Observational study of people infected with SARS-Cov-2, treated with amantadine

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Abstract
Background We conducted an observational study of 15 patients from a Southeastern area of Mexico with symptoms compatible with SARS-CoV-2, which were treated with the antiviral amantadine.
Methodology In this study, data were collected from 15 individuals with clinical symptoms of COVID-19 infection, which were treated on an ambulatory basis with 100 mg of amantadine for a period of 14 days.
Results This drug demonstrated its effectiveness, as patients recovered successfully with this treatment without the necessity of attending a hospital to use mechanical ventilation. All patients developed IgG antibodies to SARS-CoV-2.
Conclusion Amantadine can be used as a viable and cost-effective alternative for treating people with severe acute respiratory syndrome (SARS-CoV-2) on an ambulatory basis, while the vaccine is not available.

Keywords Amantadine · SARS-cov-2 · Celecoxib · Azithromycin

Introduction
The SARS-CoV-2 pandemic has left more than 40,000 deaths in Mexico [1]; this is probably because there is no effective treatment that can stop the coronavirus worldwide. Studies have been conducted with hydroxychloroquine in combination with azithromycin; however, this has not been successful [2]. Studies have also been done with the antiparasitic Ivermectin, but the results are still controversial [3].

The use of antivirals has been approved by the FDA, such as Remdesivir [4], which is an adenosine nucleotide analogue that disrupts viral replication and inhibits the RNA polymerase enzyme. However, its use requires hospital assistance, since it is administered intravenously, which increases treatment costs due to hospital attention.

In 1973 amantadine was approved by the FDA for the treatment of motor symptoms in patients with Parkinson’s disease [5]. In 1976, amantadine was developed for the treatment of influenza H1N1 [6, 7]; however, this drug is not recommended for the treatment of influenza, because it mutates and loses sensitivity to the drug [8]. Amantadine has been found to have several benefits, such as being used as an antiparkinsonian, as it is involved in the process of dopamine release [9]. It is important to note that patients with Parkinson’s disease, who are being treated with amantadine, have not shown the symptomatology of COVID-19 infection [10, 11]. It is important to mention that the neurological indications of amantadine are not related to its antiviral activity.

Molecular docking studies have shown that amantadine could enter the SARS-CoV-2 E-channel and interfere with the release of its viral content into the cell, thus inhibiting its propagation [12]. Other studies have shown that amantadine

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as a treatment for COVID-19 infection has been effective, and the patients have recovered successfully, without the necessity to go to a hospital [13].

In this observational study, 15 patients were treated in an ambulatory setting in Southern Mexico with amantadine, and it was shown to be effective for the successful recovery of SARS-Cov-2 infected patients.

**Patients and methodology**

**Study population and data collection**

This study included a sample of 15 patients of different ages, who presented a symptomatology compatible with SARS-Cov-2. No serological studies were available at the time of the study. Data were collected between April 1 and July 25, 2020, using a questionnaire about the symptoms presented, as well as their chronic diseases. IgM and IgG antibodies were detected with a labclinics ELISA kit (Barcelona, Spain). The report followed the procedures of the observational studies in epidemiology (STROBE) [14].

The inclusion criteria were as follows.

a. Patient consent to participate in the study.

b. Desire to participate in the study.

c. Male or female over 18 years of age.

d. Clinical symptoms compatible with SARS-Cov-2

Exclusion criteria.

a. Legal incapacity.

b. Medical or psychological condition in which the investigator’s opinion would not allow completion of the questionnaire.

c. Invasive ventilation.

**Case studies**

Ambulatory patients who stayed at home during the quarantine period in a small town in Southeastern Mexico in the state of Tabasco, Mexico.

**Objectives of the study**

The main objective of this observational study was to determine if treatment with the drug amantadine would be effective for ambulatory treatment of people manifesting symptoms of COVID-19 infection.

Family members who lived with the patients were suggested to take amantadine prophylactically, 100 mg once a day.

**Results**

**Demographic and clinical characteristics**

A total of 15 patients over 18 years of age with clinical symptoms compatible with SARS-Cov-2 were included in this study. Table 1 shows the characteristics of the patients and their major comorbidities. The average age of the people in the study was 48 years ± 16. Five of them were men and 10 were women. Four per cent suffered from hypertension and three per cent from diabetes mellitus. Only one person was reported to have a heart disease.

Table 2 shows the symptomatology presented by the patients when they were infected with the coronavirus. Most of them presented fever, dyspnea, a headache, nausea, nasal congestion. Ten of them lost their sense of smell and taste.

Table 3 shows the treatment they were recommended to follow. The 15 patients received 100 mg of amantadine, one tablet in the morning and one in the afternoon, over a period of 14 days. Most of them received 500 mg
of azithromycin for a period of 6 days. They received celecoxib 200 mg orally as an anti-inflammatory and 500 mg of aspirin for 6 days as an anticoagulant. Three of the patients had to be nebulized with ipratropium bromide/salbutamol, 3 times a day for 5 days, as they had difficulty breathing. Two of the patients had to be given oxygen (4 Lpm) as they had an oxygen saturation below 90%.

After 14 days of treatment, they were tested for IgG and IgM antibodies to SARS-Cov-2, all were positive for IgG antibodies.

### Discussion

In this study, 15 patients were treated with amantadine as an antiviral. All patients recovered successfully with amantadine treatment, were not required to go to the hospital, and were not connected to a mechanical ventilator.

Studies have shown that amantadine is effective in decreasing the effects caused by coronavirus [13]. It has been shown that people with Parkinson’s disease who have been positive for COVID-19, have not exhibited symptoms [10, 11]. The effect of amantadine is that it can stop the coronavirus, giving the body the opportunity to generate IgG-type antibodies.

Autopsy reports have demonstrated diffuse alveolar damage, edema, hyaline membrane formation, accumulation of megakaryocytes, platelets and neutrophils in the alveolar capillaries, generating pulmonary thrombotic microangiopathy that often results in fibrin thrombi in the alveolar capillaries and small pulmonary arteries [15].

For this reason, azithromycin was added to amantadine treatment as an antibiotic capable of reducing the exaggerated production of macrophages and pro-inflammatory cytokines [16] as well as preventing bacterial aggregation generated in respiratory processes [17].

Also, as part of the treatment, aspirin was used as an anticoagulant to reduce the risk of venous thromboembolism [18]. Celecoxib was used in most patients as a protective measure for the vascular endothelium [19].

Three patients received ipratropium bromide combined with salbutamol, because they presented respiratory distress [20]. None of the patients were administered dexamethasone [21], because steroids inhibit the immune response and the effect we expect with amantadine was that the virus would stop and the body would develop IgG-type antibodies against the coronavirus.

### Conclusion

It is important to point out that amantadine is an effective antiviral that can stop the symptoms of the coronavirus and gives the body the opportunity to defend itself by generating protective antibodies. Family members reported that they did not have the symptoms generated by the coronavirus.

Amantadine can be used as a viable and cost-effective alternative for treating people with severe acute respiratory syndrome (SARS-Cov-2) on an ambulatory basis, while the vaccine is not available.

### Author contributions

GEA-A: Project design and article writing. JDA-M: consultation and follow-up of patients. RAL: patient monitoring. MEH-A: discussion of results. DH-Co: data collection. FR-D: data collection.

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### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no competing interests.
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