

Anticoagulation in COVID-19 “Benefit Exists But we Need Trials”

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LETTER TO EDITOR

Dear Editor,

The pandemic we are facing has been devastating in some regions of the globe, not only because of the rapid spread, but also because of the unpredictability form of presentation and course of the disease. In fact, COVID-19 in its most severe form (SARS-CoV-2 pneumonia) and its systemic consequences have been described by several colleagues on the ground. The variety of multiorganic consequences, particularly cardiovascular, and the little expected response to therapeutic strategies as in the case of ventilation, makes us realize that knowledge about the virus is still scarce.

Severe disease in COVID-19 is usually in the form of ARDS with hypoxic respiratory failure. This will be responsible for increased blood viscosity and activation of the hypoxia-induced factor responsible for the thrombotic process. In addition, endothelial dysfunction caused by viral cytopathy promotes over-activation of thrombin and inhibition of fibrinolysis, culminating in a systemic microthrombotic process. Thus, in the most severe cases, phenomena of venous thromboembolism and disseminated intravascular coagulation are found, such as in sepsis-induced coagulopathy (SIC) [1]. Myocardial injury is frequent and can occur through ischaemic processes such as acute coronary syndrome, but also through direct injury such as myocarditis, infectious process

in sepsis, hypoxia caused in acute respiratory distress syndrome (ARDS) and cardiac effects of pulmonary thromboembolism [2]. Tang N et al. [3] demonstrated that anticoagulation with low molecular weight heparin (LMWH) and non-fractionated heparin in a subgroup of patients (D-Dimers > 3000ug/l or SIC score ≥ 4) decreased mortality in 20%, with benefit in mortality from the cutoff of D-Dimers > 1000ug/l.

The anti-inflammatory properties of anticoagulants, particularly LMWH, are increasingly studied. In addition to the benefit in coagulopathy, it may also play a major role in hyperinflammatory syndrome, with decreased levels of circulating IL-6 and increased percentage of lymphocytes [4].

Its use is defended by experts in the field throughout Europe and the USA, described in numerous local protocols and recommended in Portugal by the Portuguese Society of Intensive Care. Current recommendations point to the benefit of anticoagulation in patients with COVID-19, conveying its importance in combating the systemic microthrombotic process.

It is important to highlight that when we talk about anticoagulants, LMWH is the most cited and used in clinical practice. The most controversial is the dose of LMWH to be used, as although most international consensuses recommended prophylactic dose

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of LMWH in these patients, we know that many experts use it in a therapeutic dose 5 and others according to D-Dimers and weight [5]. In fact, COVID-19 can have several presentations and degrees of severity which implies a different approach taking into account the type of patient, as they are not all the same. It is permissible to think that a patient at an early stage and without criteria for severe disease may benefit from LMWH in a prophylactic dose.

In the case of severe disease, is the prophylactic dose sufficient in patients with inflammatory markers (Il-6, ferritin) and coagulopathy (D-Dimers) excessively increased? The truth is that we do not know, but it will not be correct from a clinical point of view to treat these patients equally, taking into account the increased risk of hypercoagulability in a hyperinflammatory state.

Faced with this dilemma, we urgently need clinical trials that can answer us the best anticoagulant strategy according to the stage of the disease. At the moment there is no doubt about the benefit of anticoagulation in COVID-19 patients. Benefit exists but we need trials.

AUTHORS CONTRIBUTION

All authors participate in drafting the article or revising it critically for important intellectual content and all give final

approval of the version to be submitted.

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