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P91 REAL-TIME BREATH ANALYSIS OF ANTIEPILEPTIC DRUGS

[1,2]KD Singh*, [1]V Ziesenitz, [1]J Usemann, [1]U Frey, [1]J van den Anker, [1]A Datta, [1,2]P Sinues. [1]*University Children's Hospital Basel (UKBB)*; [2]*Department of Biomedical Engineering, University of Basel, Basel, Switzerland*

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Background In the field of medicine, serum concentrations of drugs with a narrow therapeutic window, used to treat seizures, are measured to assure the most efficacious and safe way of treating every individual patient. This form of personalised medicine is called therapeutic drug monitoring (TDM). We have explored the possibility to measure and monitor drugs in exhaled breath (EB), to perform completely painless and non-invasive TDM for a future clinical application especially in pediatric patients.

Methods We employed secondary electrospray ionisation in combination with high resolution mass spectrometry to obtain highly resolved EB mass spectra. We then statistically compared these EB mass spectra between patients taking antiepileptic drugs against controls (no drugs), to find potential EB-based bio-markers for drugs. Suspected drug metabolites detected in breath will be compared with systemic blood concentrations. We will screen a total of 15 drugs requiring TDM.

Results So far we have successfully measured EB mass spectra of patients undergoing treatment with Valproic acid (VPA, n = 27), Lamotrigine (n = 19), Levetiracetam (n = 15) and Oxcarbazepine (n = 11). Exploratory data analyses are still ongoing for these drugs. However, for VPA we have identified few candidate ions which enables us to predict free VPA blood concentrations (RMSE 1.5 mg/L). Additionally, we have positively identify two molecules involved in free VPA prediction, based on LC-MS/MS of the exhaled breath condensate. In the near future we will continue to perform data analyses and LC-MS/MS on ions of interest to confirm their identity.

Conclusions This work is a part of an ongoing study and it is too early to come up with a definite conclusion. However, we observed several differentially abundant ions between controls and epileptic patients for various drugs, but the identity and clinical significance of these ions is yet to be determined.

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P92 METABOLOMICS IN CHILDREN WITH HEART FAILURE USING ACE-INHIBITORS, AN EXCITING OPPORTUNITY?

[1]N Smeets*, [2]M Dalinghaus, [1,3]S de Wildt. [1]*Pharmacology and Toxicology, Radboudumc, Nijmegen*; [2]*Pediatric Cardiology*; [3]*Intensive Care and Pediatric Surgery, Erasmus MC – Sophia Childrens Hospital, Rotterdam, The Netherlands*

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Introduction ACE inhibitors (ACEi) have a prominent place in the treatment of heart failure in children. However, there is a significant interpatient variability in efficacy and safety in those children that is not completely understood. Metabolomics provides an interesting innovative approach to better understand underlying mechanisms for variation in disease and response to therapy. With this review, we aim to provide an overview of metabolomics in the field of heart failure therapy with or without ACEi in both adults and children and try to identify gaps in this field.

Methods The PubMed database was systematically searched using several search strategies. Articles were labelled as relevant when they included information on either metabolomics of adult patients with heart failure and/or ACEi-therapy or in children. This yielded 42 relevant articles

Results 24 articles were found describing metabolomics in adults with heart failure, either with or without ACEi-therapy. In addition, several metabolites were identified in adults correlating with either ACEi-efficacy or safety. No metabolomics articles were found in children with heart failure or in children on ACEi-therapy. Several papers (18) were found on metabolomics in children for other diseases and/or treatments.

Conclusion Metabolomics in adult heart failure patients has helped to unravel part of observed disease and therapy variability, and appears helpful in identifying patients at risk for therapy failure as well as detecting novel targets for heart failure therapy. In children, a significant information gap exists. This provides exciting opportunities for personalized treatment of heart failure.

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P93 SEMI-MECHANISTIC MODELLING OF HYDROCORTISONE PHARMACOKINETICS IN PAEDIATRIC PATIENTS WITH ADRENAL INSUFFICIENCY

[1]V Stachanow*, [2]J Melin, [1]R Michelet, [3]O Blankenstein, [3]U Neumann, [4]R Ross, [4]M Whitaker, [5]W Huisinga, [1]C Kloft. [1]*Freie Universität Berlin, Berlin, Germany*; [2]*AstraZeneca, Gothenburg, Sweden*; [3]*Charité-Universitätsmedizin Berlin, Berlin, Germany*; [4]*The University of Sheffield, Sheffield, UK*; [5]*Universität Potsdam, Potsdam, Germany*

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Background Patients with congenital adrenal hyperplasia (CAH) have low to no biosynthesis of cortisol and require lifelong cortisol replacement. Optimisation of hydrocortisone (HC, synthetic cortisol) therapy in this population is important, since too low or high cortisol concentrations increase the risk of adrenal crisis or Cushing's syndrome[1]. HC has nonlinear pharmacokinetics (PK) caused by saturable binding to corticosteroid binding globulin (CBG)[2]. The objective of this analysis was to extend an established paediatric HC PK-model[3] with dried blood spot (DBS) data in order to further characterise the binding behaviour of HC in children.