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RELIABLE RESULTS IN CONTINUOUS BIOANALYSIS OF PAEDIATRIC RENIN SAMPLES – COMPREHENSIVE QUALITY ASSESSMENT WITHIN CLINICAL STUDIES IN CHILDREN

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Background As the initiator of the Renin-Angiotensin-Aldosterone-system, renin plays an essential role in the vicious circle of heart failure. Therefore, renin was determined in the investigators driven ‘Labelling of Enalapril from neonates up to adolescents’ (LENA) study to evaluate its role in paediatric heart failure. Due to the often long-lasting periods of recruitment of paediatric subjects, the assay performance has to be guaranteed over the whole recruiting time. Therefore, to ensure the high quality of the determined renin study samples after successful assay validation,¹ a multi-step quality approach was used to get reliable results over a period of 30 months.

Methods Based on a multi-step quality approach consisting of calibration standards (CSs), quality controls (QCs) and incurred sample reanalysis (ISR), study samples of unknown renin concentrations were determined. Results within predefined limits of CSs (6 levels) and QCs according to European Medicine Agency (EMA) guidelines were required for evaluating the study samples.² ISR was performed for randomly selected paediatric samples to evaluate the long-term accuracy of the validated assay.

Results 133 analytical runs were conducted for renin from February 2016 to August 2018. In 119 (88.8%) valid runs, a total number of 1414 of CCs and 952 of QCs were determined. Thereof 99.9% of CCs and 98.3% of QCs were in the predefined limits according to EMA. 143 incurred sample pairs were reanalysed resulting in 95.8% of samples within EMA guidelines. Using this multi-step quality approach, the reliable determination of 965 LENA paediatric study samples was guaranteed.

Conclusion In addition to the assay validation, the multi-step quality approach ensured the reliability of the determined renin concentrations in the continuous bioanalysis of the paediatric study samples and guaranteed the high quality of the collected data in the LENA study.

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APREPITANT IN THE PREVENTION OF CARDIOTOXIC ADVERSE EFFECTS OF DOXORUBICIN IN THE PAEDIATRIC POPULATION – A SYSTEMATIC LITERATURE INVESTIGATION

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Background In cell line experiments, the selective NK-1-receptor antagonist Aprepitant was able to inhibit the cardiotoxic adverse effects of Doxorubicin,¹ a common cytostatic used in paediatric cancer therapies. Cytostatic therapy is one of the principal reasons for toxic cardiomyopathy in children, resulting in dilated cardiomyopathy and consequently leading to heart failure. However, Aprepitant is currently licenced for adults and children and is indicated amongst others in the antiemetic supportive therapy of Doxorubicin regimes. To address the hypothesis of any indication of Aprepitant in preventing cardiotoxic adverse effects of Doxorubicin, systematic literature research is needed.

Methods Systematic literature research was examined using PubMed in January 2019. Selected inclusion criteria were: ‘Substance P’ or ‘Aprepitant’ and ‘Doxorubicin’/‘cardiac inflammation’/‘cardiomyopathy’ or ‘Aprepitant’ and ‘paediatrics’/‘neonates’/‘children’. The use of Aprepitant in adults and children as an antiemetic agent and the involvement of Substance P in (neurogenic) inflammation, cardiac infarction or diabetes led to the exclusion of publications.

Results The PubMed search resulted in 220 identified publications whereby 33 were relevant concerning the potential use of Aprepitant in the prevention of cardiotoxic adverse effects of Doxorubicin. It emphasises the potential use of Aprepitant in the prevention of toxic cardiomyopathy by antagonizing the inflammatory effects of the endogenous NK-1-agonist Substance P regarding cell and animal models.^{1 2} Based on these models, Substance P is associated with adverse cardiac remodelling and cardiac inflammation. However, in children, Aprepitant was only used as an antiemetic agent and no off-label indication was described.

Conclusion Since toxic cardiomyopathy is a severe adverse effect in the Doxorubicin therapy in children, the evaluation of the role of Substance P is a promising and worthy approach to condense the knowledge about a potential use of Aprepitant in preventing paediatric toxic cardiomyopathy.

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