CHARTER-Ireland Study Summary

Background: Nebulised unfractionated heparin may attenuate COVID-19 ARDS by reducing pulmonary microvascular thrombosis, blocking SARS-CoV-2 entry into cells, and decreasing lung inflammation. COVID-19 patients with a raised D-dimer have areas of pulmonary hypoperfusion on CT perfusion scans of the lung and have increased mortality risk. This was a phase Ib/IIa open label multi-centre, randomized controlled trial. The study was designed to evaluate whether nebulised unfractionated heparin decreased the procoagulant state related to COVID-19 induced ARDS, with safety as a co-primary outcome.

Results: Forty patients were recruited, with 20 patients into each group. Mean age was 56.6 (SD 11.5) in the heparin group and 51.3 (SD 14.7) in the standard care group, while 60% of participants were male. In terms of the primary efficacy outcome, area under the D-dimer concentration curve was not different between the groups ($p = 0.61$). In terms of the co-primary outcome of safety, fourteen patients suffered at least one serious adverse event, 9 patients the Heparin group and 5 in the control group. Eight patients had one or more bleeding events, 5 in the heparin group and 3 in the control group, but were no cases of pulmonary bleeding, of severe haemorrhage or of heparin-induced thrombocytopaenia. Patients receiving heparin therapy had lower PaO_2/FiO_2 Ratios, increased Oxygenation Indices, and decreased ROX index profiles, up to day 10. The time to separation from respiratory support, and the time to ICU or hospital discharge was similar in both groups. There were 3 deaths in the Heparin group and 2 in the control group.

Conclusions: Nebulised unfractionated heparin was safe and well tolerated, but did not alter the primary outcome, and worsened oxygenation indices in patients with COVID-19 ARDS.

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