(LDL), high density lipoprotein (HDL), triglycerides (TG), alanine-aminotransferase (ALT) and aspartate aminotransferase (AST), liver size and fibrosis before and during treatment with sebelipase alfa, and adverse events. From the outpatient programme were obtained dose, administrations and weeks of treatment. The efficacy was evaluated by normalising the analytical values of the lipidic and liver profiles in three patients who participated in the clinical trial until April 2018.

Results Three male brothers 12, 15 and 17 years' old diagnosed with LALD before 5 years, heterozygous for mutation in the LIPA gene c.894G>A, c.256C>T. Before the trial, patients presented abnormal analytical values (except TG), hepatomegaly and fibrosis. Patients received continuous treatment with sebelipase-alfa at a dose of 1 mg/kg/2 weeks intravenously. Preparation of the medication was carried out by the hospital pharmacy service. In April 2018, after 225, 183 and 114 weeks of treatment respectively, all three patients maintained the values analysed in the range of normality (except HDL in two and TG in one patient). Hepatomegaly reversed in all patients. The means of the values and of the percentages of variation to the basal were: cholesterol 150.66 ± 22.89 mg/dL (−34.19%), LDL 89.33 ± 12.20 mg/dL (−46.90%), HDL 35.66 ± 6.35 mg/dL (+1.55%), AST 30.66 ± 4.04 IU/L (−64.88%), ALT 21.33 ± 4.93 mg/dL (−65.99%) and TG 130 ± 85.91 mg/dL (+2.12%). Concerning safety, two patients who suffered diarrhoea, and adverse effects related to the infusion were not reported.

Conclusion LALD is a rare disease, and sebelipase-alfa is the first drug authorised for its treatment. The response to treatment with sebelipase-alfa has been favourable from the beginning, with an improvement in the studied variables and a good safety profile in the reported cases.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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No conflict of interest.

5PSQ-008 CYP2C19 SNP'S INFLUENCE ON CLOPIDOGREL RESPONSE IN PERIPHERAL ARTERY DISEASE PATIENTS

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Background Clopidogrel is a prodrug, metabolised to its active metabolite especially by the CYP2C19 enzyme. The effect of CYP2C19 polymorphisms on clopidogrel efficacy in coronary disease had been widely researched. The clopidogrel label recommends testing the CYP2C19 loss of function alleles before the start of the treatment and the DPWG and CPIC pharmacogenetic dosing guidelines recommend switching clopidogrel in case of carrying the CYP2C19*2 SNP in coronary patients with stent. This remains unstudied in peripheral artery disease (PAD) patients.

Purpose Explore the influence of CYP2C19 genetic polymorphisms on clopidogrel response in PAD patients.

Material and methods Peripheral artery disease patients treated with clopidogrel after percutaneous transluminal angioplasty were recruited. They were tested for carrying the CYP2C19*2, *3 (loss of function (LOF)) and *17 (gain of function (GOF))

allele. The primary endpoint was the occurrence of atherothrombotic ischaemic events, diagnosed by ultrasound imaging, during 12 months' follow-up. Furthermore, we collected data about clinical parameters (age, sex, ethnicity), co-medication during follow-up, vascular risk factors and surgical parameters.

We tested the association between carrying LOF or GOF alleles and the primary endpoint in a univariate analysis, and multivariate analysis including those clinical parameters previously related to clopidogrel response. OR and HR were calculated and P-values<0.05 were considered statistically significant.

Results Seventy-two patients were recruited, mean age 67.4 ± 9.4 years, 22.2 females and 100% were caucasians. Carrying CYP2C19 LOF alleles was significantly associated with the primary endpoint in the single analysis (OR=4.49; 95% CI: 1.45 to 13.84; p=0.009), in the multivariate analysis (OR=4.89; 95% CI: 1.32 to 12.83; p=0.018). This association remains significant if we perform a survival analysis (HR=4.07; 95% CI: 1.80 to 9.20; p≤0.001). On the other hand, carrying CYP2C19 GOF alleles was not related to the primary endpoint.

Conclusion CYP2C19 LOF polymorphisms show a higher effect on clopidogrel response in PAD patients than that provided in acute coronary syndrome patients. These SNPs may be used as genetic markers of clopidogrel response in PAD patients. Clopidogrel treatment may be guided by CYP2C19 genotyping, although further analysis should be performed.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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No conflict of interest.

5PSQ-009 CYP2C19 SNP'S INFLUENCE ON CLOPIDOGREL RESPONSE IN CEREBROVASCULAR DISEASE PATIENTS: FINAL RESULTS

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Background Clopidogrel is a prodrug, which is metabolised to its active metabolite especially by the CYP2C19 enzyme. Carrying some polymorphisms, contained in the DNA region encoding the CYP2C19 expression, have shown a significant association with a lack of clopidogrel efficacy among coronary patients. This association had been widely researched and the clopidogrel label recommends testing the CYP2C19 loss of function alleles before the start of the treatment, even DPWG and CPIC pharmacogenetic dosing guidelines, and recommend switching clopidogrel in case of carrying the CYP2C19 loss of function alleles in coronary patients with stent. This remains unstudied in cerebrovascular-disease patients.

Purpose Explore the influence of CYP2C19 genetic polymorphisms on clopidogrel response in cerebrovascular disease patients.

Material and methods Patients after stroke or transient ischaemic event (TIA) treated with clopidogrel after hospitalisation were recruited. These were tested for carrying the CYP2C19*2, *3 (loss of function (LOF)) and *17 (gain of function (GOF)) alleles. As primary endpoint we considered

the combined occurrence of stroke, TIA, cardiovascular death and acute coronary syndrome (ACS). Furthermore, we collected data about clinical parameters (age, sex, ethnicity), co-medication during follow-up and vascular risk factors.

We tested the association between carrying LOF or GOF alleles and the primary endpoint in a univariate analysis, and multivariate analysis including those clinical parameters previously related to clopidogrel response. OR and HR were calculated and P-values < 0.05 were considered statistically significant.

Results Sixty-seven patients were recruited, 53 (79.1%) because of stroke, mean age 68.2 ± 9.83 years, 35.8% females and 100% caucasians. Carrying *CYP2C19* LOF alleles was significantly associated with the primary endpoint in the single analysis (OR=3.82; 95% CI: 1.1 to 13.2; $p=0.028$), in the multivariate analysis (OR=5.07; 95% CI: 1.2 to 21.45; $p=0.023$). This association remains significant if we perform a survival analysis (HR=3.01; 95% CI: 1.01 to 9.0; $p=0.048$). Carrying *CYP2C19* GOF alleles was not related to the primary endpoint in the univariate analysis but, in the multivariate analysis, it was significantly associated with a protection against the primary endpoint.

Conclusion *CYP2C19* LOF polymorphisms may be used as genetic markers of clopidogrel response in cerebrovascular disease patients. Among these patients, *CYP2C19* GOF allele may be considered as a protector against the primary endpoint.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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No conflict of interest.

5PSQ-010 MANIPULATION OF WARFARIN TABLETS IN PAEDIATRIC CARE: DO WE GIVE THE RIGHT DOSE?

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Background Manipulation of drug formulations to achieve an appropriate dose is often necessary in the paediatric ward (e.g crushing and dispersion of tablets, followed by extraction of a fraction). However, such manipulation has previously been shown to result in inaccurate dosing for some tablet formulations of the poorly soluble anticoagulant aspirin. Using the same manipulation procedure, a dispersible tablet formulation of aspirin yielded 99% of the intended dose while a chewable tablet yielded only 9%.¹ Warfarin is another anticoagulant used in paediatric care. Despite having good solubility, ensuring a reliable dose of this substance is important, considering the narrow therapeutic index of the drug.

Purpose To investigate the dose accuracy and dose precision attained after manipulation of two different warfarin tablets, using validated ultra high-performance liquid chromatography (UHPLC-analysis).

Material and methods Warfarin tablets: Marevan (2.5 mg; Takeda AS, Norway) and Warfarin Orion (2.5 mg; Orion Pharma, Finland). Instrument: UHPLC-system from Shimadzu Corp (Nexera, with Prominence DAD-detector). Analytical column: Inertsil 2 μ m C8-3, 2.1 $\times$ 100 mm, (GL Sciences Inc., Tokyo, Japan). The analytical method was validated for linearity, precision and specificity. Dosing accuracy study: six tablets

from each of the two formulations were individually dissolved in 10 ml water. After 8 min, a sample (1 ml) was withdrawn. Dosing accuracy and precision was recorded and compared between formulations.

Results For Warfarin Orion (2.5 mg) 96.5% (SD 4.8; range 89.8%–101.4%) of the intended dose was found. For Marevan (2.5 mg) 101.4% (SD 4.2; range 96.3%–107.2%) of the intended dose was found.

Conclusion Using a validated UHPLC-method, the dosing accuracy upon dispersion and dose extraction from two warfarin tablets (Marevan and Warfarin Orion) was found to be both accurate and precise – unlike that which had previously been published for different aspirin tablets. These results underline the importance of considering both formulation and drug characteristics when manipulating tablets.

REFERENCES AND/OR ACKNOWLEDGEMENTS

1. Notaker N, Brustugun J, Tho I, Bjerknes K. Manipulation and formulation – the tale of two aspirin tablets. Poster abstract. EAHP 2016.

No conflict of interest.

5PSQ-011 VENOUS THROMBOEMBOLIC EVENTS AND TOTAL HIP OR KNEE ARTHROPLASTY: INCIDENCE AND ASSOCIATED FACTORS

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Background Orthopaedic surgery is associated with a high risk of venous thromboembolism events (VTE), especially in total hip arthroplasty (THA) or total knee arthroplasty (TKA). The incidence of VTE with pharmacological prophylaxis after THA or TKA was 0.7%.¹ Although this incidence is low, these adverse events are serious and usually preventable.

Purpose The aims of this study were to evaluate the incidence of VTE and the factors associated with a VTE after THA or TKA.

Material and methods To evaluate this incidence in 2017, the numerator (number of stays with VTE after THA or TKA) and the denominator (number of stays of patients hospitalised to THA or TKA) were obtained from diagnosis related groups (DRG) data. Some demographic and medical characteristics of stays were extracted from DRG data. Information related to the thromboprophylaxis were obtained by analysing prescriptions of the whole stays. The factors associated with a VTE were identified according to Fisher's exact test.

Results A total of 833 stays of THA and TKA were identified. The patients' mean age was 72.2 years. The most common thromboprophylaxis was the use of low-molecular weight heparin (LMWH) in postoperative and rivaroxaban over the following days.

The incidence of VTE was 0.48%. The patients' mean age with VTE was 74 years. The most common thromboprophylaxis was the use of LMWH in postoperative and dabigatran. In the study, any factors were not significantly associated with VTE ($p>0.05$).

Conclusion In our study, the incidence was low. Our prescription software proposed protocols of thromboprophylaxis standardised according to patients' characteristics, especially age. The prescriptions were always performed by senior physicians. The thromboprophylaxis recommendations were respected. This study did not find characteristics significantly