Correlation between activated partial thromboplastin time and diluted Russell's viper venom time in the presence of lupus anticoagulant

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Lupus anticoagulant (LA) is a heterogeneous group of antibodies that interfere with phospholipid-dependent coagulation tests, which result in abnormally prolonged clotting times *in vitro*. The prevalence of LA in a healthy individual is 1-5%^{1,2}. LA is also associated with antiphospholipid syndrome (APS).

Activated partial thromboplastin time (APTT) is one of the most used coagulation tests. LA acts as a phospholipid inhibitor and affects phospholipid-containing reagents, affecting those with less phospholipid content³. Thus, different commercial APTT reagents present different sensibilities to LA⁴. International guidelines for large population, primary care, service giving laboratories recommend using APTT reagents that are not sensitive to LA, or ideally, the inclusion of reagents with different sensitivity levels to phospholipid inhibitors⁵⁻⁷.

The most frequently used tests for LA detection are diluted Russell's viper venom time (DRVVT) and a sensitive APTT. If both are positive, LA's presence is highly confident^{8,9}. Considering that LA can cause APTT prolongation depending on the reagent's sensitivity, we aimed to evaluate our APTT reagent's behavior in patients with LA by DRVVT.

We performed a retrospective, cross-sectional study including records of samples of patients with clinical suspicion of APS analyzed with DRVVT and simultaneous APTT in our hematology laboratory from January 2018 to February 2019. For LA evaluation, we used DRVVT (DRVVT Screen and Confirmation, STA-STA-CLOT); for APTT, Automated STA-PTT (cephalin reagent with a silica activator). All analyses were performed on an STA Compact Max (Diagnostica Stago, France), according to the manufacturer's specifications.

A total of 131 samples, in which simultaneous evaluation of APTT and DRVVT was performed, were included, corresponding to patients of a median age of 36 (25-46) years. We observed LA presence in 30 (23%) samples, 21 (70%) of which had prolonged APTT. The median DRVVT ratio observed in these samples was 1.49 (1.31-1.68). Thus, we classified positive LA as low concentration LA (LCLA) when DRVVT ratio < 1.5 (16 cases) and high concentration LA (HCLA) when DRVVT ratio ≥ 1.5 (14 cases). LCLA samples included 8 (50%) that reported prolonged APTT and 8 (50%) with normal APTT; in the HCLA samples, 13 (93%) had prolonged APTT and 1 (7%) normal APTT.

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Thirteen (12.9%) of the 101 cases with negative LA also reported prolonged APTT. We observed a moderate positive association when we correlated the DRVVT ratio with APTT in the LA-positive ($r = 0.679$, $P < 0.001$) group. After performing a ROC curve, APTT yielded a sensitivity of 70% and a specificity of 86.1% for detecting LA by DRVVT (AUC = 0.860, SD = 0.040, 95% CI, 0.782-0.939).

LA analysis is complex and many pitfalls restrain its interpretation as a result of the heterogeneous nature of LA antibodies, non-standardized reagents, and the lack of gold standard⁹. We found a prolonged APTT in 70% of the samples with LA positivity by DRVVT, with a greater prevalence in higher concentrations of LA (93% in HCLA and 50% in LCLA samples). Similarly, Yao et al. assessed classified LA concentrations according to DRVVT ratios as weak (1.2-1.5), moderate (1.5-2), and strong (> 2). They found a higher prevalence of prolonged APTT in moderate and stronger LA concentrations (41.2% and 83.3%, respectively) compared to weaker concentrations (9%)¹⁰.

The limitations of our study were a small sample size, the absence of a second assay other than the DRVVT to detect LA, and the lack of inclusion of healthy individuals. We must keep in mind that DRVVT and APTT can measure different populations of antiphospholipid antibodies, which may be a reason not to expect a high correlation between values.

The present results indicate that our laboratory's APTT reagent is sensitive to LA, with a moderate association between the DRVVT ratio and APTT values. It is essential to know an APTT reagent's sensitivity before LA studies for its accurate interpretation and, if needed, complementation with further assays in accordance with recommendations from LA diagnosis guidelines.

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Conflicts of interest

This paper's authors have no conflicts of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

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