OPEN ACCESS Freely available online

Journal of Clinical & Experimental Pharmacology

Research Article

Chlorpheniramine Maleate Nasal Spray In COVID-19 Patients: Case Series

Joselit Torres[1], Camille Celeste Go[2], Farah Chohan[2], Genesis Camacho L[2], Marcos A Sanchez-Gonzalez[1], Gustavo Ferrer[2,3]*

[1]Institute of Immunodiagnosis. Urb. El Rosal, Caracas, Venezuela; [2]Division of Research & Academic Affairs, Larkin Health System, South Miami, Florida, USA; [3]Aventura Pulmonary Institute, Miami, Florida, USA; [4]Nova Southeastern University Fort Lauderdale, Florida, USA

ABSTRACT

The pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) posted a devastating global health crisis. Very little is known about this virus that it is difficult to find treatments of this novel virus. The vaccine that can potentially combat this virus is under works hence, the repurposing of existing medical treatments such as chlorpheniramine maleate (CPM) could be a possible treatment. CPM is a safe and effective antihistamine with potent antiviral activity against various strains of influenza A/B, thus highlighting its great antiviral potential.

The coronavirus disease 2019 (COVID-19) has a droplet mode transmission with a notably high viral load especially the nose. Several studies postulated that the nose is possibly the primary route of entry of SARS-CoV-2 owing to the high expression of Angiotensin 2 converting enzyme receptors. We hypothesize that utilizing (CPM) nasal spray as an adjunct treatment to COVID-19 patients and reduce their clinical course and hasten their time to negativization via RT-PCR via nasopharyngeal swab. We present four symptomatic patients with mild-moderate risks. CPM nasal spray was added to their current supportive treatment. All four patients showed rapid improvement of their clinical symptoms with a shorter than average time to negativization on repeat nasopharyngeal swab via RT-PCR. No safety issues were encountered during the course of treatment. Given its years of excellent safety profile with remarkable clinical results as shown in this case series, we conclude that CPM nasal spray may be a potential adjunct treatment option in patients with mild to moderate COVID-19 symptoms.

Key words: COVID19; Intranasal; Chlorpheniramine maleate; Therapeutics; Nasal spray; SARS-CoV-2

INTRODUCTION

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or coronavirus disease 2019 (COVID-19) led the World Health Organization to recognize it as a global pandemic in March 2020 [1].

There are no effective chemo-prophylactic drugs against SARS-CoV-2 so the main intervention strategy is the control of transmission. Scientists had to find alternative treatments, with clinical trials focused on investigating potential therapeutic agents and repurposing existing treatments.

Nasopharynx has been recognized as the port of entry of SARS-CoV-2 and has a high viral shedding from the nasal cavity before and after onset. [2] Nasal secretions are swept by rapid nasociliary clearance into the oropharynx and aspirated into the lower respiratory tract [3].

On the basis of a previously published case report, this study is focused on understanding the potential effectiveness of chlorpheniramine maleate (CPM) in suppressing the replication of SARS-CoV-2 in the nose [4].

In a study conducted in vitro and in animal models by Xu et al, carbinoxamine maleate (CAM) and S-(+)-chlorpheniramine maleate (SCM) showed potent antiviral activity against influenza A strains and one influenza B strain and protection from potentially lethal avian H7N9 influenza virus. By penetrating the blood-brain barrier, they inhibit the influenza virus by targeting the early stage of virus life cycle, and its entry into the host cells. Additionally, they can be used prophylactically in healthy individuals for prevention of influenza virus infection [5].

We aim to utilize existing medications, particularly CPM nasal spray, for reducing the clinical course of the disease and decrease

***Correspondence to**: Gustavo Ferrer, Aventura Pulmonary Institute, Miami, Florida, USA, Tel: +1954482-474; E-mail: gferrer@pulmonary-institute.com

Received: January 08, 2021; **Accepted**: January 23, 2021; **Published:** January 30, 2021

Citation: Torres J, Go CC, Chohan F, Genesis Camacho L2, Sanchez-Gonzalez MA, Ferrer G (2021) Chlorpheniramine Maleate Nasal Spray In COVID-19 Patients: Case Series. J Clin Exp Pharmacol. 10:275. doi: 10.35248/2161-1459.21.10.275

the time to negativization.

This case series will show how four COVID-19 positive patients enrolled in a study utilizing CPM nasal spray showed positive outcomes. All patients have expressed written informed consents.

CASE PRESENTATION

Case 1

An elderly white female, with hypertension with unknown treatment and asthma treated with desloratadine and albuterol, tested positive for COVID-19 in September 202. The patient is a non-smoker, no past surgical history. After testing positive with COVID-10, she was enrolled in this case series and was given the experimental treatment. She was instructed to spray two puffs of CPM nasal spray per nostrils twice a day for seven days. She continued to use albuterol as needed, and supportive treatment. She was followed for seven days and was assessed for symptoms. On day 1, she complained of waking up at night due to the cough, fever and diarrhea, runny, itchy and stuffy nose, sandy sensation in her eyes, chest pain, anosmia, ageusia, fatigue, cough. She had mild symptoms most of the time on Symptoms Assessment Score (SAS). She rated generalized pain as nine on the Visual Analogue Score (VAS) and the Numerical Rating Scale (NRS). On day 2, oxygenation was 91%. On day 4, she noted improvement in her runny, itchy and stuffy nose. On day 6, VAS was reported as three. She also had mild to nonexistent congestion. Although mild anosmia was still present, it was markedly improved compared to day 1. She remained afebrile after the fourth day of the trial. She was tested via nasopharyngeal swab RT-PCR and tested negative on day 7. A follow-up was done on day 14 and reported return to baseline health.

Case 2

A young adult white woman with chronic rhinitis and sinusitis treated with cetirizine, tested positive for COVID-19 in September 2020. She is a non-smoker with no past surgical history. Three days prior, she started experiencing runny and stuffy nose, itchy and painful eyes, anosmia, chest pain, fatigue and fever at 102.2 Fahrenheit (F). She also reported difficulty in sleep due to nasal symptoms and has been using albuterol as needed. Upon consultation, she was tested for COVID-19 RT-PCR via the nasopharyngeal swab. Following the positive test, she was enrolled in the case series experimental group. On day 1, she complained of stuffy nose, sneezing, congestion, sandy and watery eyes, fever 102.2°F, anosmia, and eye pain. she reported fever 100.4° (F) and mid-effort shortness of breath that was worse on day 3 when saturation was 92%. On Day 4, she was afebrile and was able to smell strong substances. On day 7, she reported all the symptoms were mild or non-existent. Repeat nasal swab RT-PCR was negative. She returned to baseline health on Day 14.

Case 3

An elderly Hispanic female, with history of chronic rhinitis and allergies treated with cetirizine, tested positive for COVID-19 in October 2020. She is a non-smoker with no past surgical history reported. She sought consult on day 3 and was tested for COVID-19 via nasal swab RT-PCR with positive results. On day 1, she had runny and stuffy nose, anosmia, tiredness, itchy and painful eyes and mild cough. Normal oxygen saturation was detected. On day 3, she noticed an improvement of symptoms but with mild presentation of nasal symptoms and persistent eye pain. On day 6, she reported mild eye pain. On day 7, her sense of smell completely recovered. She was retested on day 7 and tested negative. She returned to baseline health on day 14.

Case 4

A young adult white female, with history of chronic rhinitis treated with desloratadine. She tested positive for COVID-19 on October 2020. She is a non-smoker, with no surgical history. She reported fatigue, restless, runny, itchy and stuffy nose, anosmia and eye pain, fatigue, shortness of breath with minimum physical activity, eye pain, runny nose, anosmia, ageusia and diarrhea two days prior. A consultation was followed by a COVID-19 RT-PCR test which was positive. She was enrolled in this case series and was given the experimental treatment. On day 1, she complained of a stuffy nose, anosmia, ageusia, tiredness, cough, and congestion. She reported mild symptoms on SAS, rated generalized pain as nine on the VAS and the NRS. She had diarrhea on day 3 and 4. Improvement of symptoms was noted on day 7 and a repeat COVID-19 RT-PCR via nasopharyngeal swab was done with negative results. She reported return to baseline health by day 14.

DISCUSSION AND CONCLUSION

The above-mentioned cases are showing the potential efficacy of utilizing CPM containing nasal spray as a possible adjunct treatment against COVID-19 and augment the time to negativization on nasal RT-PCR. Although this does not guarantee definite proof of efficacy, this case series provides a framework for initiating a broader scope randomized placebo-controlled clinical trial in the potential efficacy of chlorpheniramine nasal spray in COVID-19 patients.

Patients in this study reported several risk factors that could potentially increase morbidity and mortality in COVID-19 infected individuals. Patient 1 was an elderly, with hypertension and asthma, patient 2, 3 and 4 had chronic rhinitis and sinusitis. These patients had more than average risk of morbidity and mortality of COVID-19. [6] All patients had a benign course of disease and all showed improvement of symptoms with the use of chlorpheniramine.

Patients were asked to spray two puffs of CPM nasal spray per nostrils two times per day for seven days. A study conducted on SARS-cov-2 stock to highlight the virucidal potential of CPM showed a reduction of 99.7% in viral load in Vero 76 infected cells [7].

Mostafa et al in a study on FDA approved drugs that have antiviral activity against SARS-CoV-2 concluded that besides antimicrobial drugs like Azithromycin, Niclosamide, and Nitazoxanide, several antihistamines and anti-inflammatory drugs could reduce SARS-CoV-2 replication. CPM, a competitive histamine H1 receptor antagonist, exhibited strong virucidal activity against a variety of influenza viruses [8].

In addition, CPM is generally safe and effective for use with the main side effect being drowsiness. A study also reviewed the systemic bioavailability and overall safety of a nasal spray solution that delivers doses of 1.12 and 2.24 mg CPM intranasally (0.4% nasal spray) and has found no adverse events [9].

Lastly, the improvement of symptoms and time to negative PCR test are important to highlight. A study conducted by Vaira, L.A. found

that olfactory and gustatory dysfunctions are common symptoms in COVID-19 patients. [9] Furthermore, Al-Ani RM et al. also highlighted that patients who have nasal and paranasal problems have longer time in recovery from the smell because of interference with air current from reaching the olfactory epithelium to the roof of the nose. [10] Spethet. Al also stated that patients with allergic rhinitis, chronic rhinosinusitis, and asthma, have increased severity in symptoms. [11] In our study, resolution of symptoms was notable as early as Day 4 with no progression to severity. Furthermore, when patients were tested via nasal RT-PCR on Day 7, all of them tested negative, a 50 % reduction to negativization compared to the average 14-day course of the disease [12].

In summary, the cases reported in this case series, who have minimal to moderate morbidity and mortality risk from COVID-19 showed significant improvement in symptoms and a 50% reduction in the clinical course with the use of CPM nasal spray. This could potentially pave the way in improving clinical outcome and reduce clinical burden in areas heavily affected with COVID-19. We recommend a larger randomized, placebo-controlled clinical trials which could further shed light on this potential treatment.

COMPETING INTERESTS

The authors declared that they do not have any conflict of interest.

FUNDING

Not applicable

AUTHORS' CONTRIBUTION

T.J, G.F. are the one who conceptualized and gathered the data. C.C.G, F.C, G.C.L and M.S.G collated and analyzed the data for this case series. All authors have equal contribution with this paper. All authors agreed to the final manuscript and submission of this case report.

ACKNOWLEDGMENT

None.

REFERENCES

1. Grech V, Cuschieri S. COVID-19: A global and continental overview of the second wave and its (relatively) attenuated case fatality ratio [published online ahead of print, 2020 Oct 3]. Early Hum Dev. 2020;105211.
2. Cegolon L, Javanbakht M, Mastrangelo G. Nasal disinfection for the prevention and control of COVID-19: A scoping review on potential chemo-preventive agents [published online ahead of print, 2020 Aug 18]. Int J Hyg Environ Health. 2020;230:113605.
3. Lipworth B, Chan R, Rui Wen Kuo C. COVID-19: Start with the nose. J Allergy Clin Immunol. 2020;146:1214.
4. Go CC, Pandav K, Sanchez-Gonzalez MA, Ferrer G. Potential Role of Xylitol Plus Grapefruit Seed Extract Nasal Spray Solution in COVID-19: Case Series. Cureus. 2020;12:e11315.
5. Xu W, Xia S, Pu J, Wang Q, Li P, Lu L, et al. The Antihistamine Drugs Carbinoxamine Maleate and Chlorpheniramine Maleate Exhibit Potent Antiviral Activity Against a Broad Spectrum of Influenza Viruses. Front Microbiol. 2018;9:2643.
6. Jian L, Yi W, Zhang N, Wen W, Krysko O, Song WJ, et al. Perspective: COVID-19, implications of nasal diseases and consequences for their management. J Allergy Clin Immunol. 2020;146:67-69.
7. Westover JB, Ferrer G, Vazquez H, Bethencourt-Mirabal A, Go CC. In Vitro Virucidal Effect of Intranasally Delivered Chlorpheniramine Maleate Compound Against Severe Acute Respiratory Syndrome Coronavirus 2. Cureus. 2020;12.
8. Mostafa A, Kandeil A, AMM Elshaier Y, Kutkat O, Moatasim Y, Rashad AA, et al. FDA-Approved Drugs with Potent In Vitro Antiviral Activity against Severe Acute Respiratory Syndrome Coronavirus 2. Pharmaceuticals. 2020; 13:443.
9. Vaira LA, Deiana G, Fois AG, Pirina P, Madeddu G, De Vito A, et al. Objective evaluation of anosmia and ageusia in COVID-19 patients: Single-center experience on 72 cases. Head Neck. 2020;42:1252-1258.
10. Al-Ani RM, Acharya D. Prevalence of Anosmia and Ageusia in Patients with COVID-19 at a Primary Health Center, Doha, Qatar [published online ahead of print, 2020 Aug 19]. Indian J Otolaryngol Head Neck Surg. 2020;1-7.
11. Speth MM, Singer-Cornelius T, Oberle M, Gengler I, Brockmeier SJ, Sedaghat AR, et al. Olfactory Dysfunction and Sinonasal Symptomatology in COVID-19: Prevalence, Severity, Timing, and Associated Characteristics. Otolaryngol Head Neck Surg. 2020;163:114-120.
12. Walsh KA, Jordan K, Clyne B, et al. SARS-CoV-2 detection, viral load and infectivity over the course of an infection. J Infect. 2020;81:357-371.