

Therapeutic Efficacy of Ivermectin as an Adjuvant in the Treatment of Patients with COVID-19

Study conducted at the Social Security Institute for Workers of the State of Chiapas, ISSTECH, Mexico

Alberto Cundapí Núñez¹

Institute of Social Security for Workers of the State of Chiapas, ISSTECH, Tuxtla Gutierrez, Chiapas, Mexico

Jesús Miguel Leyva Cervantes²

Institute of Social Security for Workers of the State of Chiapas, ISSTECH, Tuxtla Gutierrez, Chiapas, Mexico

Marco Antonio Ordoñez Juárez³

Institute of Social Security for Workers of the State of Chiapas, ISSTECH, Tuxtla Gutierrez, Chiapas, Mexico

Gerardo Grajales Yuca⁴

Specialty Hospital Vida Mejor
Tuxtla Gutierrez, Chiapas, Mexico

Ana Paola Rubiano Murcia⁵

Specialty Hospital Vida Mejor
Tuxtla Gutierrez, Chiapas, Mexico

Jenner Josué Martínez⁶

Specialty Hospital Vida Mejor
Tuxtla Gutierrez, Chiapas, Mexico

Abstract:- This document sets out the results of a study aimed at estimating the therapeutic efficacy of ivermectin as an adjuvant in the treatment of COVID-19 patients treated at the Specialty Hospital Vida Mejor of the Institute of Social Security for Workers of the State of Chiapas, ISSTECH, Mexico. Ivermectin as an adjuvant in the treatment of COVID-19 patients is more effective (92%) outpatient patients. In critical hospitalized and severe hospitalized patients, ivermectin had a significant impact, both in improving patients' health and decreasing lethality.

Keywords:- Ivermectin, COVID-19, Efficacy.

I. INTRODUCTION

In late 2019, in December, cases diagnosed as pneumonia began to be seen in Wuhan, China. The abrupt increase in the number of cases with this diagnosis and the report of the first fatal case resulted in it being officially recognized as an emerging health problem in January 2020 and 23 days later the World Health Organization declared SARS-CoV-2 virus infection an international public health emergency (WHO 2020, a,b; Kofi et al, 2020; Wang et al, 2020).

The SARS-CoV-2 virus can affect individuals of any age, with a slight predominance in the male sex. The mortality from this virus, which we will call from now on, COVID-19, varies from 1.5-3%. To date, several risk factors are identified; but it is advanced age and comorbidity the main ones, within these comorbidities with hypertension, diabetes, cardiovascular diseases and possibly immunosuppression (Carbaño, 2020).

Data on the number of cases, worldwide, as of 20 June 2020 were recorded 8,741,136 and 462,088 deaths (WHO, 2020 a.b). The figures for Mexico are 170, 485 cases (55.11% men and 44.89% women), with 20, 394 deaths. Among comorbidities, high blood pressure adds up to 20.11% of cases; obesity, 19.76%, diabetes, 16.54% and smoking, 7.96% (INSP, 2020). In the case of Chiapas, the

state where the present investigation was conducted, to this day confirms 3,532 cases and 239 deaths, 2282 patients recovered (ISECH, 2020).

Within the virus-specific data, the incubation period has been calculated in 5.1 days and it is believed that 97.5% of patients will have symptoms at 11 days on average (Laurer et al., 2020). The average admission to the hospital is 7 days, with an average resolution and death time of 22 and 18.5 days, respectively (Zhou et al., 2020). Mortality is estimated at 5.7% (Wang, 2020).

The COVID-19 clinic is still uncertain; but within the most common symptomatology presented in patients are fever, cough, fatigue, and shortness of breath. These symptoms usually appear between 1-14 days after exposure. Depending on the severity of these symptoms, the disease is classified into (Gralinski and Menachery, 2020; Graham et al., 2020; Zhou and Liu, 2020; Xu, Lai, and Liu, 2020; Fang et al., 2020):

- Mild-moderate, which occurs in most patients and is considered as non-severe pneumonia.
- Severe, when the disease progresses into severe pneumonia that requires specific treatments and admission into intensive care units
- Critical, evolves in SARS, sepsis and shock, and so far, occurs in approximately 5% of cases.

So too, although rarely, some patients have atypical initial symptomatology such as (Zhou and Liu, 2020; Chang, 2020; Tian, 2020):

- Digestive (mild anorexia, nausea, vomiting, diarrhea, abdominal pain, etc.)
- Neurological (headache);
- Cardiovascular (such as palpitations, chest tightness, etc.)
- Mild pain in the limbs or dorsal myalgia
- Ophthalmological symptoms as the first manifestation (conjunctivitis)
- Asymptomatic infections

The prognosis of this disease is usually favorable in children and adults up to 24 years, for people between the ages of 25 and 65 years varies depending on the comorbidity, being more vulnerable to complications, people with cardiovascular disease, high blood pressure, diabetes, liver or kidney lung conditions (Villegas, 2020).

However, about treatment for COVID-19, one has not yet been shown to be completely effective or decisive, supporting drugs are used. In this regard Caly and collaborators (2020), reported that the antiparasitic ivermectin has antiviral activity against this virus having performed in vitro tests. In terms of lethality, SARS-CoV-2 appears to be less virulent than SARS-CoV (10% less lethal) and MERS-CoV (35% less lethal), with the exception of the elderly and those with underlying health conditions (Gralinski and Menachery, 2020; Cohen, 2020; Chen et al, 2020).

Among the studies for the use of ivermectin in COVID-19 patients are:

- The first published study of the use of ivermectin in COVID-19 patients is entitled "Usefulness of Ivermectin in COVID-19 Illness" (Patel, 2020); it had participants from 169 hospitals around the world. The results are quite significant from the reduction in the fatality rate, as this was 6.1 times lower compared to patients who did not use ivermectin (1.4 vs. 8.5%). Specifically, the fatality rate of patients in need of mechanical ventilation, lethality was reduced 2.9 times (7.3% vs. 21.3%) which is also significant, despite being an advanced stage of the disease. It should also be noted that these results have been obtained with an average dose of 150 mcg/kg, which is below the usual dose of 200 mcg/kg in the use of ivermectin.
- Tavaréz (2020), reported 247 cases with COVID-19 treated with ivermectin by pneumologist in the Dominican Republic. He explained that the treatment he performs consists of giving 2 tablets of 6 mg (12mg of ivermectin) per day for 2 days, this equates to one dose per day of between 150 to 200 mcg per kilo. In those who have more than 80 kilos the dose is 3 tablets of 6 mg (18mg) per day for 2 days; equivalent to one dose per day of between 150 to 225 mcg per kilo. The ivermectin provided from the early stages of the disease is amazingly effective and the results are particularly good, in most cases before 24 hours were left without symptoms.
- Aguirre (2020) in Lima Peru, included ivermectin as the first line of therapeutic action for COVID-19. He established a treatment scheme, consisting of ivermectin bottle of 6mg/ml, applying 1 drop per Kilo, 1 time per day for 2 days. In 6 mg tablets, the adult dose is 2 tablets per day for 2 days. As results found from 82 treated patients, the Fatality Rate has been 0% and it is also observed that in 100% of cases treated with ivermectin there is an improvement in the disease and resolution of fever within 48 hours of initiation of treatment.

So far, treatment for COVID-19 has been with oseltamivir in the first suspected cases of SARS-CoV-2 (Chen et al., 2020; Lu, 2020); some cases where remdesivir has been used (Wang et al., 2020; Lai et al, 2020; Holshue et al., 2020), lopinavir-ritonavir (Cao et al, 2020) and aminoquinolins chloroquine and hydroxychloroquine (the latter also in combination with azithromycin) (Gautret et al, 2020).

Within the high insulation criteria (WGNC, 2020; Shen et al., 2020) are:

- You must not have a fever for more than 3 days
- Respiratory symptoms improved significantly
- Significant absorption of inflammation in the pulmonary image
- Two consecutive negative tests of respiratory pathogenic nucleic acid (PCR), with a sampling interval of at least 1 day.

In this study, the objective was to estimate the therapeutic efficacy of ivermectin as an adjuvant in the treatment of COVID-19 patients treated at the Specialty Hospital Vida Mejor of the Institute of Health at the Service of Workers of the State of Chiapas, ISSTECH, in Chiapas, Mexico.

II. METHODS

This article is the result of a descriptive, prospective case study, approved by the Ethics and Biosecurity Committee of the Specialty Hospital of ISSTECH. The study population was patients disease SARS-COVID2-19 by RT-PCR attended at the in this hospital in Chiapas, Mexico, during the period from April to June 2020.

Sampling was non-probabilistic of consecutive cases served, meeting inclusion criteria:

Patients with clinical suspicion and/or SARS-VOC22-19 pneumonia who received outpatient treatment with ivermectin (days 1 and 2), acetaminophen, ketorolac and atorvastatin; treatment of severe hospitalized patients with ivermectin (days 1,3 and 5), acetaminophen, azithromycin, oseltamivir, atorvastatin, omeprazole; ivermectin (days 1,2,3,4 and 5), atorvastatin, azithromycin, oseltamivir, enoxaparin and critical support.

For the purposes of this research, treatment based on patient classification was used, namely:

- **Outpatients:** Ivermectin 12 mg V.O; Repeat doses: 12 mg v.o at 48 hours; Paracetamol 500 mg v. for 5 days; Ketorolaco 10 mg v.o c-8 hs in case of pain and Atorvastatin 40 mg c-24 hours a month
- **Severe hospitalized patients:** Ivermectin: 12 mg V.O. days 1, 3 and 5 atorvastatin 40 mg v.o c/24 hs, Azithromycin: 500 mg v. or day 1; 250 mg v.o. 2,3,4 and 5 and Osetalmivir :150 mg V.O c/12 hours

➤ **Critical hospitalized patients:** Ivermectin: 12 mg SNG, days 1, 3 and 5 atorvastatin 40 mg SNG c/24 hs, Azithromycin: 500 mg SNG day 1; 250 mg SNG days 2,3,4 and 5 and Osetalmivir :150 mg SNG c/12 hours, Enoxaparin 1 mg/KG c-24 hs i.v. and Critical Support, more narcotic, sedation, muscle relaxant.

III. DISSCUTION

107 patients with confirmed SARS-Cov2-19 were identified. The age of the patients was 60 x 4, minimum age of 23 years and maximum age of 90 years, 52% were men and 48% female. The average admission to the hospital was 5.4 days, with an average resolution and death time of 21 to 25 days.

Although there is a difference between frequencies by gender, this is not statistically significant. The average age falls within the age group of older adults, confirming the vulnerability of this group to COVID-19. However, within the range we can find a large amplitude.

When assessing the place of origin, it is the large and middle cities, which have the highest number of cases; this would be relative if not that, in this study, the state's capital city, Tuxtla Gutierrez, reports a frequency (71 cases) that exceeds the second city by 700% with the highest number of cases reflected (9 cases). Other cities are infrequent in cases ranging from 1-5.

In relation to the type of patient occupation, the highest percentage were those in the household with 25%, followed by retirees with 22%, employees 10%, teachers 8%, doctors and nurses with 7% respectively.

As for occupation, it is interesting to note that the greatest number of cases is represented by housewives, dedicated to the household (27), and retirees (24). I mean, they are people who do not have a job that is forcing them to leave the house. For the specific case of housewives, when leaving home in search of basic satisfactory with the likelihood of exposure to the virus. About people who, if they are working, 22 cases are for health care workers, as frontline staff are at risk they are at vulnerable risk as they care for patients with COVID-19.

24 patients were treated (23%) external consultation and 83 patients (79%) in the emergency room of the hospital. The admission service demonstrates the high number of hospitalized, severe, and critical cases related to COVID-19, as most were admitted by adult emergency and intensive care unit, in equal proportions.

Symptoms began 10 to 1 days before admission. The most common symptoms were headache, general condition attack, cough, fever and dyspnea coinciding with previous studies in different parts of the world (Gralinski and Menachery (2020); Graham et al., 2020; Zhou and Liu, 2020; Xu, Lai and Liu, 2020; Fang et al., 2020). 93% of patients had headache and general status attack respectively, cough 90%, fever 88% and dyspnea 79%.

In 33% of cases there are no comorbidities, 26% with a single comorbidity and 41% with two or more comorbidities. Among the most common comorbidities are, high blood pressure; diabetes mellitus plus high blood pressure; diabetes mellitus, high blood pressure and obesity; diabetes mellitus, obesity and smoking; health conditions that affect the immune system, caused mechanisms of defense of the organism are altered and therefore there is a greater propensity to any disease, in this case COVID-19. This coincides with what was found in the studies of Carbaño (2020) and INSP (2020).

Regarding the type of patients, 24 were outpatient (23%), hospitalized severe 41 patients (38%) and hospitalized critics' 42 at 39%. In relation to the diagnosis of patients to confirm it, 100% of the patients were tested the RT-PCR test collected by nasopharyngeal swab, resulting in a positive result in the entire target population.

Of the total number of patients treated, 38% (41) died, of which two (2%) outpatients, 18 (17%) severe inpatients and 21 (19%) patients cared for in critical condition. Among the findings were found factors associated with mortality, namely age, which showed an average of 68 x 6 greater than patients recovered 55 x 5; only 9 patients who died were not comorbidity and 32 patients had 1 to 2 comorbidities, of these, diabetes mellitus, high blood pressure and diabetes mellitus plus high blood pressure were much more common in deceased patients. In addition to this factor, the critical condition, since 50% of the patients who died had this condition.

Ivermectin as an adjuvant in the treatment of COVID-19 patients proved to be more effective in patients with outpatient treatment, 24 patients recovered 22, corresponding to 92% efficacy in this group of patients. The results are in addition to what was found by Patel (2020); Tavarez (2020) and Aguirre (2020).

For the critically ill patient group, out of a total of 42 patients treated, 50% of patients (21) were recovered, and for the severe hospitalized group, 41 patients were treated and 44% (23) of the sick were recovered. In both groups of patients, apart from the increased viral load and severity of the disease, they have a longer period of elimination of the virus, ivermectin had a significant impact on both improving patients' health and lethality.

IV. CONCLUTIONS

In this investigation, the following is concluded, based on the classification of groups and type of treatment:

- Ivermectin given in the early stages of the disease was shown to be highly effective.
- Ivermectin as an adjuvant in the treatment of COVID-19 patients is more effective (92%) outpatient patients.
- In critical hospitalized and severe hospitalized patients, ivermectin had a significant impact on both improving patients' health and decreasing lethality.

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