COMMENTARY

Remdesivir in COVID-19 management: availability and relevance to low- and middle-income countries

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Background

Coronavirus disease 2019 (COVID-19) comprises a spectrum of pathologies, including serious respiratory illness such as pneumonia and lung failure, and is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) [1]. Treatment guidelines and protocols for the management of COVID-19 have been prepared globally by various healthcare organizations and regulatory agencies; however, to date, no specific treatment option has been proven to cure COVID-19.

On 1 May 2020, the US FDA granted an Emergency Use Authorization for remdesivir [2], a nucleotide analog prodrug that inhibits viral RNA polymerase. Having previously undergone research in the treatment of Ebola, the focus has recently been on the use of remdesivir in the treatment of COVID-19 [3].

With COVID-19 cases in Nepal rising to 70,614 as of 25 September 2020, with the death of 459 patients [4], Nepal is seeing a steep rise in cases. A major share of the population is of low socioeconomic status, and with no production of remdesivir within Nepal, the relevance and significance of the use of this drug to treat COVID-19 in that country, as well as in other low- and middle-income countries (LMICs), is questionable.

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Clinical evidence

In common with most antiviral drugs, remdesivir is more efficacious when administered early in the course of the disease than when administered in the later critical stage [5]. With its broad spectrum of activity, remdesivir inhibits RNA-dependent RNA polymerases and causes arrest in RNA synthesis, most probably by delaying RNA chain termination [6].

Several clinical trials have been conducted to determine the efficacy of remdesivir in COVID-19 patients. Studies have suggested a shortened course of treatment, a reduction in viral load, and clinical efficacy when the drug is administered early in the course of the disease. The significant clinical improvement in respiratory status (68% of 61 patients) and shortening of the disease course was reported in the study by Grein et al. [7]. These results are supported by those of a larger study ($n = 1026$) by Beigel et al., with the median recovery time being shortened from 15 days with placebo to 10 days with remdesivir, but with no significant reduction in mortality rate [8]. The study conducted by Goldman et al. ($n = 397$) showed clinical improvement of ≥2 points on a 7-point ordinal scale in 64% and 54% of patients receiving a 5- or 10-day regimen of remdesivir, respectively, with those receiving 10 days of treatment being at a clinically worse status at the beginning of the trial [9]. Remdesivir significantly reduced viral load in a study conducted in China, but the study was terminated early as COVID-19 became controlled during the early stages of the trial and no new patients were available for randomization [10]. Overall, the efficacy of remdesivir in the treatment of COVID-19 is currently questionable as the main purpose of a therapeutic agent during the COVID-19 pandemic is to reduce mortality, not to decrease the length of hospital stay [11].

The adverse effects associated with remdesivir include hypoalbuminemia, constipation, anemia, hypokalemia, increased bilirubin, thrombocytopenia, and acute respiratory

failure [9, 10]. The study by Beigel et al. suggested that adverse effects did not differ significantly between placebo and remdesivir [8]. Forty-four clinical trials of remdesivir for COVID-19 are currently registered [12]. Studies with larger populations, and which also compare the efficacy of remdesivir with that of other antiviral drugs, are needed to confirm the relevance of remdesivir in treating COVID-19.

Cost and availability

Gilead Sciences stated that by April 2020 they would have produced enough remdesivir for 140,000 courses of treatment, and that most of this will be supplied to the US market [13]. Beximco Pharmaceuticals Limited in Bangladesh is the first South-Asian company to start the production of a generic version of remdesivir. Gilead's recent agreements with India's Cipla and Jubilant Life Sciences, as well as with Pakistan's Ferozsons Laboratories, will increase the production of remdesivir in this region. Substantial amounts of the drug need to be distributed. Given that Pakistan had 309,581 cases and India had 5,908,748 cases of COVID-19 as at 25 September 2020, the supply of remdesivir to Nepal and other LMICs will certainly be limited.

In the USA, the official cost of remdesivir is US$520 per vial for those with private insurance and US$390 per vial for those without insurance [14]. The required dose of remdesivir is two vials on the first day and one vial per day for the remaining course of the treatment. This brings the cost to US$2340–3120 for a 5-day course and US$4290–5720 for a 10-day course. Cipla International has distributed the drug at a price of US$53.34 per vial in India, although a higher price of up to US$818 per vial has been reported due to insufficient production and black marketing [15, 16]. Heavily criticized for its initial cost of US$84,000 for one course of sofosbuvir [17], the pricing policy of Gilead has been considered predatory by some. At current costs, the financial burden of a course of remdesivir might be unbearable for many patients. With the economy falling apart, the next logical question is will Nepal, as well as other LMICs, be able bear the costs of such medications, even if the availability of these medications can be established?

Use in low- and middle-income countries

Remdesivir appears to be more potent when administered early in the course of disease [5]. This makes it difficult to select which patients are to be administered the drug, considering the uncertainty of progression of the disease and significant demographic variation. As a result, a large proportion of patients would require the drug, which is difficult to acquire and very expensive in LMICs such as Nepal. Thus, the use of remdesivir is relatively insignificant for routine treatment regimens to treat COVID-19 in LMICs.

Conclusion

Currently, no therapies have established efficacy and safety for the management of COVID-19. Given the experimental phase of the management of the disease, the use of remdesivir has shown some positive results, and its compassionate use during the early stages of the disease is justified. Remdesivir may be a promising medication for COVID-19 but the results of well-designed clinical trials are necessary to clarify its effectiveness, tolerability, and safety. However, for LMICs such as Nepal, the use of remdesivir in the treatment of COVID-19 is currently insignificant due to its unavailability and the high acquisition cost of the drug, as well as the lack of evidence regarding its effects in reducing mortality. To make this drug relevant to COVID-19 management in LMICs, production should be commenced at the national level, followed by government implementation of price reduction strategies after its mass production.

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