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had been exposed to nitrofurantoin during the first trimester of pregnancy. Exposure to nitrofurantoin was not associated with an increased risk of birth defects in general (adjusted OR, 0.850 [95% CI, 0.669–1.080]) or specific malformations.

Conclusion: First-trimester exposure to nitrofurantoin was not associated with increased risk for major birth defects as well as other specific malformations.

Disclosure of Interest: None declared.

PP221—DRUG USE IN THE PAEDIATRIC WARDS IN DENMARK – A NATIONWIDE STUDY WITH FOCUS ON LEGISLATION

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Introduction: Understanding the gap between evidence-based medicine and clinical practice is necessary to improve clinical outcomes in children. This study aimed to investigate the most used drugs, analyzed in defined daily doses (DDD), in the Danish paediatric wards within 1 year.

Patients (or Materials) and Methods: Data were extracted from a Danish database, which contains information about the number of DDD sold to the hospital pharmacies including what is sold to the pediatric wards, hereby estimating the pediatric drug use. Two analyses were made regarding the drug consumption. A main analysis covering the 90% most used drugs where the extent of off-label use and the number of drugs having a Pediatric Investigation Plan (PIP) were explored. Nationwide, 16 hospitals were included representing both general and specialized pediatric departments. Secondly, a test sample analysis was made regarding drug use during hospital admission, covering 80% of the pediatric standard medicine assortments from 3 hospitals; results from the remaining hospitals are being prepared.

Results: One hundred drugs constituted the 90% most used drugs in the pediatric wards. Divided by anatomical classification (ATC), treatment of infections (J), drugs used for alimentary tract and metabolism problems (A), and antineoplastic and immunomodulating agents (L) were most prescribed. The subgroup L has not been among the most used ATC groups before, the expenses for this subgroup constitutes 25% of the entire pediatric medicine budget. Fifteen drugs (15%) were by all indications off label, the amount of DDD used off label accounted for 9.2%. A PIP existed on 25% of the PIPs and adolescents in 64%.

In the test sample 71% of the drugs were repeated when compared with the results from the main analysis. The immunomodulating agents were not included. Contrary to the main analysis, drugs aimed at the nervous system (N) were among the most used subgroups.

Conclusion: The PIP is a fairly new step toward evidence-based medicine ensuring the safety, efficacy, and positive risk-benefit balance by assessing clinical trials in children. However, only one fourth of 100 most used drugs in pediatric wards have a PIP and only 8 of these are completed. As a consequence, off-label drug use is frequent in Danish children and rational guidance regarding prescriptions in several areas is needed.

Disclosure of Interest: S. Haaslund-Krog; Other: An article addressing the same results and subjects will be submitted to a journal in April 2013. R. Mathiasen: Other: An article addressing the same results and subjects will be submitted to a journal in April 2013. H. Holst: Other: An article addressing the same results and subjects will be submitted to a journal in April 2013.

PP222—THERAPEUTIC DRUG MONITORING OF DAPTOMYCIN: A RETROSPECTIVE MONOCENTRIC ANALYSIS

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Introduction: Daptomycin is a lipopeptide antibiotic with rapid concentration-dependent bactericidal action against Gram-positive organisms. Target daptomycin plasma concentrations have been determined in animal models for some pathogens, but data on optimal exposure in humans are still lacking. Measurement of daptomycin plasma concentration is available at our institution since 2009 and is performed regularly. The aim was to assess variability of daptomycin plasma concentrations and the main determinants influencing daptomycin exposure.

Patients (or Materials) and Methods: We retrospectively collected data in patients with at least 1 determination of daptomycin plasma concentrations during the period of January 2009 to February 2012 at the University Hospital of Zurich. Samples were analyzed by LC-MS/MS. Because daptomycin is mainly eliminated by the kidneys, exposure in patients with no renal replacement therapy (nRT), intermittent RT (iRT), and continuous RT (cRT) was compared. A trough level (Cmin) of at least 10 mg/L and a minimal peak level (Cmax) of 50 mg/L were defined as optimal based on animal data.

Results: Ninety patients were identified with a mean (SD) age of 59 (16) years and a mean body weight of 74 (21) kg with 15 (16%) patients having a BMI > 30. The mean total daptomycin dose was 448 (133) mg (range, 175–1000 mg). In 22%, daptomycin was administered every 48 hours and in 1% every 36 hours. Mean Cmax was 66.2 mg/L (n = 247; range, 20–236 mg/L) and mean Cmin was 16.7 mg/L (n = 116; range, 2–68 mg/L). Cmax and Cmin levels were significantly lower in cRT (52 [20] mg/L and 9.5 [7] mg/L, respectively) compared with nRT (75.6 [42] mg/L and 21.4 [16] mg/L, P < 0.0001). Cmin below 10 mg/L was found in 69% of cRT, in 35% of iRT, and 26% of nRT. When controlling for plasma creatinine and albumin concentrations, dose interval, administered dose/kg and BMI, cRT remained significantly associated with an increased risk of a Cmin level below 10 mg/L (OR = 3.1; P = 0.001) compared with nRT. There was an inverse and independent association between administered dose/kg and Cmax below 50 mg/L (OR = 2.0; P = 0.003). Trough levels >20 mg/L were mainly seen in nRT patients with renal impairment with only 2 cases of mild CK elevation.

Conclusion: Daptomycin exposure is highly variable depending on renal function and renal replacement therapy used. Patients undergoing cRT had the highest proportion of low daptomycin exposure with the highest risk for possible under dosing.

Disclosure of Interest: None declared.

PP223—PERCEPTIONS TOWARDS BENZODIAZEPINE DISCONTINUATION IN NURSING HOMES

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Introduction: Guidelines caution prescribers and patients against chronic benzodiazepine use (BZD). Nevertheless, BZD use among nursing home residents remains high. We focused on individual residents and explored benefit and harm of chronic BZD use, willingness to try, and barriers against the discontinuation of chronic BZD use by questioning the general practitioner (GP) and the nurse.

Patients (or Materials) and Methods: In this cross-sectional study, we selected nursing home residents with at least 3 months of BZD use. A resident-specific questionnaire was addressed to the GP and nurse. For every resident, the GP and nurse had to score 8 barrier statements on a 10 point Likert scale. Additionally, we collected 10 general attitudes scored by GPs and nurses. The questionnaire was based on an expert meeting and was pretested.

Results: We received data for 109 chronic BZD users. GPs and nurses indicated that the BZD still had the desired effect in, respectively, 87% and 83% of the residents, and that except for dependence; there were no observed side effects in 75% and 70% of the residents. Overall, GPs had higher barriers than the nurses. Nevertheless, the willingness to stop among GPs was higher (respectively 33% vs. 21%). Both caregivers were willing to stop in 13% of the residents. The most common barriers against discontinuation was for both caregivers the fear that initial problems will come back and the preference of a pharmacologic treatment instead of a nonpharmacologic treatment. The GPs perceived the resident's motivation as a larger barrier than the nurses (median, 9 vs 7; P = 0.001) and indicated more often that discontinuation of BZDs can lead to an increase in care burden (median, 8 vs 6; P = 0.028). Of all 10 general statements, the most common attitude among both GPs and nurses was that the longer the resident takes the medication, the more difficult it is to stop (median, 8), and the resident's old age makes it difficult and unnecessary to stop. Nurses, in contrast to the GPs, indicated that there is little knowledge on alternative strategies to handle troubles when stopping BZDs (median, 7 vs 2; P < 0.001) and little scientific information available for stopping (median, 6 vs 2; P = 0.004). The scores for resident-specific barriers were higher than for general statements.

Conclusion: The perceived effectiveness, the absence of side effects and the presence of dependence in most residents that use BZD chronically, result in a low willingness to stop. Implementation of discontinuation initiatives have to address different barriers of different parties requiring multidisciplinary evaluation of residents.

Disclosure of Interest: None declared.