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Editorial

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EDITORIAL

Covering coronavirus—emerging tools for the fight against the common enemy

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'Zoom' meetings, self-isolation and 'flattening the curve' are just some phrases that have crashed into our usual vocabulary. An abrupt change from January 2020, when the faint whisperings of an emerging, novel coronavirus in China seemed remote to the average person in the UK as they continued their daily normalities. Since then, estimates reveal an exponential spread with coronavirus disease 2019 (COVID-19) impacting over 3.5 million people and sadly, causing over 240 000 deaths internationally, as of 3rd May 2020 [1]. The spread of this respiratory disease has overtaken the ability of our healthcare systems to test, track and contain those with suspected infections. This has led to an unprecedented need for specific tools to treat those who are unwell.

Currently, there is very limited evidence from randomised control trials (RCTs) showing that any medical treatment can potentially improve outcomes in patients with COVID-19 [2]. Broadly, current areas of interest can be split into antiviral drugs and medications that alter immune response. Lopinavir/ritonavir and chloroquine/hydroxychloroquine are the medications with the most clinical evidence.

Lopinavir is a protease inhibitor and ritonavir increases the half-life of lopinavir, both of which have been previously used to treat human immunodeficiency virus. Two RCTs performed in China have evaluated the efficacy of lopinavir/ritonavir in patients with COVID-19 [3, 4]. Cao et al. conducted an open-label RCT at a single hospital in Wuhan, demonstrating that there was no significant difference in the time to clinical improvement compared to supportive care alone [3]. Furthermore, the ELACOI trial, a single-blind RCT, found that there was no difference in the primary outcome of time to negative pharyngeal SARS-CoV-2 PCR test between the treatment and control groups. [4]

Chloroquine and hydroxychloroquine are long-established agents that have been used to treat malaria and chronic inflammatory diseases such as 'lupus' and 'rheumatoid arthritis'. Its beneficial use for COVID-19 patients has been controversial. The first open-label, RCT was published on 14th April 2020, which demonstrated that there was no significant difference in oxygen saturations and time length for recovery from symptoms between patients receiving high doses of hydroxychloroquine, compared to those receiving supportive treatment alone. However, it recorded an increase in adverse effects from hydroxychloroquine, most notably diarrhoea [5]. It should be noted that these clinical trials are subjected to their own individual limitations, including small sample sizes, being single-centre and lack of blinding [3–5].

Particular medical agents that have caught media attention include remdesivir and immunoglobulin therapy (IVIG). Remdesivir is a nucleotide analogue that inhibits viral RNA polymerase with its first clinical use for the treatment of Ebola [6]. A study published in the New England Journal of Medicine found that for patients hospitalised with severe COVID-19, treated with compassionate use of remdesivir, 36 of 53 patients showed a clinical improvement in oxygen support status. [7] The United States Food and Drug Administration has authorised emergency use of remdesivir for treating severe coronavirus [8]. Randomised, placebo-controlled trials of remdesivir therapy for COVID-19 will

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be needed to further establish its potential uses [7]. IVIG has been considered as a possible adjunctive therapy for COVID-19. The rationale for this treatment is that antibodies from recovered patients may aid immune clearance of infected cells [9]. A RCT, containing 80 participants evaluating the efficiency of high-dose IVIG therapy in severe COVID-19 has been initiated in Wuhan, China. This will provide more evidence for IVIG use in treating such patients [10].

Further research has been planned, with the RECOVERY trial beginning in the UK, it is the world's largest RCT that aims to evaluate multiple potential COVID-19 treatments including lopinavir–ritonavir, low-dose dexamethasone, hydroxychloroquine, azithromycin and tocilizumab. It hopes to provide definitive results on whether the treatments are safe and effective within a timescale of months, having already recruited over 1000 patients from over 132 different hospitals [11].

Current clinical management guidance from the World Health Organization emphasises the role of infection prevention and supportive management of complications and at the moment, do not advocate specific medical treatments for COVID-19 [12]. With every day passing scientists are gathering more information to further understand the new disease and navigate through this uncertain science. A robust research effort is currently underway to develop a vaccine against COVID-19. Imperial College London is progressing towards phase II clinical trials for a self-amplified RNA vaccine [13]. Additionally, Oxford University are starting accelerated clinical trials in humans, aiming to recruit 510 volunteers, who will receive either the ChAdOx1 nCoV-19 vaccine or a control injection [14]. This hopes to provide information on its safety profile and its ability to generate an immune response against the virus.

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The COVID-19 pandemic presents the greatest global public health emergency of this generation. Despite the fact that no medical therapy has definitively been shown to be effective against COVID-19, it is clear that huge efforts are being made around the world to ensure success as soon as possible. Though there is nothing about this scientific process that is certain; through technology, knowledge and collaboration, rapid progress is being made in understanding and equipping ourselves for a united fight against the common enemy. In the meantime, stay safe, remain kind and protect your healthcare system.

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