Review of: "Safety and Efficacy of the combined use of ivermectin, dexamethasone, enoxaparin and aspirin against COVID 19"

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This is a prospective single center experimental study done without controls (the protocol of the study suggests they will use patients who were treated with other options). The rationale supporting the combination of treatments is mostly based on experimental data, and in the case of aspirin lacking. Any conclusions about the benefits of the combination therapy have the potential to have severe bias. The most important limitations are: 1-This study should have been a randomized controlled trial in order to fully evaluate the efficacy of the treatment strategy. A single arm study, without a clear hypothesis of the effect size and well defined outcomes does not answer the clinical question. The inclusion and exclusion criteria are poor (a patient with a recent GI bleeding could have been included?). The intervention used for anticoagulation in the moderate group changed between the protocol available at Clinical trials they used enoxaparin 1mg/Kg BID (https://clinicaltrials.gov/ProvidedDocs/63/NCT04425863/Prot_SAP_000.pdf), in the manuscript it was aspirin 250mg for 30 days) 2-The outcomes were not adjudicated by a blind group of experts, so it is unclear if the study investigators adjudicated their events which is major limitation 3-They do not report how the primary outcome progression was defined and adjudicated 4- Although they followed up on mortality for up to 30, how was this conducted. Did they call the patients? Did they have study personnel conducting these tasks? 5-They include 167 participants but no estimate of the effect of the treatment is given and the study has no sample size calculations. How much reduction in the primary outcome did they expect? 6-They included patients with different severity of disease, they should have conducted three separate studies for each group (outpatient and inpatient) 7-The information provided about the population is scarse. How many patients did not accept to participate in the study? If they were collecting information about their mortality, did they sign inform consent so they could use 8-The authors do not acknowledge any limitations in their manuscript 9-Finally, the conclusion about the efficacy is not supported by the results of the study. The 95% CI for mortality of the IDEA cohort is 0.59 (0.03-2.9), is not statistically different to the 2.1% percent seen at the same time in Argentina (Two-sided p-value=0.1761 using the One-Sample Test for Binomial Proportion, Normal-Theory Method) The conclusions of this study should be tested in a well design multicenter randomized controlled trial. Until then, only the interventions with high quality evidence should be used.