How do laboratories interpret unexpected APTT prolongation?

Post-analytical external quality assurance survey in laboratories of 35 countries

E. Ajzner, Sz-Sz-B County'sTeaching Hospital, Central Laboratory, Nyíregyháza, Hungary
On behalf of the EFLM Working Group on Post-analytical External Quality Assurance

Activated Partial Thromboplastin Time (APTT) is a simple clotting test that is used for monitoring conventional heparin therapy and also for screening intrinsic pathway coagulopathies. Although the test is simple, abnormal APTT results induce series of laboratory actions in post-analytical phase of laboratory testing until interpretative laboratory report is generated.

We developed a web-based questionnaire in order to get insight into the existing post-analytical procedures induced by unexpected APTT prolongation. Laboratories participating in coagulation EQA schemes were invited through EQALM and ECAT organisations to the survey. A case history about unexpected APTT prolongation was presented and participants were asked to answer multiple choice questions about the following fields of post-analytical laboratory testing: 1, the considered pre-analytical errors and anticoagulant therapy and their exclusion in practice 2, the use of mixing study and its technical details 3, the interpretation of mixing study in theory and through three potential laboratory scenarios when participants were asked to discriminate between inhibitor and non-inhibitor caused coagulopathies 4,further investigations and reporting. This presentation summarises the answers of 902 laboratories.

The responses show considerable variation in handling unexpected prolonged APTT. Majority of the laboratories (66%) consider heparin contamination as the main pre-analytical error to be excluded, but interestingly only 37% of laboratories use laboratory approach (heparinase or anti-factor Xa assay etc.) to verify presence of heparin in the sample. 22% of laboratories do not consider any pre-analytical errors during investigations. 27% of participating laboratories do not perform mixing studies and 12% of laboratories do only at physician request passing this way the decision about the necessity of a simple reflex test in haemostasis investigation to the clinicians. 90% of those who do mixing studies use 1:1 ratio in the mixture. The main sources of normal plasma are pooled in house (44%) and purchased plasmas (36%) meanwhile quite high portion (17%) of laboratories do mixing with single donor's plasma. 45% of those laboratories that perform mixing study do not use pre-incubation in their investigations losing the chance for detection of type 2 inhibitory coagulopathy. Although principles stated to be used in decision-making of mixing studies are guideline-based in majority of laboratories, the case scenarios were not interpreted because of lack of competence by 6%-17% of laboratories. Presence or lack of inhibitor in the sample was inversely diagnosed by 7% (scenario A), 14% (B), 8% (C) of laboratories. Mixing study results of non-inhibitory factor deficiency (scenario B) were classified best, 80% of the laboratories gave correct interpretation. Scenario A representing inhibitor with type 1 kinetics was interpreted correctly only by 35% of laboratories meanwhile 52% of laboratories selected only one of the inhibitor types, not considering the fact that mixing studies cannot discriminate between non-factor specific and coagulation factor specific-inhibitors with type 1 kinetics. Presence of type 2 inhibitor (scenario C) was diagnosed correctly by 51% of laboratories, 24% of laboratories suspected presence of non-factor specific inhibitor. In agreement with previous observations lack of step-by-step investigations could be seen in our study also: only half of those laboratories that perform mixing studies and would do further investigations would base them on the result of previous mixing studies; 23% of those laboratories that don't perform simple mixing study do either factor activity or lupus anticoagulant tests or both as the next step after APTT in investigations.

Majority of laboratories in the study seem to have no clear protocol of step-by-step investigation of APTT prolongation. Misinterpretations are frequent, especially in inhibitory coagulopathies. Summary and distribution of the survey's experience and also guideline recommendations on APTT testing and interpretation can help to improve interpretative thinking and skill of participant laboratories.