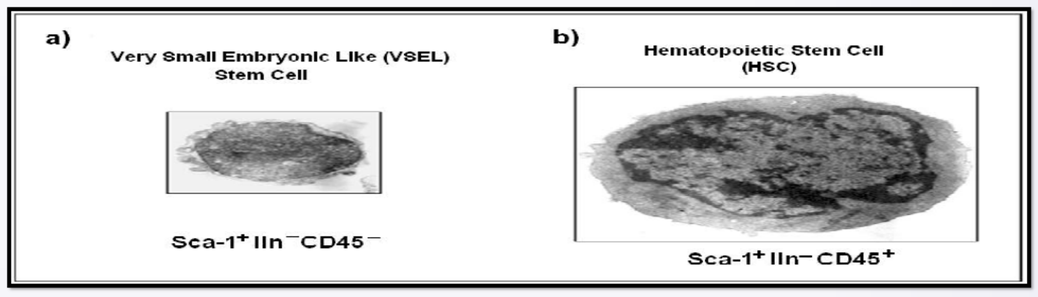
Objectives

Growth hormone deficiency (GHD) is an endocrine condition, caused by problems arising in the pituitary gland that does not produce sufficient quantities of growth hormone (GH). GHD is treated by replacing GH with one daily injections. Recent studies suggested that GH could be involved in regulation of certain stem cell subset potential and function. However, the exact effects of GH therapy on biology of stem cells in pediatric patients were not studied in detail.

The aim of the study was to evaluate the levels of very small embryonic-like cells (VSELs) delineated by Lin-CD133+CD45- phenotype and hematopoietic stem/progenitor cells characterized by Lin-CD133+CD45+ phenotype in relation to treatment with GH.

Characteristic of VSEL(CD133 ⁺ /CD45⁻) & HSC (CD133⁺/CD45 ⁺)



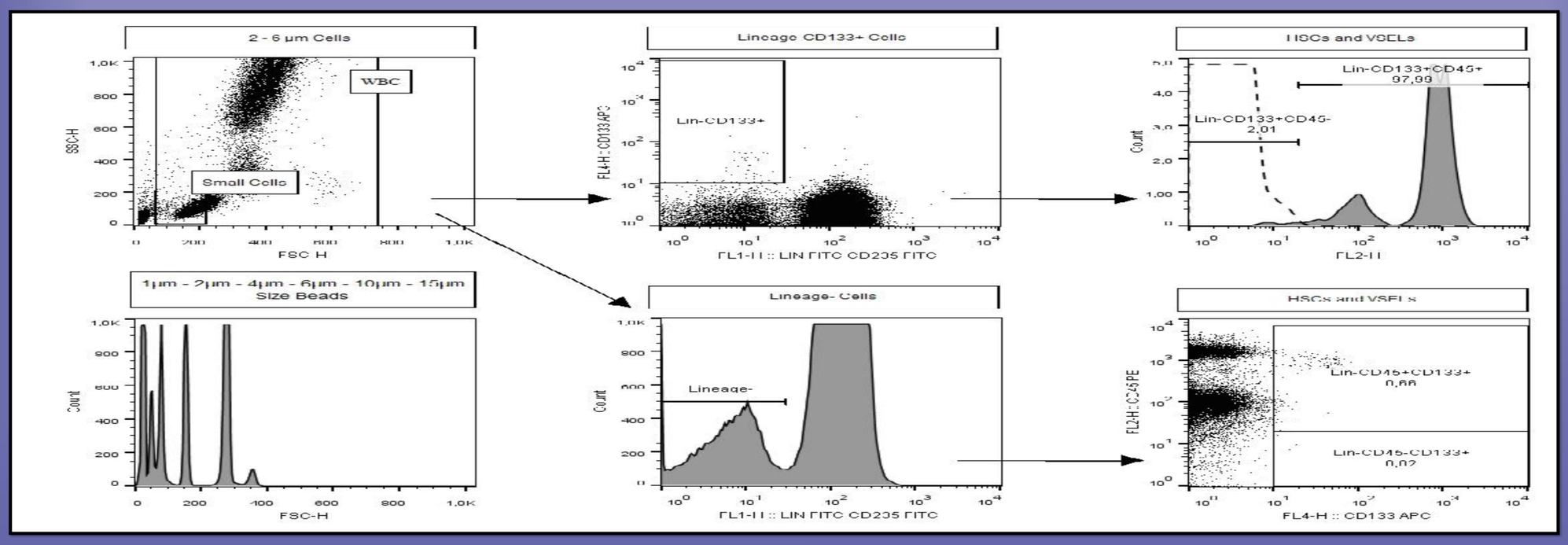
VSEL(CD133 ⁺ /CD45⁻): a)

- ✓Very small embryonic-like cells
- ✓Cells with the characteristics of embryonic stem cells
- ✓Found in tissues of the adult's body
- ✓Combined ESC pluripotent potential and lack of the oncogenic properties

HSC (CD133⁺/CD45 ⁺): b)

- ✓Hematopoietic stem cells
- ✓ Multipotent potential
- ✓Bone marrow, umbilical cord blood, peripheral blood
- ✓Precursor of all the other blood cells
- ✓Ultimately responsible for the constant renewal of blood

Fig1. The strategy of HSC and VSEL gating



Material and methods

	Untreated GHD patients	GHD patients after 2-5 years of GH therapy	Healthy controls	*p, **p
Female/male (n)	18 (6/12)	15 (5/10)	15 (5/10)	
Age (years)	12.5±3	15.2±1.2	14.3±3	NS, NS
Weight(kg)	43.5±2.39	56±5.28	54.2±7.8	p<0.001, NS
Height (cm)	145.3±3.69	156.6±4.3	154±3	p<0.001, NS
fT4 (ng/dl)	1.14±0.7	1.0±0.63	1.2±0.46	NS, NS
fT3 (ng/dl)	3.19±2.27	2.2±0.5	3.2±0.38	NS, NS
TSH (µU/ml)	1.47±1.1	2.57±4.37	2.04±0.72	NS, NS
GH doses (mg/kg/d)	-------	0.025-0.035	------	

Peripheral blood samples were subjected to extracellular staining using fluorochrome-conjugated monoclonal antibodies: anti-CD235 FITC, anti-CD45 PE, anti-CD133 APC, and Lin 1 FITC mixture. Following incubation immunostained blood samples were incubated for with BD FACS Lysing Solution and washed twice to get rid of erythrocytes.

Results

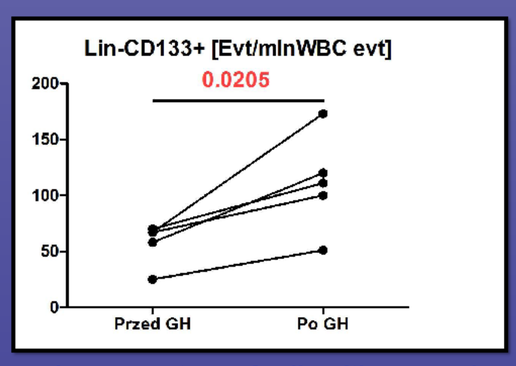


Fig 2. Study shows increasing percentage of cells with expression markers for the progenitor cells

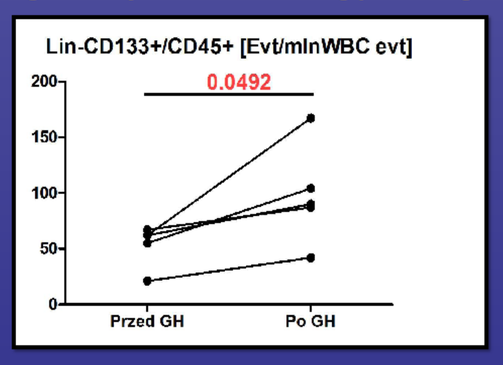


Fig.3 Analysis of HSC befor and after GH therapy in GHD patients

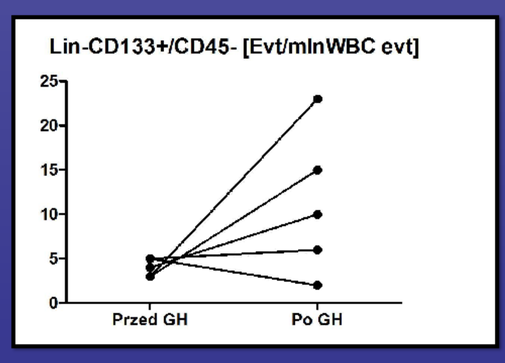


Fig 4.No difference between number of VSEL before and after GH therapy

We conclude that GH therapy in GHD patients can be associated with expansion of peripheral blood stem and progenitor cells. Further studies assessing the longevity of such phenomenon are still warranted.

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