

Anti-phospholipid Syndrome and PT/INR

Background

Anti-phospholipid syndrome is a thrombotic condition which can result in the following clinical conditions; venous thrombosis, arterial thrombosis, recurrent pregnancy loss or thrombocytopenia¹. Patients with Anti-phospholipid Syndrome and thrombosis are treated with warfarin to prevent recurrence of thrombotic episodes.

Anti-phospholipid antibodies (APA) are auto immune antibodies directed against phospholipid-binding proteins and can be called anti-cardiolipin antibodies (ACA) or lupus anticoagulants (LA) depending on the method used to detect them. A patient must test positive for LA or for moderate to high levels of ACA on two occasions at least 12 weeks apart in order to confirm a diagnosis of Anti-phospholipid Syndrome². This is because APA's can appear transiently in the blood but have no connection to clinical symptoms³.

Management of patients with Anti-phospholipid Syndrome who are taking warfarin using the PT/INR is known to be problematic. This is thought to be due to the thromboplastin used in the Prothrombin Time reagent and its responsiveness to the patient's APA⁴.

APA and Lab Systems using Plasma

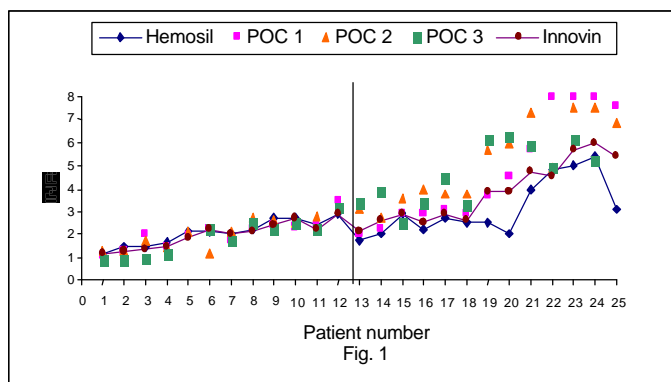
One study⁴ examined the effect of APA's on 9 commercially available plasma reagents. The study concluded that the majority of insensitive thromboplastins for the measurement of PT/INR in plasma are not significantly affected by APA. It was also concluded that thromboplastins made from recombinant Tissue Factor should be checked for their responsiveness before using them for monitoring an individual patient. This is due to the fact that APA's are so varied that some may affect a particular reagent whereas others may not.

APA and POC Systems using Whole Blood

A recent study⁵ examined the effect of APA on whole blood Point of Care systems for PT/INR monitoring. Three POC systems were evaluated together with two lab reagents (plasma samples). The study concluded the following:

- POC devices provided falsely elevated INR values in a third of the APA patients tested,
- All three systems performed equally,
- The plasma based lab systems sometimes provided falsely elevated results
- The POC devices provided reliable results in the remaining two thirds of the APA patients

Figure 1 summarizes the results of the whole blood POC study. Hemosil® and Innovin® are the two plasma based lab reagents.



Conclusion

Based on the conclusions of the studies mentioned, different methods of measuring PT/INR behave differently with different APA patients. It is therefore very important to assess the individual patient together with the responsiveness of the PT/INR reagent/system to be used to monitor warfarin therapy (lab or POC). It is also important when performing a correlation study comparing one PT/INR system to another to consider whether any of the patients included in the study have Anti-phospholipid Syndrome. The presence of such samples in the population may affect the correlation.

References

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