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Review Article

# The Use of Compassionate Ivermectin in the Management of Symptomatic Outpatients and Hospitalized Patients with Clinical Diagnosis of Covid-19 at the Centro Medico Bournigal and at the Centro Medico Punta Cana, Grupo Rescue, Dominican Republic, from May 1 to August 10, 2020

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## ABSTRACT

No antiviral has been shown to reduce mortality in SARS-COV-2 patients to date. In the present Retrospective observational study, 3,099 patients with a definitive or highly probable diagnosis of infection due to COVID-19 were evaluated between May 1st to August 10th, 2020, at the Centro Medico Bournigal (CMBO) and the Centro Medico Punta Cana (CMPC), and all received compassionate treatment with Ivermectin and Azithromycin. A total of 2,706 (87.3%) were discharged for outpatient treatment, all with mild severity of the infection. The average between the onset of symptoms and the Emergency Room (ER) visit in outpatients was 3.6 days (Early Treatment). In 2,688 (99.33%) with outpatient treatment, the disease did not progress to warrant further hospitalization and there were no deaths. In 16 (0.59%) with outpatient treatment, it was necessary their subsequent hospitalization to a room without any death. In 2 (0.08%) with outpatient treatment, it was necessary their admission to the Intensive Care Unit (ICU) and 1 (0.04%) patient died. There were 411 (13.3%) patients hospitalized, being admitted at a COVID-19 room with a moderate disease 300 (9.7%) patients of which 3 (1%) died; and with a severe to critical disease were hospitalized in the ICU 111 (3.6%), 34 (30.6%) of whom died. The mortality percentage of patients admitted to the ICU of 30.6% is similar with the percentage found in the literature of 30.9%. Total mortality was 37 (1.2%) patients, which is much lower than that reported in world statistics, which are around 3%, by the time of completion of this study.

**Keywords:** Ivermectin; Azithromycin; Retrospective observational study; COVID-19; Early treatment

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## INTRODUCTION

In December 2019, a new Coronavirus (SARS-COV-2) was identified in Wuhan, China, and declared a pandemic in March 2020 by the World Health Organization (WHO).

It produces a disease known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) [1,2]. At Monash University in Australia, Leon Caly and a group of collaborators infected Vero-h SLAM cells with SARS-COV-2 in vitro and added Ivermectin only once within 2 hours of infecting the cells.

After adding Ivermectin, 48 hours later there was a 99.8% reduction in viral RNA compared to another control sample to which Ivermectin was not added.

The 50% effective concentration of Ivermectin was 2 micromoles (minimum viral inhibitory concentration) [3,4].The ethics committee and the COVID-19 task force of the Grupo Rescue (GR), in their weekly meeting, based on the absence of availability of Hydroxychloroquine in the 2nd and 3rd week of April 2020.

When they received a high number of critical cases of patients infected with SARS-COV-2 in the Emergency Room (ER) of CMBO, they decided to modify the institutional management guide to include Ivermectin based on the in vitro study of the Monash University [3], in conjunction with Azithromycin for both inpatient and outpatient treatment, based on their anti-viral and anti-inflammatory properties.

The present study is a report of the observed results [5-10].

### Objectives

To show that Ivermectin reduces mortality from COVID-19 infection.To demonstrate that in patients in the early symptomatic viral replication of the disease, Ivermectin slows the progression of the disease, decreases the number of hospitalizations and decreases the number of deaths.

## METHODS

### Retrospective observational study

From May 1st to August 10, 2020, the drug Ivermectin was indicated as a compassionate treatment to all patients admitted in the ER of the CMBO and the CMPC, with the definitive diagnosis of COVID-19 due to chain reaction of real-time Polymerase Transcription (rt-PCR) or with a highly probable diagnosis due to the presence of at least 1 of the major criteria and at least 3 of the minor criteria (Table 1) [11-16].

Pregnant women, breast feeding women, children under 2 years or under 15 kg, patients allergic to the drug or those who are anticoagulated with coumarins are excluded for the administration of Ivermectin.

In addition, patients who, once informed of the pros and cons of the use of the drug for the treatment of COVID-19, refused its use and refused to sign the informed consent designed for this purpose, were also excluded from treatment with Ivermectin.

| Mayor criteria | Minor criteria | Comorbidity criteria |
|---|---|---|
| rt-PRC-COVID-19 positive test | Fever >38°C | Age >65 |
| | Dyspnea | Diabetes mellitus |
| IgM-COVID-19 positive test | Dry cough | Obesity (Body Mass Index (BMI) >30) |
| | Anterior chest pain | Thromboembolic disease |
| Pulmonary CT-scan with typical changes associated with COVID-19 infection | Asthenia | Chronic smoker |
| | Ageusia/Anosmia | Obstructive pulmonary disease |
| | Diarrhea | Renal insufficiency |
| | Nausea | Cardiac insufficiency |
| | Myalgias | Coronary cardiopathy |
| | Headache | Systemic arterial hypertension |
| | Skin rushes | Cancer |
| | Elevated reactive C protein | Immunosuppressed |
| | Lymphocytopenia | |

**Table 1:** Major, minor and comorbidity criteria for the diagnostic of COVID-19 infection.

**All patients received in the ER undergo:** rt-PCR or Immunoglobulin M (Ig M) by the rapid qualitative test for COVID 19 depending on availability and timeline of the disease, pulmonary Computed Tomography (CT) scan and laboratory tests, complete blood count, quantified reactive C protein, glycemia, creatinine, transaminases, Lactate Dehydrogenase (LDH), ferritin, D-dimer, swab for Influenza A and B, and a standard 12-lead electrocardiogram [13,15,16].

A scale of severity was established to decide the patients to be treated outpatient or hospitalization namely:

**Grade 1 (mild):** Patients with arterial oxygen saturation greater than 93% room air, heart rate less than 125/minute, respiratory rate less than 24/minute, no decompensated organs and no deterioration of comorbidities (Table 1).

**Grade 2 (moderate):** Sustained arterial oxygen saturation (3 minutes) equal to or less than 93% room air, dyspnea, respiratory rate greater than 24/minute, heart rate greater than 125/minute.

**Grade 3 (severe):** Sustained arterial oxygen saturation (3 minutes) equal to or less than 80% ambient air, arterial hypotension.

**Grade 4 (critical):** Patients Grade 3 who does not respond to support measures and require mechanical ventilation, administration of vasopressors or hemodialysis.

Grade 1 patients were treated on an outpatient basis and followed up by our medical staff, with instructions to return immediately to the ER if they had disease progression. Grade 2 patients were hospitalized in isolation rooms in the COVID-19 area, and grade 3 and 4 patients were hospitalized in the Intensive Care Unit (ICU) in the COVID-19 area.

The outpatients were administered Ivermectin at 0.4 mg/kg, orally (PO) in a single dose in the ER and Azithromycin 500 mg PO per day for 5 days, with follow-up of the outpatients.

Hospitalized patients were administered Ivermectin PO at 0.3 mg/kg, days 1 and 2, and the dose was repeated on days 6 and 7. They were given Azithromycin 500 mg PO daily, for 7 days.

If they presented a D-dimer greater than 1,000 mg/ml or an increase of 50% from the initial value, they were started with Enoxaparin at 1 mg/kg subcutaneously, every 12 hours. Patients with an elevated D-dimer, but less than 1,000 mg/ml received Enoxaparin at 1 mg/kg subcutaneously, every 24 hours. Enoxaparin was not administered if there was thrombocytopenia less than 50,000 [17].

Patients who required oxygen received Dexamethasone at 0.1 mg/kg PO per day, maximum 10 mg per day, for 10 days (or Methylprednisolone at an equivalent dose) [18].

Critically ill patients with suspected cytokine cascade syndrome were administered Interleukin 6 blockers, of the Tocilizumab type, 400 mg intravenously and the dose was repeated after 24 hours if there was no clinical improvement. If Tocilizumab was not available, they were administered Methotrexate, a Jak /Stat blocker at 1 mg/kg on days 1, 2 and 3 intramuscularly or intravenously. At 48 hours after the last dose of Methotrexate, Folic Acid 15 mg daily was started PO for 7 days [19,20].

## RESULTS

A total of 3,099 patients were evaluated in the ER of the CMBO and CMPC from May 1st to August 10, 2020 and treated with Ivermectin.

| | #Patients (%) | Deaths (%) |
|---|---|---|
| Outpatients who do not warrant subsequent hospitalization | 2688 (99.33%) | 0 (0%) |
| Outpatients who merited subsequent hospitalization in rooms in the COVID-19 area | 16 (0.59%) | 0 (0%) |
| Outpatients who merited subsequent hospitalization in the ICU in the COVID-19 area | 2 (0.08%) | 1 (0.04%) |
| Total | 2706 (100%) | 1 (0.04%) |

**Table 2:** Patients discharged from the centro medico bournigal and the centro medico punta cana emergencies for outpatient treatment.

Initially, 2,706 patients (87.3%) received treatment on an outpatient basis, of which 2,688 (99.33%) did not progress the disease, so they did not merit new admission to the ER and subsequent hospitalization and there were no deaths. Of the patients treated as outpatients, 16 (0.59%) subsequently merited hospitalization in the COVID-19 area room with 0 (0%) deaths and 2 of them (0.08%) required hospitalization in the ICU, of which 1 died (0.04%) (Table 2).

In total, 411 patients (13.3%) were hospitalized, including patients initially treated on an outpatient basis and later merited hospitalization, of which 300 patients were admitted to rooms in the COVID-19 area, representing 9.7% of all patients admitted in the ER. On the other hand, in the COVID-19 ICU, 111 patients were hospitalized, representing, 3.6% of the cases originally treated in ER (Table 3).

Of the total number of hospitalized patients, 37 deaths were reported. Three of them occurred in the regular isolation area, while 34 occurred in the COVID-19 ICU (Table 3). The total mortality of the patients initially evaluated in the ER was 37 (1.2%) (Table 3).

From the patients admitted to the ICU, 30.6% with degrees of severity 3 and 4 of the disease died (Table 3).

| | #Patients (%) | #Deaths (%) | % Deaths in each subgroup |
|---|---|---|---|
| Outpatients who do not warrant subsequent hospitalization | 2688 (86.7%) | 0 (0%) | 0% |
| Patients Hospitalized in rooms in the COVID-19 area | 300 (9.7%) | 3 (0.1%) | 1% |
| Patients Hospitalized in the ICU in the COVID-19 area | 111 (3.6%) | 34 (1.1%) | 30.6% |
| | 3099(100%) | 37 (1.2%) | 1.2% |

**Table 3:** Centro Medico Bournigal and Centro Medico Punta Cana.

The average between the onset of symptoms and the ER visit in outpatient treated patients was 3.6 days, while in patients hospitalized in a COVID-19 isolation room it was 6.9 days, and in patients hospitalized in ICU-COVID-19 of 7.8 days.

The distribution by gender of all patients admitted to the ER was as follows: 50.02% male and 49.98% female. While the distribution in hospitalized patients was 63.5% male and 36.5% female.

The average age of the patients hospitalized in rooms of the Covid-19 isolation area was 52 years, while in the ICU patients it was 58 years.

COVID-19 rt-PCR tests were performed only on a total of 685 patients, equivalent to 22% of all patients admitted in the ER with a clinical diagnosis of Covid-19 according to the Institutional Management Guide, of these, 360 (52.5%) were

reported positives (DETECTED) and 325 (47.5%) negatives (NOT DETECTED).

On the other hand, IgM COVID-19 tests were performed on a total of 2,041 (65%) patients, of which 413 (20%) were positives and 1,628 (80%) negatives [21-23].

## CONCLUSION

In 99.3% of the outpatients who were treated with Ivermectin, the establishment of early treatment (on average 3.6 days from the onset of symptoms), was effective since the infection did not progress, they did not merit subsequent hospitalization and had no deaths.

The mortality of the severe to critical patients hospitalized in the ICU was similar to that reported in the international literature of 30.9% versus 30.6% in the patients of the present study.

Total mortality adding up outpatients and hospitalized patients treated with Ivermectin was 1.2%, well below the average 3% reported in most series and overall mortality worldwide, by the time of completion of this study.

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