Response to: 'Correspondence on 'EULAR recommendations for the management of antiphospholipid syndrome in adults" by Gao and Qin

We thank Gao and Qin[1] for their interest in the 2019 European League against Rheumatism (EULAR) recommendations for the management of antiphospholipid syndrome (APS) in adults.[2]

The authors raised a question about the management of individuals 'with threatened abortion or threatened premature delivery, no history of delivery<34th week of gestation and <10th week of spontaneous miscarriage, but the results of laboratory tests show that antiphospholipid antibodies (aPL) are positive and other pathogenesis is not found'. In addition to recommendations for the management of women fulfilling the classification criteria for definite obstetric APS (premature birth<34th week of gestation due to severe pre-eclampsia or eclampsia, ≥3 unexplained spontaneous abortions<10th week or ≥1 unexplained fetal death>10th week of gestation), EULAR recommendations for APS management have also addressed the non-criteria obstetric APS manifestations (section 9C). Non-criteria obstetric manifestations included the presence of two recurrent spontaneous miscarriages<10th week of gestation or delivery≥34th week of gestation due to severe pre-eclampsia or eclampsia. An expert opinion-based statement was made due to limited evidence since most studies reported on mixed populations of criteria and non-criteria pregnancy complications, indicating that treatment with low-dose aspirin (LDA) alone or in combination with prophylactic dose heparin might be considered based on individual's risk profile. For women with no history of pregnancy complications (with or without systemic lupus erythematosus (SLE) but with a high-risk aPL profile, it was stated that treatment with LDA (75–100 mg daily) during pregnancy should be considered (section 8, expert opinion).[2]

Gao and Qin commented that 'management recommendations for obstetric patients with APS before pregnancy are lacking' and they asked if 'it is necessary to start using LDA before pregnancy for patients at high risk of aPL'. EULAR Recommendations for the management of APS stated that LDA in obstetric APS should be preferably started prior to conception (section 9A).[2] In their next point, Gao and Qin reported that 'in women with recurrent pregnancy complications despite combination treatment with LDA and heparin at prophylactic dosage, addition of hydroxychloroquine (HCQ) in the first trimester is considered' and they have asked 'whether it is necessary to start using HCQ 3 months before the next pregnancy since HCQ needs to be used 3 months in advance to reach the effective concentration'. EULAR recommendations stated that in women with recurrent pregnancy complications despite combination treatment with LDA and heparin at prophylactic dosage, increase of heparin to therapeutic dose or addition of HCQ or low-dose prednisolone in the first trimester may be considered (section 10). The evidence for the potential use of HCQ was based on two small observational studies with limited representativeness[3] where no mention about HCQ initiation before conception was made.[4 5]

Gao and Qin also commented that 'obstetricians tend to intensify monitoring and detect aPL regularly during pregnancy', and since 'studies have shown that the aPLs level will change dynamically during pregnancy', they asked whether 'these changes have any effect on our prescription'. This question was not included in our systematic literature review; however, current evidence from isolated studies addressing this issue does not support any changes in management practice based on aPL titre changes during pregnancy because although modest decreases in all aPL tests were observed during pregnancy, these changes were not associated with changes in pregnancy outcomes.[6] Finally, Gao and Qin raised the question if 'it is necessary to monitor platelet changes during pregnancy' given that 'studies have shown that decreased platelet count may be an indicator of poor prognosis in patients with APS'. Regular blood testing during pregnancy is crucial in patients with APS to rule out potential APS complications manifested with thrombocytopenia, including hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome and catastrophic APS.

We agree that more evidence is needed to address these questions that hopefully will be answered by the updated EULAR recommendations for APS management.

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