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Does remdesivir have any neuropsychiatric adverse effects?

On 1 May 2020, the US Food and Drug Administration issued an emergency use authorisation for remdesivir in the treatment of hospitalised COVID-19 patients (Food and Drug Administration, 2020). Remdesivir is a nucleotide analogue antiviral drug. It is an investigational drug against COVID-19 and to date there is relatively little known about remdesivir from human trials.

Experience from previous viral pandemics suggests that the immunological response to viruses themselves has the potential to cause neuropsychiatric manifestations including encephalopathies and psychosis (Troyer et al. 2020). It is too early in the course of the current COVID-19 pandemic to evaluate such associations for COVID-19 (Bilbul et al. 2020). Antiviral drugs, such as those used in the treatment of human immunodeficiency viruses, have been associated with effects on the central nervous system; neuropsychiatric manifestations include mania and psychoses (Abers et al. 2014). Little is known, however, about the potential neuropsychiatric adverse effects of remdesivir. We conducted a PubMed search to elicit any early reports of such effects.

Evidence from Ebola virus disease

In a case report of remdesivir therapy for Ebola meningoecephalitis treated with high-dose corticosteroids and intravenous remdesivir therapy, no serious clinical or biochemical events were reported apart from a transient rise in serum amylase level (Jacobs et al. 2016).

One patient experienced neurological complications after receiving remdesivir for Ebola treatment in a phase 1 study; however, it was not clear if this was due exclusively to having received remdesivir (European Medicines Agency Committee for Medicinal Products for Human Use, 2016; Barlow et al. 2020).

No adverse effects were recorded in a neonate treated with remdesivir for Ebola in Guinea (Dörnemann et al. 2017).

A randomised controlled trial (RCT) with remdesivir as one of four agents for Ebola virus in 175 patients in the Democratic Republic of Congo limited enrolment during the trial to two non-remdesivir agents once two of the other trial agents had shown superiority over remdesivir in respect of mortality outcomes. There were no significant clinical or biochemical side effects related to remdesivir apart from one report of hypotension and death possibly related to the drug (Mulangu et al. 2019).

Evidence from COVID-19 disease

An RCT of intravenous remdesivir in Hubei, China in COVID-19 patients found no aggravation of depression or schizophrenia leading to treatment discontinuation in the treatment group of 158 patients (Wang et al. 2020).

A case report of a COVID-19 patient from Washington, USA treated with remdesivir reported no significant adverse effects (Holshue et al. 2020).

Of the first 12 US patients with COVID-19 confirmed by the Centre for Disease Control, 3 patients received remdesivir. After starting remdesivir, all patients had transient gastrointestinal symptoms. No other post-remdesivir symptoms were observed (Kukawski et al. 2020).

In an open-label cohort of 61 COVID-19 patients from the USA, Canada, Europe and Japan, 60% reported adverse events. The most common adverse events were increased hepatic enzymes, diarrhoea, rash, renal impairment and hypotension. Delirium was reported in two patients (Grein et al. 2020).

The Adaptive COVID-19 Treatment Trial recruited patients from 68 sites worldwide. Data on adverse effects are yet to be published (National Institute of Allergy and Infectious Diseases, 2020).

A study of remdesivir use in four COVID-19 patients in Naples, Italy (Durante-Mangoni et al., 2020) highlighted a predominantly cardiac and hepatic adverse effect profile.

A prospective, open-label study of remdesivir, conducted in Milan, Italy, with 35 COVID-19 patients found that the adverse effect profile included increased liver enzymes, acute renal injury and in one case a serious maculo-papular rash (Antinori et al. 2020).

Summary

The limited data available do not seem to highlight any specific neuropsychiatric adverse effects associated with remdesivir, save for the occurrence of delirium in two patients in one open-label study in COVID-19 disease (Grein et al. 2020) and a possible report of neurological complications in a phase 1 trial in Ebola virus disease (Barlow et al. 2016). This position cannot, however, be taken as definitive because it is not known whether trial protocols specifically evaluated for such effects, apart from the RCT in Hubei in which placebo (but not remdesivir) was associated with exacerbation.
of depression and schizophrenia (Wang et al. 2020). Further, this preliminary review did not use a systematic review methodology. Remdesivir is a drug that is investigational and trial data are limited. The neuropsychiatric adverse effect profile, if any, will only become apparent following controlled trials with large sample sizes.

Conflicts of interest

GG and BDK have no conflicts of interest to declare.

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