



Letter to the Editor

Prevalence of older in-patients at risk of clopidogrel resistance according to the STIB score. Results from REPOSI registry



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Clopidogrel and acetylsalicylic acid are cornerstones of treatment of the acute coronary syndromes (ACS) and percutaneous coronary interventions (PCI) [1]. The problem of clopidogrel resistance was the object of numerous studies which showed that high platelet reactivity (HPR) in patients treated with this drug is a strong predictor of the risk of ischemic events in patients undergoing PCI [2]; [3]; [4]; [5]; [6]. Matetzky and colleagues showed that 25% of patients undergoing PCI after a previous STEMI were resistant to clopidogrel and therefore at an increased risk of adverse cardiovascular events [7]. In another study, Price and colleagues measured HPR in patients treated with clopidogrel with a point-of-care test, showing that HPR was associated with cardiovascular adverse events that occurred after patient discharge from hospital [8].

Legrand analyzed platelet function in a group of patients with the point-of-care VerifyNow test, showing that HPR in patients treated with clopidogrel was associated with an increased risk of ischemic complications during or after coronary interventions and involved more than 50% of patients undergoing PCI [1]. With the aim to identify patients prescribed with HPR using clinical information available at the bedside, Legrand showed that anemia, body mass index (BMI) and diabetes mellitus, which together define the STIB score, act as independent variables with similar weight in predicting the risk of clopidogrel resistance [1]. The aim of this study was to calculate the STIB score in the older population enrolled in the REPOSI (Registro POLiterapie Società Italiana Medicina Interna) register and treated with clopidogrel.

The REPOSI register is an independent project of the Italian Society of Internal Medicine (SIMI), Foundation IRCCS Cà Granda Policlinic Hospital in Milan and IRCCS Institute of Pharmacological Research “Mario Negri” in Milan. 87 Italian hospital wards of Internal Medicine and Geriatrics contributed to the compilation of the register. Patients aged 65 years and older admitted to the participant wards were enrolled in the study, during a period of 4 weeks, 3 months apart (one week per season), in different years (2010, 2012 and 2014). A total of 3915 patients were enrolled.

The project was approved by the Ethics Committee of each participating hospital and informed consent was signed by all enrolled patients. The register collected data on drug prescription at hospital admission, during hospitalization and at discharge. For the aim of this study data on drug prescriptions collected at the time of hospital admission were used, and patients treated with clopidogrel were specifically analyzed. The classification of patients was based on Legrand's STIB score, defined by the combination of three clinical parameters: anemia,

obesity and diabetes mellitus. According to this score, the probability of HPR in patients taking clopidogrel was 77.8% in those with anemia, obesity and diabetes mellitus, 62.6% in those with at least two of these variables, 44.1% in those with only one of these variables, and 38.5% in patients with no variables [1]. Patients were considered anemic if hemoglobin (Hb) was equal or less than 13.9 g/dl, obese if BMI values were equal or greater than 28 kg/m² and diabetics according to the International Classification of Diseases 9 revision (ICD-9) codes [9] or if fasting blood glucose was equal or greater than 126 mg/dl.

333 of 3915 (8.5%) patients were treated with clopidogrel and represented our study sample. The average age of patients was 78.9 years (7.2 SD), and 53.5% of them were men. 296 (88.8%) of them had anemia, 82 (24.6%) were classified as obese and 183 (54.9%) were affected by diabetes mellitus. Patients were classified according to the four groups identified by Legrand, in order to grade the corresponding risk rate of clopidogrel resistance. Among patients 16.8% had anemia, obesity and diabetes mellitus, so they had a 77.8% probability of having HPR; 39.0% had two variables, so they had a 62.6% probability of having HPR; 39.9% had only one variable, so they had a 44.1% probability of having HPR; 4.2% had no variable, so they had 38.5% probability of having HPR.

Findings from this study show that older patients prescribed with clopidogrel have a high probability of having HPR and thus resistance to clopidogrel according to the simple STIB score, that helps to predict the risk rate of clopidogrel resistance at the bedside according to the presence of anemia, obesity and diabetes mellitus. Legrand was the first to develop a simple clinical indicator in order to predict resistance to clopidogrel. However, another study by Wu and colleagues, published three months before the previous one, must be mentioned because the authors proposed a similar approach to the problem. They showed that obesity and diabetes mellitus were significantly associated with clopidogrel resistance, after proving that clopidogrel induces a lower antiplatelet effect in patients with ACS and metabolic syndrome than in those without metabolic syndrome [10]. The role of anemia was also studied by Giustino and colleagues, showing that anemic patients have HPR higher than non-anemic [11].

The phenomenon of resistance to clopidogrel catches the attention of a growing number of clinicians because of its frequency and the severity of adverse events related to it. The identification of patients with HPR may help to improve their therapy applying the concept of personalized medicine, most important in the older people treated with polypharmacy. The existence of such a simple clinical method as the STIB score, that allows to predict the possible resistance to clopidogrel at the bedside without using expensive laboratory investigations, provides an attractive approach to the problem.

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