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Case Report

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Novel and Effective Treatment for Patients with COVID-19 in Stages I to IIIA of the Infection

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Abstract

We report here a novel treatment for patients with Covid-19, stages I to IIIA of infection. The combination of Nitazoxanide, Hydroxicloroquine and Zinc effectively eliminated the SARSCov2 virus after 10 days of treatment in 165 of the 172 patients studied, as determined by RT-PCR and antigen in nasal swabs. This triplet of medicines along with Deflazacort and Ribaroxaban successfully treated patients in stages IIB to IIIA of the infection .The treatment described here is readily available, inexpensive and should prove useful to control dissemination and spread of the virus by symptomatic and asymptomatic persons as well as to decrease the mortality.

Keywords: Nitazoxanide • SARS-CoV-2 • Hydroxychloroquine • Antibodies • Coronavirus

Introduction

In a preliminary study, we found that the treatment of 76 patients with COVID-19 in phases I to IIA of the infection, with the novel treatment integrated by the joint use of 3 drugs, Nitazoxanide, Hydroxychloroquine and Zinc, for 10 days, eliminated the SARS-CoV-2 virus in 95.58% of the cases and that was superior to the control groups that did not receive any treatment or that received the mixture of hydroxychloroquine, Azithromycin and Zinc [1-3].

Here we describe the results obtained in 172 additional patients carried out in order to: 1) increase the number of patients treated with the triplet Ni tazoxanide+hydroxychloroquine+zinc and 2) report the results obtained in patients in a more advanced phase of the infection, phases IIB to IIIA, who were treated with the triplet of drugs indicated above, and who also received concomitantly Deflazacort and Ribaroxaban.

Case Presentation

Universe of patients

The 172 patients were treated in private consultation. All patients were symptomatic and diagnosed as COVID-19+by RT-PCR (85 patients) and by detection of antigen (S1) in nasal swabs (87 patients). The patients were subjected to determination of specific IgG and IgM anti-SARS-CoV-2 antibodies, 14 to 25 days after completing the treatment, by ELISA. The laboratory studies were carried out in the Endogenetics LES, Clinica Foianini, BioCenter, El Remanso Medical Center and IBC laboratories, all in the city of Santa Cruz, Bolivia. 157 patients had O2 saturation above 95% and 15 patients showed O2 saturation between 92% to 94% at the beginning of their diagnosis.

In 118 patients a Computed Tomography of the Thorax (CT-Thorax) was performed; changes with COVID-19 pneumonitis affecting 5% to 20% of the lung fields were detected in 103 patients. In 15 patients, pneumonitis affected between 30% and 50% of the lung fields. Patients with more than 30% but less than 50% involvement of the lung fields and with O2 saturation between 92% to 94% were classified as having phases IIB to IIIA of infection and these 15 patients received treatment with Nitazoxanide, hydroxychloroquine, and Zinc during 10 days, plus deflazacort and ribaroxaban for 25-30 days.

The universe of patients studied between November 1, 2020 and May 5, 2021: 172.

- Age: 18 to 75 years.
- Sex: 74 female and 98 male.
- Patients without previous underlying disease: 88.
- Baseline diseases present: some patients had one or more concomitant underlying diseases: patients with Hypertension (65), Diabetes Mellitus (52), Allergic bronchial asthma (11), Systemic Lupus Erythematosus (34), Rheumatoid Arthritis (22), Obesity (43), primary hypothyroidism (9), and less than 1 to 5 patients per entity were patients with Primary Sjögren's Syndrome, Necrotizing Polyangitis, Celiac Disease, Mixed Connective Tissue Disease, Autoimmune Polymyositis, Scleroderma, Leukocytoclastic Vasculitis, Wegener's Granulomatosis, and Graves-Basedow's Disease. Three patients presented concomitant infection with Dengue and COVID-19.

Control group

15 patients infected with COVID-19 in phase I of the infection that received symptomatic treatment, but no antiviral treatment and had no underlying disease.

Age: 31 to 50 years old.

Sex: 9 males and 6 females.

Treatment scheme

157 patients in phase I to IIA of infection were treated with:

- Hydroxychloroquine 200 mg every 12 hours × day.
- Nitazoxanide 500 mg every 12 hours × day.

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- Zinc 50 mg × day.

For 10 days: 15 patients in phases IIB to IIIA of infection were treated with:

- The triplet of medications listed above × 10 days.
- Deflazacort (30-45 mg x day) and Ribaroxaban (10-20 mg × day)

During 25-30 days: Paracetamol, and Bequium or Flemex Forte syrups, and PeptoBismol in suspension were prescribed as symptomatic, according to requirements. Patients in phase IIIA were recommended to maintain the prone position in bed for at least 12 hours × day. 6 patients received supplemental oxygen at home (they had oxygen saturation of 92% initially) until saturation improved to 95% and was discontinued (Table 1).

Patients				**Treatment Response***
		Number Treated	PCR/Ag Negative	ELISA IgG anti-SARSCoV2
Without underlying disease		88	88	88
	Stage I-IIA	85	85	85
	Stage IIB-IIIA+	3	3	3
With underlying disease		84	77	77
	Stage I-IIA	72	65	65
	Stage IIB-IIIB+	12	12	12
	Required 2nd Cycle treatment #	7	7	7

Table 1. Group of patients and response to treatment; (*) - Treatment: Nitazoxanide +Hydroxychloroquine+Zinc for 10 days; (+) - Treatment: Nitazoxanide+Hydroxychloroquine+Zinc for 10 days and Deflazacort+Ribaroxaban for 25-30 days; (#) - Seven patients were still PCR/Ag SARSCoV2 positive after the 10 days of treatment. All underwent a second cycle of treatment with Nitazoxanide+Zinc for 10 days.

Results

165 patients were negative by RT-PCR or nasal swab antigen for SARS-CoV-2, determined 14 days after initiation of treatment. 7 patients remained antigen SARSCov2 positive after completing the 10-day treatment. They were given a new cycle of treatment with Nitazoxanide and Zinc for additional 10 days. At the end of the second cycle, all 7 patients were negative for SARS-CoV-2 virus determined by RT-PCR/Nasal swab antigen (Table 1).

The 15 patients with phases IIB to IIIA of infection were practically asymptomatic 30-50 days after starting their treatment. All 172 patients had serum IgG-specific against SARS-CoV-2 determined by ELISA, 14-25 days after the start of treatment (Table 1). The most frequent undesirable effects to the medications were nausea and diarrhea, which improved when dividing the intake of Zinc to 25 mg every 12 hours. In the control group that received no specific treatment, 5 patients were SARS-CoV-2 negative after 14 days of their diagnoses and 4 patients were negative for the virus at days 21-28 after diagnoses. 6 patients clinically deteriorated and evolved into phase IIB of the infection and had to be treated with the triplet of medicines along with Deflazacort and Ribaroxaban [4-11].

Conclusion

The results described here extend, confirm and reinforce the effectiveness of the novel treatment constituted by the Nitazoxanide+hydroxychloroquine+Zinc triplet against COVID-19, originally described in the previous study carried out with 76 patients in phases I to IIA of infection with COVID-19. Much of the therapeutic success of this treatment is due to the use of Nitazoxanide. We must highlight the efficacy of Nitazoxanide for its virucidal activity. Nitazoxanide suppresses virus replication in cultures. This drug also inhibits the replication of other RNA and DNA viruses in addition to SARSCov2, including respiratory syncytial virus, parainfluenza, coronavirus (SARS1, MERS2), rotavirus, norovirus, hepatitis B, hepatitis C, dengue, yellow fever, Japanese encephalitis virus, and Ebola, in cell culture assays. The virucidal effect of Nitazoxanide has been documented in doses of 0.39 uM in culture and this concentration of 0.39 uM of Nitazoxanide is readily achieved in the plasma of people who receive 500 mg every 12 hrs. It must be emphasized that this dose is the one that has been used in patients infected with COVID-19 reported in the present and in our previous preliminary studies.

Zinc at doses of 50 to 100 mg has an inhibitory effect on the RNA polymerase of the virus and hydroxychloroquine exerts an ionophore effect, facilitating the entry of Zinc into cells, in addition to its widely documented effects on the innate immune response to viral infections. Another practical contribution of the study reported here for the treatment of patients with COVID-19 in phases IIB to IIIA of the infection, is the very good response to the triplet of antiviral drugs together with the use of Deflazacort and the anticoagulant Ribaroxaban, as a treatment for moderate to severe inflammatory phases and the known alteration in blood vessel endothelium and platelets caused by SARS-CoV-2, with the consequent formation of micro and macro thromboses in various organs. Given the mechanisms of action of each of the components of the triplet of drugs to treat COVID-19 described here, it is practically impossible for variants of SARS-CoV-2 to emerge resistant to this treatment , since in principle, they would be incompatible with viability and replication of the virus. It is therefore very important to strongly emphasize that this is a very effective treatment for patients infected with COVID-19 in phases I to IIIA. The fact that the treated patients cleared the virus clearly indicates the use of this treatment not only to treat the infection quickly, but also offers the opportunity to prevent the spread of the viral infection to others. With the advent of vaccines against COVID-19, there are now satisfactory conditions to propose a rational and scientifically proven strategy for the control of COVID-19, which I would like to detail below:

1. Carry out RT-PCR and nasal swab antigen tests to the population.

2. People who test positive for SARSCov2 should immediately start treatment with the Nitazoxanide+hydroxychloroquine+Zinc triplet. It would be ideal and desirable for this treatment to be delivered free of charge when the positive result of the RT-PCR and/or antigen tests for diagnosis of COVID-19 is reported.

3. Continue efforts to vaccinate the majority of the population as soon as possible. This strategy allows, on the one hand, to treat already infected patients in order to reduce mortality, and spread of the virus (remember that asymptomatic or slightly symptomatic infected people are the ones that most spread SARS-CoV-2) and on the other hand, vaccines prevent infection and reduce mortality caused by this virus.

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