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LETTER TO THE EDITOR

Comparison is not reason: Pitfalls in reporting thrombin generation results in anticoagulated patients

In their recent article, Helin et al[1] reported on a comparative study involving 43 frozen samples assessed on the ST-Genesia using the STG-DrugScreen among which 20 of them were also analyzed on the calibrated automated thrombogram (CAT) using the PPP-reagent. The authors concluded that "the ST-Genesia remains limited in its practical use, failing to measure over-anticoagulation using warfarin and heparin, as well as showing normal ETP with DOAC."

The conclusion of the authors has to be tempered because their results do not permit stating such ending remarks. First, it is not surprising that the STG-DrugScreen behaves differently to the PPP-Reagent. The PPP-Reagent contains 5 pM of tissue factor (TF) with 4 μM of phospholipids. The STG-DrugScreen is closer in its composition to the PPP-Reagent High, which contains 20 pM of tissue factor and 4 μM of phospholipids. We already demonstrated that with lower TF concentrations the sensitivity of thrombin generation toward anticoagulant drugs is increased.[2] Nevertheless, this is at the expense of a higher interindividual variability (ie, the coefficients of variation reported in rivaroxaban-treated subjects varied between 9.8% and 29.6% for the STG-DrugScreen versus 12.6% and 50.0% for the STG-ThromboScreen, respectively),[3] which could be problematic when patient categorization will be needed to set up cutoff for clinical decision making. Second, the authors seemed to rely on the endogenous thrombin potential (ETP) for the evaluation of the intensity of anticoagulation. It has been reported that the ETP is not the most representative parameter to assess the degree of anticoagulation in direct oral anticoagulant–treated patients.[4] The ETP rather should be used in conditions where the anticoagulant system is also involved, for example, by addition of thrombomodulin or activated protein C.[3] Other parameters like the peak height, the mean/max velocity index, or the lag time are more appropriate to assess the degree of anticoagulation, especially with direct factor Xa inhibitors.[2,4] Third, in their study, less than half of the cohort has been "compared" on the two analyzers, that is, 20 samples. The comparison would have been more informative and relevant if the authors had assessed their whole cohort on the two analyzers, using the same triggers and comparing the appropriate counterparts within the two brands, that is, the PPP-Reagent versus the STG-ThromboScreen and the PPP-Reagent High versus the STG-DrugScreen.

Several groups have reported on the use of the ST-Genesia with the STG-DrugScreen application in anticoagulated patients with great success.[3,5,6] While we acknowledge that trying to reach the maximal sensitivity of a test is an important parameter to consider when designing bioanalytical testing, one should keep in mind that the test variability is also a mandatory consideration. Thus, even if the STG-ThromboScreen, or equivalent, may be of interest in anticoagulated patients, the analytical performance and the clinical relevance of a possibly higher sensitivity of this reagent in this context remains to be investigated. Therefore, it seems that Helin et al stand virtually alone in their assumption, and we encourage the researchers to further explore and investigate the possibilities that are brought to us for routinely assessing thrombin generation in anticoagulated patients.

RELATIONSHIP DISCLOSURE

Among the authors, JD is the CEO and founder of QUALIblood s.a., a contract research organization manufacturing the DP-Filter; is a coinventor of the DP-Filter (patent application number: PCT/ET2019/052903); and reports personal fees from Daiichi-Sankyo, Mithra Pharmaceuticals, Stago, Roche, and Roche Diagnostics outside the submitted work; TL reports nonpersonal fees from IRIS and Stago. FM reports institutional fees from Stago, Werfen, Nodia, Roche, Sysmex, and Bayer; and reports speaker fees from Boehringer Ingelheim, Bayer Healthcare, Bristol-Myers Squibb-Pfizer, Stago, Sysmex, and Aspen, all outside the submitted work. The other authors have no conflict of interest to disclose.

AUTHOR CONTRIBUTIONS

JD was responsible for the first draft and the writing of the final version of the manuscript. The other authors reviewed and provided comments on the first draft.

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