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?

¹J Brustugun*, ²E Birkedal AAS, ³I Tho, ³K Bjerknes. ¹Hospital Pharmacy Enterprises- South Eastern Norway, Sao- Rikshospitalet, Oslo, Norway; ²School of Pharmacy- University of Oslo, Pharmaceutics, Oslo, Norway; ³Hospital Pharmacy Enterprises- South Eastern Norway, Hospital Pharmacy- Lørenskog, Lørenskog, Norway

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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.

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No conflict of interest.

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

A Etangsale*, B Kadri, C Balouzet, E Snobbert, S Pargade, S Camps. Institut Mutualiste Montsouris, Paris, Paris 14th, France

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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

associated with VTE. It could be interesting to perform a national study to identify the factors associated with VTE after THA or TKA. This will allow the establishment of corrective measures to improve patient care and share professional and organisational practices of hospitals with low incidence of VTE.

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5PSQ-012 IMPACT OF THERAPEUTIC PATIENT EDUCATION IN THE PREVENTION AND TREATMENT OF VENOUS THROMBOEMBOLISM IN PATIENTS WITH CANCER

¹L Le Meur*, ² Benzidia, ²A Hij, ¹ Madelaine, ³C Frere, ¹L Deville, ²D Farge. ¹Saint Louis Hospital, Pharmacy, Paris, France; ²Saint Louis Hospital, Internal Medicine, Paris, France; ³Pitié-Salpêtrière Hospital, Biological Haematology, Paris, France

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Background Venous thromboembolism (VTE), including deep-vein thrombosis (DVT) and pulmonary embolism (PE), is a frequent and severe complication in cancer patients, which is the second leading cause of death in this population. International guidelines recommend a low-molecular weight heparin (LMWH)-based treatment during at least 3 months and until chemotherapy begins. The pharmacy and the internal medicine department have developed a patient education programme (PEP) dedicated to patients treated for cancer-associated thrombosis (CAT).

Purpose The objective of PEP is to increase adherence and compliance to long term-treatment, to strengthen the autonomy and to prevent or limit the recurrent VTE or bleeding complications. We describe our cohort of patients and the impact of the PEP programme.

Material and methods From 2014 to 2017, data were retrieved from the electronic patient files. A minimum number of sessions for each patient was set at three, allowing funding by our supervisory authorities. Characteristics of the patients, the number of PEP sessions, anticoagulant, recurrences and bleeding were collected.

Results In the programme, 48 patients were included. The main cancers represented were breast cancer (35%) and lung cancer (13%). Sixty per cent of cancers were metastatic at baseline, 44% of patients were diagnosed with DVT, 12% with catheter related-thrombosis and 44% with PE. Tinzaparin was prescribed in 86% of patients. The average number of sessions performed per patient was 3.5. Nearly 30% of patients did not have this minimum of three sessions, either because of death, treatment break or relay by another drug class. PEP sessions increased the self-injection rate from 40% to 67%, injections by another person from 9% to 12% and reduced the rate of injections by a nurse from 51% to 21%. Nearly 12% of patients had recurrent thrombosis under anticoagulant therapy. Only 4% of patients experienced a bleeding event. In more than 85% of cases, patients reported being observant.

Conclusion The programme fulfilled its objectives, including understanding, treatment adherence and allowing patients to be more independent with injections. This programme is the first to describe a cohort of patients treated for CAT and the

result of a good collaboration between physicians, pharmacists and nurses.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.

5PSQ-013 PRESCRIPTIONS OF DIRECT ORAL ANTICOAGULANTS IN PATIENTS ADMITTED

S Ruiz García*, E Alañón Plaza, A Calvo García, I Cidoncha Muñoz, M Ruiz López, C Martínez Nieto, A Ibáñez Zurriaga, A Morell Baladrón. *Hospital Universitario la Princesa, Farmacia Hospitalaria, Madrid, Spain*

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Background Direct oral anticoagulants (DOACs) require different follow-up than vitamin K inhibitors. DOACs dose adjustment depends on indication, age, renal function and weight, which could made dosage errors easier.

Purpose To analyse the use of DOACs and their prescription profile in the indications funded by the national health system.

Material and methods The retrospective observational study considered patients admitted in February 2017 with a prescription of some DOACs included in the Hospital Pharmacotherapeutic Guide (apixaban, dabigatran and rivaroxaban). Data sources: electronic medical records, primary care prescription and hospital electronic prescription. Data collected: age, sex, DOAC, previous anticoagulant and reason for change, dose, schedule, indication and creatinine level at admission and discharge.

Results Thirty-five patients were included, of whom 51.4% were female; median age was 82 (IQR 78.75–86.25) years. Sixteen (47.1%) patients had previously received acenocoumarol, owing to overdose or haemorrhage (five patients), stroke (four), poor control of INR (four) and patient preference (three). Thirty-six DOACs were prescribed: dabigatran in four (11.1%) patients, rivaroxaban in eight (22.2%) and apixaban in 24 (66.7%).

Two (5.7%) patients were treated with rivaroxaban to prevent thromboembolism in knee replacement with 10 mg every 24 hours for 34 and 49 days, respectively (2 weeks is the optimal duration).

In 33 (94.3%) patients, the indication was prevention of stroke and embolism in patients with non-valvular atrial fibrillation with some risk factor. Twenty-four patients were admitted with DOACs: four with dabigatran, one of them (25%) underdosed; six with rivaroxaban, two of them (33.3%) underdosed; 14 patients with apixaban, five (35.7%) underdosed; and three (21.4%) impossible to evaluate because the weight was unknown. During the admission 10 treatments were initiated, four suspended and three patients died. Three patients were discharged with dabigatran, one of them (33.3%) underdosed; three with rivaroxaban, two of them (66.7%) underdosed; and 23 with apixaban, nine of them (39.1%) underdosed; and three with weight undocumented.

Conclusion DOACs require less follow-up than classic anticoagulants, however it is necessary that the dose adjustment is optimised, the control of treatment length and the promotion of the use of these drugs for their approval indications to ensure their safety and efficacy.

REFERENCES AND/OR ACKNOWLEDGEMENTS

No conflict of interest.