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## The L-arginine/NO pathway, homoarginine, and nitrite-dependent renal carbonic anhydrase activity in young people with type 1 diabetes mellitus

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High circulating levels of asymmetric dimethylarginine (ADMA) and low circulating levels of homoarginine (hArg) are known cardiovascular risk factors in adults. While in adults with type 1 diabetes mellitus (T1DM) circulating ADMA is significantly elevated, in children and adolescents the reported ADMA data are contradictory. In 102 children with T1DM and 95 healthy controls (HC) serving as controls, we investigated the L-arginine (Arg)/nitric oxide (NO) pathway. Children with T1DM were divided into two groups, i.e., in children with newly diagnosed diabetes mellitus [T1DM-ND; n=10; age, 8.8 (4.4–11.2) years; HbA<sub>1c</sub>, 13 (8.9–13.9) %] and in those with long-term treatment [T1DM-T; n=92; age, 12.5 (10.5–15.4) years; HbA<sub>1c</sub>, 8.0 (7.2–8.6) %]. Amino acids and NO metabolites of the Arg/NO pathway and creatinine were measured by GC-MS or GC-MS/MS. There was a significant difference between T1DM-T and HC with regard to plasma nitrite [0.53 (0.48–0.61) vs. 2.05 (0.86–2.36)  $\mu$ M,  $P<0.0001$ ] as well as to urinary nitrite [0.09 (0.06–0.17) vs. 0.22 (0.13–0.37)  $\mu$ mol/mmol creatinine,  $P<0.0001$ ]. Plasma, but not urinary nitrite, differed between T1DM-ND and HC [0.55 (0.50–0.66) vs. 2.05 (0.86–2.36)  $\mu$ M,  $P<0.0001$ ]. The urinary nitrate-to-nitrite molar ratio ( $U_{NOX}R$ ), a measure of nitrite-dependent renal carbonic anhydrase (CA) activity, was higher in T1DM-T [1173 (738–1481),  $P<0.0001$ ] and T1DM-ND [1341 (1117–1615),  $P=0.0007$ ] compared to HC [540 (324–962)], but did not differ between T1DM-T and T1DM-ND ( $P=0.272$ ). The lower nitrite excretion in the children with T1DM may indicate enhanced renal CA-dependent nitrite reabsorption compared with healthy children. The Arg/NO pathway is altered in T1DM in childhood and adolescence, yet the role and the importance of hArg and ADMA in T1DM remain to be elucidated.

### Biography

Christina Carmann is a Doctoral candidate in the Department of Neuropediatrics of the University Children's Hospital in Bochum, Germany. The results of her dissertation were published in the *Journal of Amino Acids* in July 2015 entitled "The L-arginine/NO pathway, homoarginine, and nitrite-dependent renal carbonic anhydrase activity in young people with type 1 diabetes mellitus". Her main focus of the study is the L-Arginin/NO-pathway in different pediatric diseases. She is working in the University Hospital of Berne, Switzerland, Department of Pediatric Surgery.

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