Decrease of small dense LDL and lipoproteinassociated phospholipase A2 due to human growth hormone treatment in short children with growth hormone deficiency and small gestational age status



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Growth hormone deficiency (GHD) and small for gestational age (SGA) status are associated with cardiovascular risks (1-4). We therefore investigated antiatherogenic effects of growth hormone (GH).

Methods:

Subfractions of LDL and HDL, lipoprotein-associated phospholipase A2 (Lp-PLA2), and high-sensitivity Creactive protein (hsCRP) were measured at baseline, after 8 and 52 weeks of GH treatment in 51 short children born SGA (n=33) or with GHD (n=18).

Table 1 Characteristics of 51 children with growth hormone deficiency (GHD) or born small for gestational age (SGA)

| | Baseline | 8 weeks | 52 weeks | P * | |
|----------------------------------|----------|---------|----------|--------|--|
| GHD (n=18, male=12) | | | | | |
| Age (yr) | 9.0 | - | 9.9 | _ | |
| Height SDS | - 2.8 | - 2.6 | - 2.2 | <0.001 | |
| Weight SDS | - 1.9 | - 1.7 | - 1.38 | 0.001 | |
| Body mass index SDS | - 0.24 | - 0.12 | - 0.35 | NS | |
| Systolic blood pressure (mmHg) | 103 | 106 | 103 | NS | |
| Diastolic blood pressure (mm Hg) | 58 | 64 | 64 | NS | |
| HbA1c (%) | 5.35 | 5.2 | 5.4 | NS | |
| GA (n=33, male=18) | | | | | |
| Age (yr) | 6.5 | - | 7.4 | _ | |
| Height SDS | - 2.7 | - 2.5 | - 2.1 | <0.001 | |
| Weight SDS | - 2.8 | - 2.8 | - 2.29 | <0.001 | |
| Body mass index SDS | - 1.3 | - 1.3 | - 1-11 | NS | |
| Systolic blood pressure (mmHg) | 103 | 101 | 103 | NS | |
| Diastolic blood pressure (mmHg) | 61 | 60 | 62 | NS | |
| HbA1c (%) | 5.55 | 5.6 | 5.5 | NS | |

Table 3 Follow-up of inflammation- and growth factor-related parameters in 51 children with growth hormone deficiency (GHD, n=18)) or born small for gestational age (SGA, n=33))

| | Baseline | 8 weeks | 52 weeks | <i>P</i> * |
|---------------|----------|---------|----------|------------|
| Lp-PLA2 (U/I) | | | | |
| Overall group | 369.5 | 339.0 | 333.0 | 0.001 |
| GHD | 407.0 | 346.0 | 339.0 | NS |
| SGA | 367.0 | 331.5 | 328.5 | 0.002 |
| hsCRP (mg/l) | | | | |
| Overall group | 0.60 | 0.20 | 0.30 | 0.005 |
| GHD | 0.80 | 0.30 | 0.50 | NS |
| SGA | 0.60 | 0.20 | 0.20 | 0.037 |
| IGF-1 (ng/ml) | | | | |
| Overall group | 87.0 | 174.5 | 207.0 | <0.01 |
| GHD | 51.5 | 112.0 | 120.0 | <0.01 |
| SGA | 100.5 | 205.0 | 232.5 | <0.01 |
| | | | | |

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Conclusions:

Children with GHD or born SGA may benefit from GH treatment by growth acceleration and simultaneous reduction of their cardiovascular long-term risk.

Results:

For the overall group, we found post-treatment reductions of LDL cholesterol, small-dense LDL cholesterol, Lp-PLA2, and hsCRP, but increases of HDL2a cholesterol. SGA children showed reductions of small-dense LDL cholesterol Lp-PLA2, hsCRP and increases of HDL2a cholesterol. GH deficient children had non-significant decreases of small-dense LDL cholesterol, Lp-PLA2, hsCRP and increases of HDL2a cholesterol.

Table 2 Follow-up of lipids (mg/dl) in children with growth hormone deficiency (GHD, n=18)) or born small for gestational age (SGA, n=33)

| | | <u>Baseline</u> | 8 weeks | 52 weeks | P * |
|---------------------------------|---------------|-----------------|---------|----------|--------|
| LDL-C | Overall group | 87.9 | 82.4 | 78.4 | 0.016 |
| | GHD | 92.4 | 83.2 | 84.8 | 0.046 |
| | SGA | 85.9 | 81.6 | 75.9 | NS |
| non-sdLDL-C | Overall group | 65.6 | 64.8 | 61.0 | NS |
| | GHD | 67.4 | 64.8 | 67.4 | NS |
| | SGA | 65.6 | 63.4 | 57.3 | NS |
| sdLDL-C | Overall group | 21.3 | 18.7 | 17.9 | <0.001 |
| | GHD | 21.5 | 18.8 | 18.3 | NS |
| | SGA | 20.7 | 18.0 | 17.3 | 0.020 |
| HDL-C Overall gr GHD SGA | Overall group | 51.0 | 50.0 | 50.5 | NS |
| | GHD | 51.0 | 53.0 | 53.0 | NS |
| | SGA | 50.0 | 50.0 | 49.0 | NS |
| HDL2a-C Overall group GHD SGA | Overall group | 16.4 | 16.7 | 17.6 | 0.025 |
| | GHD | 16.4 | 16.0 | 17.2 | NS |
| | SGA | 16.4 | 17.0 | 17.8 | 0.004 |
| HDL2b-C Overa GHD SGA | Overall group | 13.3 | 14.2 | 13.7 | NS |
| | GHD | 13.9 | 15.7 | 16.6 | NS |
| | SGA | 13.1 | 13.7 | 12.4 | NS |
| HDL3-C Overal GHD SGA | Overall group | 14.1 | 13.3 | 12.7 | NS |
| | GHD | 14.4 | 13.0 | 11.6 | NS |
| | SGA | 14.1 | 13.3 | 13.1 | NS |
| TG Overa | Overall group | 63.0 | 72.0 | 65.0 | NS |
| | GHD | 63.6 | 70.0 | 61.0 | NS |
| | SCA | 56.5 | 72.0 | 66.0 | 0.025 |

References

- 1. Huxley R, Owen CG, Whincup PH, Cook DG, Rich-Edwards J, Smith GD, Collins R. Is birth weight a risk factor for ischemic heart disease in later life? Am J Clin Nutr 2007;85:1244-50
- 2. Capalbo D, Esposito A, Di Mase R, Barbieri F, Parenti G, Vajro P, Pignata C, Salerno M. Update on early cardiovascular and metabolic
- risk factors in children and adolescents affected with growth hormone definciency. Minerva Endocrinol 2012;37:379-89. 3. Lanes R, Soros A, Flores K, Gunczler P, Carillo E, Bandel J. Endothelial function, carotid artery intima-media thickness, epicardial adipose tissue, and left ventricular mass and function in growth hormone deficient adolescents: apparent effects of growth hormone treatment on these parameters. J Clin Endocrinol Metab 2005;90:3978-82.
- 4. Libby P, Ridker PM, Hansson GK, for the Leducq Transatlantic Network of Atherothrombosis. Inflammation in atherosclerosis. J Am Coll Cardiol 2009;54:2129-38.







