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Letter to the Editor

„How to optimize individualized strategy for antiplatelet drugs administration/discontinuation management using platelet function testing?“

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We read with great interest the recently published case-control study by Mannacio et al[1]. In regard to preoperative clopidogrel administration management, patients were divided into three equally matched groups with aim to evaluate whether individually tailored preoperative clopidogrel discontinuation management based on platelet function testing may reduce postoperative blood loss and transfusion requirements in patients exposed to clopidogrel in proximity to surgery[1]. Put briefly, the strategy to guide clopidogrel discontinuation management using platelet function testing significantly reduced postoperative bleeding and blood consumption[1]. In addition to, platelet function testing based strategy provided shorter waiting time for surgery after clopidogrel discontinuation, than it is recommended by the current guidelines[1]. Nowadays, different types of devices to measure drug specific platelet reactivity are available. Despite some device specific advantages and disadvantages, some basic principles in preoperative decision making should inevitably be considered as they are applicable to each device providing drug specific platelet function quantification. This study certainly adds to the current knowledge, however, some methodological considerations should be addressed too. Even though case-control matching was used to reduce the effect of potential confounders and calculated propensity scores included preoperative aspirin administration management, the lack of aspirin specific platelet function testing remains to be the drawback of the study[1]. Noteworthy, multivariate analysis confirmed preoperative aspirin as independent predictor for need of 3 or more packed red blood cells (PRBCs)[1]. There is evidence that certain patients have an accentuated response to the usual doses of preoperative aspirin that may result in increased perioperative blood loss[2, 3]. Recently, our research group found that patients who received packed red blood cells (PRBCs) transfusion had significantly lower aspirin sensitive platelet function test values compared to the patients not exposed to PRBCs ($p= 0.002$)[3]. Therefore, it seems reasonable to use concomitantly platelet function assays sensitive to clopidogrel and aspirin. Growing proportion of patients is being

preoperatively exposed to dual antiplatelet therapy (aspirin and clopidogrel). Awidi et coworkers found that the combination of aspirin and clopidogrel had greater inhibitory effects on platelet aggregation than either agent alone[4]. Furthermore, there is evidence that clopidogrel, when administered concomitantly with aspirin reduces the incidence of aspirin resistance[5]. Therefore, platelet inhibitory response to aspirin and consequent risk for excessive bleeding and transfusion requirements in cases of pronounced platelet inhibition should not be underestimated. The influence of aspirin and clopidogrel on bleeding should separately be assessed by drug specific platelet function tests, facilitating individual therapeutic approach for each antiplatelet agent preoperatively. Prospective studies evaluating the relationship between drug specific platelet function test values and outcomes in this particular population should provide firm cutoff values that delineate not only bleeding tendency but also proclivity towards ischemic events in cases of patients with high on treatment platelet reactivity in whom too early discontinuation may cause platelet hyperactivity followed by rebound phenomenon that may finally result in ischemic events while awaiting surgery. In this way it would be possible to frame “safety window” range in platelet drug specific reactivity. Lower bound would delineate bleeding tendency whilst upper bound would delineate proclivity towards ischemic events. We congratulate authors on this timely and elegant study. Further studies using platelet function testing and sufficiently powered to assess possible benefits in clinical outcomes are needed in order to provide the most precise and reliable information about benefits and risks of point-of-care guided preoperative administration/discontinuation for each antiplatelet agent, thus facilitating individual approach to patients with aim to reduce both bleeding and adverse ischemic events.

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