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Letter to the Editor

Is Remdesivir a Good Choice for a COVID-19 Treatment in an Outpatient Setting?

Running Title: Remdesivir and an outpatient setting

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Dear Editor

Remdesivir (RDV) has been considered a “molecule of hope” for the treatment of COVID-19 (1). Existing literatures show some inconsistent results about its efficacy in clinical settings. The trial results showed that RDV treatment was associated with improved recovery time in hospitalized adult patients who experienced infection of the lower respiratory system (2). A Spanish study showed that in patients who had less than one week of symptoms before hospitalization, RDV reduced the risk of death (3). A meta-analysis showed that RDV is beneficial in reducing mortality in hospitalized patients who needed no or conventional oxygen support. Its role in the treatment of ventilated patients was underpowered (4). Another systematic review demonstrated that RDV may have some benefits in the clinical period of the disease in hospitals and outpatient settings but the certainty of the evidence is limited (5).

Keywords: Remdesivir, COVID-19, Outpatients, Therapeutics

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In a randomized controlled trial of Remdesivir (RDV) in 52 Canadian hospitals, RDV in comparison to standard care was able to significantly decrease mechanical ventilation needs. Mortality was lower in all subgroups with RDV, but the effect was not significant. In a total sample of 1282 participants, 634 patients received Remdesivir and standard care for 10 days, and 648 patients received only standard care. The rate of mortality in hospitalized patients treated with RDV was 18.7% but, this rate was 22.6% in patients who received only standard care. The 60-day mortality rate was 24.8% and 28.2%, in these two groups, respectively. Furthermore, the rate of mechanical ventilation requirement was 8% and 15%, in these two groups, respectively. They concluded that RDV reduced the mechanical ventilation need significantly. Therefore, RDV has a modest effect on patients' outcomes (6).

RDV was recommended by the European Medicine Agency (EMA)for the treatment of adults who do not need supplemental oxygen and the risk of progressing to severe disease was high in them. It was previously recommended for the treatment of COVID-19 patients with pneumonia manifestations who required supplemental oxygen (7).

The results of a rapid review showed that some antiviral drugs, including RDV could improve the outcomes of mild to moderate COVID-19 in outpatients. But, it discussed that the results couldn't be generalized to the Omicron variant (8). The results of a prospective real-life study showed RDV may be beneficial in cases at highest risk of development of severe COVID-19 (9).

Iran is one of the countries with a high burden of COVID-19 morbidity and mortality (19). Despite all preventive efforts, Iran experienced several social, cultural, political, and economic challenges in COVID-19 primary prevention strategies (10). Challenges have led to a shift to the secondary prevention approach, including massive prescription of anti-viral agents such as RDV.

Another study evaluated the efficacy and safety of a three-day course of RDV for intravenous (IV) use in outpatient high-risk patients who had signs and symptoms during the previous week. The RCT involved 562 non-hospitalized COVID-19 patients who had at least one risk factor for disease progression including age 60 years or more, obesity, and history of diabetes mellitus compared with a placebo. Remdesivir significantly reduced the risk of hospitalization and death. Moreover, the risk of secondary medical visits or all-cause death by 4 weeks was reduced in Remdesivir-treated participants (11).

The American College of Physicians recommends RDV within 5 days to one week of manifestation of the disease for mild to moderate Covid-19 outpatients who are at risk of developing the severe disease (12).

Korman 2020 has discussed that even if RDV is useful to reduce disease progression it is not a good choice for outpatient therapy (13). Furthermore, the outpatient setting for COVID19 is breaking the primary prevention policy and protocol (e.g. physical distancing and isolation of infected patients for 2-3 weeks) by allowing infected patients to be in contact with un-infected population while they are commuting between home and outpatient setting for receiving RDV.

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Another aspect of the inappropriate prescription of RDV is related to the cost of this medication. The results of a cost-effectiveness analysis showed that RDV plus supportive care is not cost-effective in COVID-19 in hospitalized patients in Iran (14). In general, it seems that the administration of RDV can be useful for some hospitalized patients and in special cases for outpatients. (4, 5, 9,12). Unfortunately, the existence of high demand for the purchase of this drug and its prescription for patients by physicians in outpatient settings in Iran has raised the probability of induced demand. Physicians should be fully aware of the cost-effectiveness of medications in outpatients and avoid prescribing expensive, less-effective medications. Taheri et al recommended RDV therapy based on having some criteria including refractory fever, lowering the level of consciousness, decreased oxygen saturation, and finally the physician's opinion (15). The Spanish study showed that RDV was associated with decreased odds of 30 days mortality rate, especially in patients with 0-3 days and 4-6 days versus >6 days pre-admission duration of symptoms (3). Thus, we recommend designing a standard checklist of detailed criteria on admission and considering the pre-admission duration of symptoms as an important factor, in addition to the need for supplemental oxygen (2), as a requirement to prescribe RDV for hospitalized patients and having one or more risk factor for disease progression including age 60 years or more, obesity, history of diabetes mellitus, refractory fever, lowering the level of consciousness, and decreased oxygen saturation as a requirement to prescribe RDV for outpatient setting (11) in Iran.

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