NAME OF PROJECT

Unravelling difficulties in laboratory diagnosis of antiphospholipid syndrome by evaluation of 'real life' sample results in external quality control program

Subcommittee on Lupus anticoagulant/ antiphospholipid antibodies

Person responsible (Chair / Principal Investigator): Katrien Devreese/ Martine van Essen-Hollestelle

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Description Abstract

State the application’s broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Suggested length is 2-3 paragraphs.

In addition to the presence of clinical features, the diagnosis of the antiphospholipid syndrome (APS) fundamentally requires the finding of positive antiphospholipid antibody (aPL) test results. These comprise clot-based assays for the identification of lupus anticoagulant (LAC) and immunologic ("solid-phase") assays for anticardiolipin antibodies (aCL) and anti-β2-glycoprotein I antibodies (aβ2GPI).

The laboratory diagnosis of APS remains a challenge. LAC tests, as well as solid phase assays for aCL and aβ2GPI show methodological shortcomings, and the methodology is not standardized. Guidelines for LAC detection were published by the Scientific Standardisation Subcommittee (SSC) of the International Society of Thrombosis and Haemostasis (ISTH) in 2009. However, a number of questions on this respect remain unresolved. ISTH-SSC recommendations for aCL and aβ2GPI assays published in 2014 intended to ameliorate the performance of the solid-phase assays. Despite the efforts over the years standardization has not been reached.

For aCL and aβ2GPI testing, several factors contribute to variability in pre-, post- and analytical conditions, many factors related to the assay itself and its calibration. Likewise, methodology of LAC is complicated including at least two test systems (aPTT and dRVVT) in a multiple step procedure (screening, mixing, confirmation). Disagreement between different commercial assay kits and methods is observed particular in the lower range of antibody levels. External Quality Schemes illustrate that most laboratories are able to detect strong LAC, whereas the diagnosis of a weak LAC remains a problem. Large differences in antibody titre for aCL and aβ2GPI measured with different kits are still observed, even in the newest generation assays, a long standing problem.
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External quality assurance (EQA) is a distinct process that includes proficiency testing and an educational component. Proficiency testing helps laboratories assess their performance against those of peer laboratories, as well as monitoring performance over a period of time. These processes are critical for ensuring the quality of laboratory test results, and hence the appropriate clinical diagnosis and management of APS.

The ECAT (External quality Control of diagnostic Assays and Tests Foundation, Voorschoten, The Netherlands) sends laboratories freeze-dried patient plasmas on a regular basis for LAC and aPL analysis to diagnostics laboratories worldwide. EQA results reflect the real-world diagnostic practices.

Active in the field for many years, ECAT has built up a database of results that may be a source to explore some unanswered questions.

Design and methodology (Data expected to collect, sample size and statistical analysis):

Describe concisely the research design and methods for achieving these goals. Suggested length 2-3 paragraphs

The ECAT database with LAC, aCL and aβ2GPI results will be analysed to answer some specific questions. Comparable samples sent in different surveys on different time points over the years, are a good source to evaluate variability in results.

Aim of the study is to assess:

- inter-method variability for aCL IgG, aCL IgM, aβ2GPI IgG, aβ2GPI IgM
- inter-lab variability for aCL IgG, aCL IgM, aβ2GPI IgG, aβ2GPI IgM within a method
- variation in titer and qualitative (positive/negative) classification for aCL IgG, aCL IgM, aβ2GPI IgG, aβ2GPI IgM overall, and per method
- reproducibility of titer and qualitative classification over time of a similar samples of the same patient in different surveys
- inter-method and inter-lab variability in results over time
- correlation of aCL and aβ2GPI within one method
- correlation of aCL and aβ2GPI and LAC
- sensitivity of aPTT versus dRVVT in LAC detection
- inter-method variability within aPTT test system and dRVVT test system
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Study population (Inclusion, exclusion, eligibility) (patient population; recruitment of participating institutions/physicians and subjects; minimum number needed; expected number):

Suggested length 2-3 paragraphs

The ECAT database with results of surveys 2015-2017 will be used including samples derived from one patient per survey. Between 549 and 578 participants were present in the survey.

Expected timeline:

- Project stage/set up: 2018
- Launch: 2018
- Duration: 2018-2020
- Finalization/analysis: 2020
- Reporting: 2019-2020

Expected outcomes (ie. publications):

- Abstract ISTH 2019
- Communications on congresses
- Original articles

Description of project set/up and management, needed infrastructure and resources (summary):

The project is a collaboration between the ECAT Foundation and the lupus anticoagulant/antiphospholipid antibodies SSC subcommittee. The database of ECAT will be provided for statistical analysis. No extra funding is needed, all analyses will be performed by the investigators.
References:


