Use of APT™ T3X to decrease the COVID-19 contamination rate in humans

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Background and aim

The new coronavirus 2019 (COVID-19) was declared a pandemic by the World Health Organization (WHO) due to the alarming levels of spread, severity and inaction. COVID-19 is caused by the SARS-CoV-2 virus (severe acute respiratory syndrome of coronavirus 2). The main clinical characteristics observed in patients infected with COVID-19 are: fever, dry cough, fatigue or myalgia. Patients infected with COVID-19 can present from no symptoms to pneumonia and death. Dealing with COVID-19 must be done on different fronts, such as mitigation, treatment and prevention. Therefore, strategies and therapies that can help reduce the COVID-19 rate of contamination are still important alternatives at this time of the pandemic, especially when mutations of the virus have been observed worldwide.

The Advanced Penetration Technology™ (APT™) is intellectual property owned by Patient Focused Tele-Health, LLC, a Rockwall, Texas based company. The company's focus is improving over-the-counter (OTC) topical formulations, allowing consumers better therapeutic outcomes with non-prescription medications. The Advanced Penetration Technology™ (APT™) is a patent-pending, proprietary transdermal dual carrier formulation. This formulation provides improved dermal penetration and efficacy of topical API's. Additionally, the APT™ imparts both a mechanical and biochemical effect on the microbe/fungal cell walls providing a highly effective method of destruction of microbes. These unique properties impart the broad spectrum anti-viral capability to the APT™ Tetracycline 3% formulation, breaking barriers in pharmacology and virology.

The topical formulation APT™ Tetracycline 3% formulation (APT™ T3X), is a FDA registered, non-prescription product. This formulation is used in an off-label manner as an intranasal application for prevention of COVID-19 and other viruses. The APT™ T3X as a topical application will penetrate through and into the mucus layer and deeper. This barrier of coverage will provide a mitigation effect to decrease the viral load of exposure and infection. The efficacy of APT™ T3X is due to disrupting the lipid envelope in seconds, hence neutralizing the virus. Previous tests were performed with APT™ T3X and the results found were promising. However, these tests were performed only *in vitro* and clinical studies demonstrating the ability of the APT™ T3X to decrease viral exposure and contamination by COVID-19 are necessary to confirm the possible prophylactic effect, allowing the formulation to be widely distributed to the general population.

Therefore, the aim of this project will be to evaluate the efficacy of the APT™ T3X compared to placebo to decrease COVID-19 contamination rate in humans.

Methods

Trial design

A two-arm, parallel randomized, triple-blinded (volunteers, care provider, and outcome assessor), placebo-controlled trial will be carried out. This trial it will be prospectively registered on clinicaltrials.gov.

Ethics

This study was submitted and approved by the Research Ethics Committee of Irmandade da Santa Casa de Misericórdia de Porto Alegre – ISCMPA, Porto Alegre, Rio Grande do Sul, Brazil, under protocol number 4.485.847. This trial will be performed in accordance with the Declaration of Helsinki and the guidelines for research involving human subjects. All volunteers will sign the written informed consent before enrolment in the study.

Volunteers and recruitment

One hundred volunteers will be included in the trial (fifty volunteers per group). The inclusion criteria will be: over 18 years; good general health (without serious health problems); tested negative, by means of immunoglobulin (Ig) G and IgM serology tests and chain real-time polymerase chain reaction (RT-PCR), for COVID-19. The exclusion criteria will be: previous immunization against COVID-19; allergy to tetracycline hydrochloride; diagnosis of Lyme disease; immunocompromised; share housing with someone diagnosed with COVID-19 at the time of the baseline evaluation; serious illnesses, such as cancer, kidney failure, decompensated cardiorespiratory and metabolic diseases, etc.

Randomization and blinding

Prior to initiation of the treatment, patients will be randomized into their respective intervention groups: APT™ T3X or placebo. Randomization will be generated by a website (http://random.org/) and performed by a participating researcher not involved in the recruitment and evaluation of the volunteers. This researcher will be instructed not to disclose the

randomization codes in the intervention groups to any of the volunteers and to the other researchers involved in the study, until its completion. The intervention bottles will be exactly the same regardless of whether it was APT™ T3X or placebo. Concealed allocation will be achieved through the use of sequentially numbered, sealed, and opaque envelopes.

Interventions

Volunteers will be instructed to use the intervention, according to the prior randomization, once a day, every day, for 21 days. If the volunteer is health professional, it will be instructed to use the intervention twice a day, every day, for 21 days. Intervention specifications included:

1) APT™ T3X: The volunteers will be instructed to use 4 drops of tetracycline hydrochloride 3% (APT™ T3X) applied inside of the nasal channels and inside of nostrils.
2) Placebo: The volunteers will be instructed to use 4 drops of a formulation composed of FDA approved inactive ingredients applied inside of the nasal channels and inside of nostrils.

All volunteers will be instructed to record each intervention application and to send to a member of the research team in order to control and ensure the adherence to treatment.

Outcomes

Primary outcome

The primary outcome measured will be the rate of contamination by COVID-19 measured through the rate of how many people will be infected with COVID-19 over the course of the study in each group. This outcome will be measured 22 days after the randomization i.e., after 21 days of application with APT™ T3X or placebo.

Secondary outcomes

The secondary outcomes will be presence of adverse events, number of adverse events and frequency of adverse events measured through self-report. In addition, other virus or bacteria contamination rate will be measured through the rate of how many people will be infected with influenza or pneumonia over the course of the study in each group. All secondary outcomes will be measured 22 days after the randomization i.e., after 21 days of application with APT ™ T3X or placebo.

Statistical analysis

The results obtained will first be tested for normality using the Kolmogorov-Smirnov test. The chi-square test or Fisher's exact test for two independent proportions will be used in the statistical analysis of the primary outcome of this study, the COVID-19 contamination rate and for the secondary outcomes: presence of adverse events and another virus or bacteria contamination rate. For the other secondary outcomes, the number of adverse events and frequency of adverse events, the Wilcoxon test will be used if this outcome does not present a normal distribution. If this outcome presents a normal distribution, the two-tailed, unpaired t test will be used. The level of significance used will be 5% ($p < 0.05$).