

short review

Design of circuits for the outpatient treatment of patients with mild or moderate SARSCoV2 infection with intravenous remdesivir. Differences between a primary hospital and a tertiary hospital in the Autonomous Community of Madrid (Spain)

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The pandemic caused by SARS-CoV-2 infection during 2020 and later revealed the weaknesses of Health systems worldwide, causing a huge morbidity and mortality. Among other multiple factors involved, the availability of physical spaces and technical means for the care of these patients accounted as one of the most important. Already in the beginning of the pandemic, emphasis was placed on the need to locate and use available health resources strategically, not only to avoid overcrowding of the Health System itself, but also to ensure the better and fairest distribution of these resources [1]. As more and more details became known about the course of the infection, and increasingly effective treatments were developed, each country implemented various strategies for optimal use of such resources. These strategies included the construction of hospitals dedicated exclusively to treat patients with this infection [2], the creation of specific units

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[3], or the design of out patient's pathways to attend patients with no need of hospitalization. However, inside the same country, and even inside the same region of a country, there are hospitals with different levels of specialized care, and measures which are correct for a level 3 hospital (high degree of specialization) may not be useful for a level 1 hospital (low degree of specialization) This article reviews the particular characteristics and the most significant differences in the creation of these circuits between a level 3 and a level 1 hospitals in the Autonomous region of Madrid Community during year 2023.

Indications

Although there were initial doubts about treating patients with mild or moderate SARS-CoV-2 infection, either due to lack of evidence [4], or due to fear of causing inequalities between patients when accessing treatment [5], progressively, multiples studies have shown the effectiveness of antiviral treatments to prevent progression to severe disease in patients with very specific conditions [6]. In fact, currently, the clinical characteristics of those patients in whom early treatment with antivirals is indicated can be consulted in different guidelines, both global [7-9], national [10,11], and local [12]. Regarding the indicated treatment, symptom management should be initiated for all nonhospitalized adults. For those mentioned above, several antiviral therapeutic options are available. The main goal of therapeutic management for nonhospitalized patients is to prevent progression to severe disease, hospitalization, or death. Other goals may include accelerating symptom recovery and viral clearance and preventing long-term sequelae. Current data on the impact of therapy on these secondary goals are limited. Several factors affect the selection of the best treatment option for a specific patient.

These factors include the clinical efficacy and availability of the treatment option, the feasibility of administering parenteral medications, the potential for significant drug-drug interactions, the patient's pregnancy status, the time from symptom onset, and the in vitro activities of the available products against the currently circulating SARS-CoV-2 variants and subvariants. Most of the data that support the use of the recommended treatment options come from clinical trials that enrolled individuals who were at high risk of disease progression and who had no pre-existing immunity from COVID-19 vaccination or prior SARS-CoV-2 infection. Accordingly, the proportion of hospitalizations and deaths in the placebo arms of these trials was high compared to what has been seen more recently in populations where most people are vaccinated or have had prior SARS-CoV-2 infection. Although these trials demonstrated the efficacy of using antiviral drugs in high-risk populations, it is difficult to know their precise effectiveness in the current setting because of the low rates of hospitalization and death among those who have been vaccinated [6]. Nevertheless, some patients continue to have an increased risk of disease progression, and it is in those people that therapies are most likely to be beneficial. Patients who are at the highest risk are older patients (i.e., those aged >50 years and especially those aged ≥65 years) and patients who are unlikely to have an adequate immune response to COVID-19 vaccines due to a moderate to severe immunocompromising condition or the receipt of immunosuppressive medications. Other risk factors

include lack of vaccination or incomplete vaccination; a prolonged amount of time since the most recent vaccine dose (e.g., >6 months); and conditions such as obesity, diabetes, and chronic pulmonary, cardiac, or renal disease [6,7]. The NIH Panel's recommendations reflect the available data on the benefits of using antiviral therapies to prevent progression to severe COVID-19 [6]. Preferred therapies are Ritonavir-boosted nirmatrelvir (grade of evidence AIIa), an oral drug, which must be started as soon as possible and within 5 days of symptom onset. However, dosage must be adjusted to renal clearance and a lot of interactions with other drugs make this choice not easily eligible. Second option is Remdesivir (grade of evidence BIIa), which is an endovenous (EV) antiviral and must be also started as soon as possible and within 7 days of symptom onset. Alternative therapy for use when the preferred therapies are not available, feasible to use, or clinically appropriate Molnupiravir (grade of evidence CIIa), another oral drug, which must be started as soon as possible and within 5 days of symptom onset. Bearing in mind these indications, and knowing the non-stationary, aleatory nature of SARS-CoV-2 infection and community transmission, non-hospitalized management circuits had to be designed for those patients with remdesivir indication, as they had to receive it in EV way.

Hospitals and Pathway designing

Previous experiences on design and implementation of clinical pathways for outpatient management of patients with mild and moderate SARS-CoV-2 infection were scarce [3]. Just a previous assay in a tertiary level hospital placed in Alicante (Spain) was available as a model to follow through on [13]. However, regional differences on the baselines developed at every local community, made the model used at Alicante unable to be used at the Regional Community of Madrid. Clinical pathway objectives were assuring the treatment of all patients with criteria for receiving EV remdesivir once a day for three days. All patients were detected at the Emergency Department, as there are no developed circuits contacting Primary Care and the hospital Departments. This fact caused Emergency Departments to become occasionally overcrowded.

So, clinical pathway deemed to be absolutely necessary. Conversations between different departments took place to design it, and discuss the best way to warranty the compliance. After analysing all the intercurrent factors (number of potential patients using the circuit, day hospital attendance and daily occupation, human resources needed and disposal, Internal Medicine specialist availability to attend adverse effects during administration) there were 4 departments mainly involved: Emergency Department (ED), Internal Medicine Department (IM), Medical Direction, and Nurse Direction. Level 1 Hospital was located northwest in the Autonomous region of Madrid. It covers attention to a total of 115,000 population, has 90 beds available, and a small day-hospital able to attend 6 patients at the same time, between 08 AM and 15 PM, from Monday to Friday. It has also a small isolation room, mainly used for immunocompromised or psychiatric patients. SARS-CoV-2 infected patients follow up is attended solely by the IM whenever the patient needed to stay in the hospital; except for the ED. Infectious disease specialists were not available. Although main objective was avoiding the visit of these patients to the ED, decision was taken in a short time period (less than 1 month) as availability of the day-hospital was not feasible. So, a single room space was prepared at the ED just to administer the daily dose of remdesivir EV to those patients needing it. Level 3 Hospital is located in the urban center of the city of Madrid. 600,000 people receive attention from

this resource, which accounts for 800 beds availability, 2 medical day-hospitals, with more than 20 attending points each, and available everyday single day (even weekends days) from 08 AM to 20 PM. The amount of patients to get benefit of the pathway is quite larger on the Level 3 hospital than on Level 1.

IM has a narrow collaboration with the Microbiology and Infectious Disease Departments. As a main difference with the level 1 hospital, Hospital Pharmacy Department had to be involved on the design to ensure the availability of Remdesivir at the day-hospitals. Home hospital Department was also included on the discussion as to assure the medication to these patients who were included, but were unable to attend the hospital for mobility reasons. Meetings were held several times in the year, and it took 6 months to finally develop the pathway with the agreement of all the departments. Labour of Medical and Nurse Direction were much greater to finally achieve an accord. In this case, patients got the first dosage of Remdesivir at ED, and they got an appointment for the next 2 days at the day-hospital prior to leaving home. That pathway accomplished the primary goal (avoiding overcrowded ED) and secondary one (providing the best quality service to every patient who needed it).

Conclusion

Fight against SARS-CoV-2 infection is still in progress. Different virus variants and transitory epidemic transmission periods are on the ground yet. Apart from vaccination campaigns and social diffusion of several measures to prevent the infection, Health Systems effort to offer the best available service is mandatory. Although every Health System may show different characteristics and may have different resources, all of them must find ways of putting all of them at the patient disposal. It finally works. This article analyzes two different approaches pending on the particular features of two different levels of care hospitals. Both approaches are valid as they adapt to the hospital everyday reality. So, we encourage every single Health Resource to reach treaties using dialogue as the best way to ensure the better quality of care for its patients.

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