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Targeted screening of succinic semialdehyde dehydrogenase deficiency (SSADHD) employing an enzymatic assay for γ-hydroxybutyric acid (GHB) in biofluids

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Introduction: An enzymatic assay for quantification of γ-hydroxybutyric acid (GHB) in biofluids can be employed for targeted screening of succinic semialdehyde dehydrogenase deficiency (SSADHD) in selected populations. We used a two-tiered study approach, in which the first study (proof of concept) examined seven urine samples derived from patients with SSADHD and five controls, and the second study (feasibility study) examined a broader sample population of patients and controls, including plasma.

Objective: Aim of this study was to evaluate split samples of urine and plasma (anonymized) by enzymatic assay, gas chromatography alone (proof of concept) and gas chromatography-mass spectrometry, and the results compared.

Method: Multiple detection methods have been developed to detect GHB. We evaluated an enzymatic assay which employs recombinant GHB dehydrogenase coupled to NADH production, the latter quantified on a Cobas Integra 400 Plus.

Results: In our proof of concept study, we analyzed 12 urine samples (five controls, seven SSADHD) and in the feasibility study, we evaluated 33 urine samples (23 controls, 10 SSADHD) and 31 plasma samples (14 controls, 17 SSADHD). The enzymatic assay carried out on a routine clinical chemistry analyzer was robust, revealing excellent agreement with instrumental methods in urine (GC-FID: $r=0.997$, $p \leq 0.001$; GC-MS: $r=0.99$, $p \leq 0.001$); however, the assay slightly over-estimated GHB levels in plasma, especially those in which GHB levels were low. Conversely, correlations for the enzymatic assay with comparator methods for higher plasma GHB levels were excellent (GC-MS; $r=0.993$, $p \leq 0.001$).

Conclusion: We have evaluated the capacity of this enzymatic assay to identify patients with SSADHD via quantitation of GHB. The data suggests that the enzymatic assay may be a suitable screening method to detect SSADHD in selected populations using urine. In addition, the assay can be used in basic research to elucidate the mechanism of the underlying disease or monitor GHB-levels for the evaluation of drug candidates.

Biography

Cédric Wernli worked for about 10 years as a Lab Technician in the Clinical Chemistry laboratory in Toxicology department at the University Hospital in Basel. After his studies in Pharmacy at University of Basel (MSc in Pharmacy, 2013), he passed the board exam as a Pharmacist in October 2013. Since then, he works as a PhD-student at the University of Basel in coorperation with the University of Applied Science and Arts Northwestern Switzerland in developing quantitative lateral flow immunoassays for therapeutic drug monitoring in whole blood.

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