STUDY OFFICIAL TITLE (original title is in Spanish. This is a translation into English)

Topical Ivermectin and Iota Carrageenan

REGISTRY NUMBER (CLINICALTRIALS.GOV)

NCT04425850

DATE: May 29th, 2020 (last update approved by Ethics Committee of Eurnekian Hospital)

IVERCAR – STUDY PROTOCOL (SUMMARY)

OBJECTIVES

Evaluate the effect of the use of repeated doses of buccal ivermectin associated with nasal and buccal administration of iota-carrageenan as add-on preventive treatment on contagion and progression of COVID-19 in a population of healthy individuals exposed to SARS-CoV-2 with increased risk of contagion, i.e. health-care personnel working in Eurnekian Public Hospital, compared to standard prophylactic measures only.

STUDY HYPOTHESIS

Healthcare workers have an increased risk to become infected. The beginning of the disease is linked to quick viral replication in the oropharynx and nasopharynx. Treatment with ivermectin associated with iota-carrageenan applied locally to the nasal and buccal cavity could lower the probability of contagion and progression to severe disease and would lower the viral load in the upper airways.

STUDY PROTOCOL (SUMMARY)

Study center	Hospital Interzonal Universitario Dr. Alberto Eurnekian, EZEIZA. (Eurnekian Public Hospital, Ezeiza, Province of Buenos Aires, Argentina)
Study concept	Efficacy and safety study to evaluate the use of buccal ivermectin and associated with buccal and nasal iota carrageenan in the prophylaxis of COVID/19 in health-care workers
Study type	Prospective, single-center, two-arm parallel, comparative with standard prophylactic measures
Justification	The emergency of COVID-19 requires the urgent development of strategies to avoid the impact of the disease on our population and the saturation of the health system and to allow us to carry out adequate treatments to reduce the mortality of the disease. Upper respiratory tract infection has a major impact on the transmission and pathogenesis of SARSCoV2. The role of nasopharynx, saliva and salivary glands in the early stage of viral infection is becoming increasingly well understood. Any measure located in the nasopharynx and oral cavity to reduce viral load, will reduce the level of contagion in the social environment of each person. Given that the viral RNA detection diagnostic test is not immediate and that contagion control is essential during the first days after infection, this treatment, , could contribute to the control of contagion in the first stage of infection, even when there are no symptoms of the disease and in suspected cases of COVID-19 We propose the use of buccal Ivermectin associated with nasal and buccal iota carrageenan as a topical antiviral treatment.

Study outcomes	Primary outcome: infection rate (contagion rate) in each arm Secondary outcome: adverse events in each arm (other than those resulting from contagion and disease progression)
Study population	Healthy healthcare workers at Eurnekian Public Hospital (physicians, nurses, patient transporters, administrative staff, cleaning staff, kitchen staff) who accepted to take part in this protocol either in the treated or untreated arm of the study
Elegibility criterio	**Inclusion criteria** 1. Not younger than 18 years of either sex 2. Health personnel from the Dr. Alberto Eurnekian Interzonal University Hospital 3. No COVID-19 related symptoms 4. Able to understand and give written informed consent **Exclusion criteria** 1. Known hypersensitivity or allergy to any component of the product under evaluation 2. Age under 18 years 3. Use of immunosuppressants (including systemic corticosteroids) in the past 30 days. 4. Pregnant or nursing. 5. Patients with other acute infectious diseases. 6. Patients with autoimmune disease and / or decompensated chronic diseases. 7. Unable to fulfill the administrative tasks proposed by the study. 8. Infection with SARSCoV-2 confirmed by PCR or rapid test authorized by ANMAT. **Discontinuation criteria** 1. All subjects who use any other nasal or oral topical medication during the study period (sprays or nebulization with decongestants, corticosteroids, antibiotics, etc.) will be discontinued. 2. Development of any serious or severe adverse drug reaction that, at the discretion of the researcher, puts the subject under study at risk
Treatment	Ivermectin oral drops (6 mg/ml), Certificate No. 58.382, ANMAT Iota-carrageenan (0.17 mg / shot) nasal spray, Certificate No.57.232, ANMAT Each application consists of: One shot of iota carrageenan nasal spray in each nostril and 4 shots in the oral cavity. After five minutes, apply 1 oral drop of ivermectin (200 μg of ivermectin) on the tongue. Food and drink consumption avoided 1 hour before and after treatment.

	Posology This application must be repeated 5 times a day, each 4 hours. The last application should be just before night rest. In this case, less than 4 hours may have passed by from the previous application.
Study design	The study consists of 5 visits at Eurnekian Public Hospital and/or daily remote monitoring, according to the following schedule: • Visit 1 (Day 0): informed consent, check of eligibility criteria, physical examination, questionnaire of symptoms, explanation about remote monitoring, nasopharyngeal swabbing for COVID-19 detection by rtPCR or quick LAMP-based test, delivery of drugs to patients. • Visit 2 (Day 7): physical examination, record of adverse events, questionnaire of symptoms, nasopharyngeal swabbing for COVID-19 testing. • Visit 3 (Day 14): physical examinatioin, record of adverse events, questionnaire of symptoms, nasopharyngeal swabbing for COVID-19 testing. End of treatment: both groups continue to use standard prophylactic measures. • Visit 4 (Day 21): physical examination, record of adverse events, questionnaire of symptoms. • Visit 5 (Day 28): physical examination, record of adverse events, questionnaire of symptoms. End of study
Statistical analysis	Chi-squared test for contagion rate in each group.