Journal of Hematology & Thromboembolic Diseases

Samos and Fedor, J Hematol Thromb Dis 2014, 2:1
DOI: 10.4172/2329-8790.1000129

Letter to the Editor Open Access

Monitoring of Antiplatelet Therapy in Clinical Practice: Is it Necessary or Not?

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Abstract

Dual antiplatelet therapy forms currently the basis in acute coronary syndrome pharmacological treatment. However, there is a wide variability in antiplatelet response to clopidogrel, which may lead to antiplatelet therapy insufficient efficacy and subsequent risk of thrombotic events. Laboratory monitoring of antiplatelet therapy may help to identify patients with insufficient antiplatelet response. We discuss the benefits of routine monitoring of antiplatelet therapy in clinical practice.

To the Editor:

Dual antiplatelet therapy containing aspirin and ADP receptor antagonist forms currently the basis in Acute Coronary Syndrome (ACS) pharmacological treatment. The introduction of ADP receptor antagonists has made a major advance in the ACS treatment. Clopidogrel given in the CURE study in patients with ACS significantly improved the clinical outcome compared with patients treated with aspirin alone [1]. However, there is a wide variability in antiplatelet response to clopidogrel, which may lead to antiplatelet therapy insufficient efficacy and subsequent risk of thrombotic events. High on-treatment platelet reactivity has been associated with a substantial hazard for future cardiovascular events, including stent thrombosis [2]. Variability of antiplatelet response to clopidogrel is associated with several factors, such as variability of clopidogrel absorption, variability of the active metabolite creation, or variability in P2Y12 receptor antagonist activity [3]. These factors may be influenced by both genetic polymorphisms, together with several environmental factors, such as different drug interactions at the level of CYP P 450 2C19 and 3A4, or at the level of P - glycoprotein [3,4]. Recently, there is also growing number of data reporting a failure in antiplatelet response following clopidogrel administration, which is specifically associated with insulin resistance and diabetes mellitus [5], however the mechanism of this antiplatelet resistance is not well understood and further studies will be needed to clarify this issue. Laboratory monitoring of antiplatelet therapy may help to identify patients with insufficient antiplatelet response.

On the other hand, prasugrel–a new ADP receptor antagonist - induces more potent platelet inhibition and patients might be exposed to higher bleeding risk [6]. Prasugrel was shown to increase Non Coronary Artery Bypass Grafting (CABG) - related bleeding in ACS patients undergoing percutaneous coronary intervention. Recently published study have suggested that a VASP index <16 % after ADP antagonist loading dose was predictive of non CABG - related major bleeding [7]. This fact only underlines the importance of tailored antiplatelet therapy and careful monitoring needed for ADP antagonist treatment. High dose clopidogrel treatment might be an alternative to prasugrel therapy in patients with clopidogrel resistance and high risk of bleeding [8]; but this option is recently not generally recommended. Ticagrelor administration may be other effective step to overcome clopidogrel resistance. Ticagrelor – an active, non – thienopyridine ADP receptor antagonist – is not affected by cytochrome P450 pharmacokinetic interactions. In PLATO study [9] ticagrelor effectively reduced mortality in patients with acute coronary syndromes. In this study no difference between diabetic and nondiabetic patients was seen. Silvano et al. described a rare case of resistance to both clopidogrel and prasugrel in nondiabetic patient with acute STEMI [10] due to genetically abnormal metabolism of antiplatelet drugs (reduced activity of CYP P450 2C19 and 3A4 verified by genetic testing), which was successfully treated with ticagrelor administration. Ticagrelor administration therefore may overcome both colpidogrel and prasugrel high on treatment platelet reactivity.

Aspirin is a "classic" antiplatelet agent frequently used in primary and secondary prevention of atherothrombotic events not only in patients with ACS. Nevertheless, large numbers of patients continue to experience these events despite aspirin therapy. "Aspirin treatment failure" has a multifactorial aetiology. Treatment nonadherence and noncompliance (due to gastrointestinal intolerance, bleeding, etc.) is an important problem in clinical practice [11]. However, approximately 10% of aspirin treated patients do not respond appropriately despite adequate compliance. "Aspirin resistance" is a complex problem including drug interactions; inter individual variability in absorption, cyclo oxygenase – 1 gene polymorphism, high platelet turnover and other not yet well understood factors [11]. Simpson et al. recently reported 21.9 % prevalence of aspirin high on – treatment platelet reactivity in diabetic patients and 15.8 % prevalence in nondiabetic patients [12]. Laboratory monitoring of antiplatelet therapy efficacy may also help to identify patients with aspirin resistance, but real clinical importance of this phenomenon remains controversial.

Numerous platelet function tests are currently available for antiplatelet therapy monitoring. Light Transmission Aggregometry (LTA) with specific inducer represents nowadays a "golden standard" in antiplatelet response testing, however, several "point of care" assays had been recently introduced in clinical practice. Verify Now® assay (Accumetries, San Diego, California, USA), for example, allows rapid assessment of platelet response on aspirin, ADP receptor antagonist and glycoprotein IIb/IIIa antagonist in one blood sample [13]. VASP phosphorylation assessment by flow cytometry represents, on the other hand, a specific method for ADP receptor antagonist activity assessment

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Received December 17, 2013; **Accepted** January 22, 2014; **Published** January 24, 2014

Citation: Samos M, Fedor M (2014) Monitoring of Antiplatelet Therapy in Clinical Practice: Is it Necessary or Not? J Hematol Thromb Dis 2: 129. doi: 10.4172/2329-8790.1000129

[14]. Advantage of this examination is its specificity for ADP receptor intracellular pathway and sample stability. Our experience show, that VASP assay is more specific for ADP antagonist efficacy assessment; however LTA is more available in clinical practice. LTA is probably sensitive enough to monitor the efficacy of ADP receptor antagonist therapy. Despite several disadvantages, LTA seems to be a method well applicable in a routine clinical practice. In case of both LTA and VASP assays are not available; at least a bed site testing should be performed. Bed site antiplatelet drug efficacy testing may provide a rough guiding on how to proceed with treatment drugs and dosages.

Although monitoring of antiplatelet treatment is nowadays not generally recommended, it can significantly help to identify patients with insufficient antiplatelet response. Patients with insufficient response may benefit from new ADP receptor antagonists treatment. On the other hand, laboratory monitoring may also identify patients with increased bleeding risk. Routine laboratory monitoring of antiplatelet therapy in selected patients (e.g. in ACS patients) therefore deserves consideration.

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