Biovascular markers in children with Kabuki syndrome

D.A. Schott¹, B.L.S. Kooger¹, J. Bierau², W.J.M. Gerver¹, L. Zimmermann³, C.T.R.M. Stumpel²

¹Department of Paediatrics Endocrinology MUMC+, ²Department of Clinical Genetics MUMC+, ³Department of Paediatrics Neonatology MUMC+

Introduction
Kabuki Syndrome (KS; OMIM 147920) is a multiple anomaly syndrome mainly characterized by specific facial features, short stature, hypotonia, mental retardation and features of metabolic syndrome. Previous research in other syndromes showed a positive effect of growth hormone (GH) to metabolic parameters. Since a GH study has been started in KS children in Maastricht, it was also interesting to assess the effect of GH to metabolic parameters. A relatively new metabolic marker, which is increased in individuals suffering from metabolic syndrome, is asymmetric dimethylarginine (ADMA). This is an endogenous competitive inhibitor of endothelial nitric oxide synthase (NOS), which prevents synthesis of nitric oxide (NO). Low levels of NO are associated with endothelial dysfunction and an increased risk of cardiovascular disease. Moreover, GH treatment is associated with a significant decrease of ADMA levels.

Materials and Methods
Fifteen pre-pubertal children (age 6.76 ± 2.23 years old) with a genetically confirmed diagnosis of KS (KMT2D or KDM6A mutation) were included. The KS children received daily GH treatment. Plasma ADMA levels and lipid profile (total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides) were measured at baseline and after six months of GH treatment. Plasma ADMA levels were assessed using the LC-MS/MS tandem mass spectrometer.

Results and Discussion
After six months of GH treatment, plasma ADMA levels were decreased from 0.65 ± 0.13 to 0.57 ± 0.03, but not significantly (P = 0.08), see figure 1. In addition, TC was significantly reduced from 3.99 ± 0.82 to 3.77 ± 0.61 (P = 0.04) and LDL showed a borderline significant decrease from 2.15 ± 0.74 to 1.88 ± 0.53 (P = 0.05). HDL and triglycerides did not show a significant difference after six months of GH treatment, see figure 2.

GH treatment in KS children seems to be favourable concerning biovascular markers and their associated risk to cardiovascular disease. However, these are preliminary results with a small sample size.

Figure 1. ADMA levels (μmol/L) at baseline (T = 0) and after six months of GH treatment (T = 1).

Figure 2. Lipid profile (mmol/L) at baseline (T = 0) and after six months of GH treatment (T = 1). TC: total cholesterol, LDL: low-density lipoprotein. *: significant difference (p < 0.05) compared to T = 1.

Conclusion
Children with KS receiving GH treatment showed improved biovascular parameters after six months compared to baseline levels. A larger sample size is required to assess if the results attain significance. However, it seems to be reasonable that GH is a safe treatment on biovascular parameters in KS patients.

References

Acknowledgements
The Dutch Kabuki Syndrome Network (NKS), All referring clinicians.

Correspondence
Nina Schott: da.schott@mumc.nl

Sponsored by
Pfizer

DOI: 10.3252/pso.eu.54espe.2015