Int. J. Odontostomat.,
14(4):561-563, 2020.

Can a Nasal/Oral/Ocular Spray Inactivate and Prevent SARS-CoV-2 infection? A hypothesis

¿Puede un Spray Nasal/Oral/Ocular Inactivar y Prevenir la Infección por SARS-CoV-2?: Una hipótesis

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FUENTES, E. & SANTOS-LÓPEZ, M. Can a nasal/oral/ocular spray inactivate and prevent SARS-CoV-2 infection? A hypothesis. *Int. J. Odontostomat., 14(4)*:561-563, 2020.

ABSTRACT: The COVID-19 pandemic has created challenges that have been dealt with adopting measures such as prolonged or intermittent social distancing, which may even be necessary until 2022. Furthermore, it has been described that a SARS-CoV-2 contagion route corresponds to the inhalation of the virus. Medications via nasal/eye spray and inhalers, therefore, could fulfill the function of inactivating SARS-CoV-2. Due to the abovementioned reasons, we suggest the following hypothesis: The use of Ocular/Nasal/Oral sprays could prevent the infection and the further spread of SARS-CoV-2.

KEY WORDS: COVID-19, SARS-CoV-2, sprays, infection.

INTRODUCTION

The outbreak of the COVID-19 pandemic can be attributed to the spread of a disease called COVID-19 or Coronavirus 2 (SARS-CoV-2), which causes severe acute respiratory syndrome (Scheller *et al*., 2020). The ongoing pandemic has brought about challenges that have been dealt with taking measures such as prolonged or intermittent social distancing, which may even be necessary until 2022 (Kissler *et al*., 2020). Furthermore, scientists have pointed out that the virus has some weak points (Scheller *et al*.), aside from describing its incubation period of approximately 5 days (Lauer *et al*., 2020) and finding out that it makes more viruses in the nasopharynx (Hui *et al*., 2020).

Three issues it is necessary to discuss to develop preventive actions against SARS-CoV-2 Infection will be listed here below:

1. Can nasal spray devices be of any use to stop SARS-CoV-2 replication at the respiratory system, especially at nasopharynx?

2. Will it be possible to find any spray that will be able to inactivate SARS-CoV-2 in the ocular conjunctiva and periocular tissues/elements?

3. Are there bio-tolerated chemical materials capable of effectively inactivating SARS-CoV-2 at the respiratory system and oral/ocular/periocular mucose?

It has been elucidated that a SARS-CoV-2 contagion route corresponds to the inhalation of the virus (Pervushin *et al*., 2009) and it has also been reported that it can be transmitted through the eye (Coroneo, 2020). For this reason, medications via nasal/eye spray and inhalers could fulfill the function of inactivating SARS-CoV-2, since they could reach the levels where this virus develops at a less aggressive stage, aiming at anatomical areas such as the ocular conjunctiva, periocular tissues, pharynx and the respiratory tree reaching its deepest areas. Due to the previously mentioned reasons, the following hypothesis can be presented: The use of

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Ocular / Nasal / Oral sprays may prevent infection and replication of SARS-CoV-2.

First of all, it has to be stated that the use of nasal sprays/inhalers is intended to deposit a drug topically in the airway (Rogliani *et al*., 2017). Since the human upper airway can become deformed during inhalation (Cheng *et al*., 2019), the use of the mentioned devices may offer a safe and cost-effective intervention by achieving a rapid onset of action using small doses of medications (Rau, 2005). Furthermore, achieving a high chemical deposition in the pharyngeal space would be a desirable feature in a device created for these purposes.

Another significant aspect that needs to be analyzed is the possible concentration of SARS-CoV-2 in tears. According to scholars such as Coroneo and Wu *et al*. (2020), the virus is highly contagious, potentially lethal, with ocular tropism (Coroneo); thus, it may be transmitted through ocular secretions (Wu *et al*.). There are theories, intended to explain this phenomenon, that suggest that the transmission can occur through the inoculation of infected droplets in the ocular conjunctiva (Amesty *et al*., 2020), causing the further spread of the infection to the respiratory tract due to the anatomical connection between the lacrimal gland and the nasal cavity (Amesty *et al.*). Therefore, an eye spray system could be useful to prevent infection through the eye and, indeed, there is a spray on the market that can reduce the bacterial and viral load on the skin and eyelashes (Seah & Agrawal, 2020).

Hydroxychloroquine, azithromycin, and zinc are elements topically used in the eye because they can partially block the angiotensin-converting enzyme 2 (ACE2) receptors (Coroneo). Since SARS-CoV-2 has a high affinity for ACE2 receptor, which is present in the eye tissues, the combination of these elements can be useful to fight the virus (Hui *et al*.).

Accordingly, the high sensitivity of SARS-CoV-2 lipophilic membranes seems to be a key to its destruction (Scheller *et al*.). To reach the airways in its entirety, emphasis should be placed on the formulation of a substance with specific characteristics that can allow it to reach that area (Rogliani *et al*). Ideally, the product should be applied both via oral and nasal inhalation, however, the inhalation pattern is not a relevant factor in the administration of the substance (Rogliani *et al*.). Besides, the particle size should be less than 2 mm in diameter as it is deposited in the lower airways by log sedimentation. Moreover, it is necessary to increase the pulmonary deposition of the spray, so that it can penetrate the distal airways, and achieve more peripheral pulmonary deposition (Rau). It should also possess good substantive properties that allow it to get absorbed into the tissues corresponding to the airway and to remain in it, exercising its action for a useful period.

Antimicrobials such as halogens, aldehydes, quaternary ammonium compounds, phenolics, alcohols, peroxides, proteases, and detergents (Scheller *et al*.) could be used. However, the material should be bio-tolerated to reduce the possibility of generating side effects during its administration. With regard to this, the drug hexamethylene amiloride was reported to act efficiently inactivating SARS-CoV-2 protein E (Hui *et al*.). Also, the use of non-toxic derivatives of Saponins from Quillaja Saponaria and Quillaja brasiliensis could be proposed speculatively as a useful element in the development of a spray due to their ability to produce saponins that theoretically would disable the virus (Fleck *et al*., 2020).

Taking into consideration the concepts analyzed above, we think it is necessary to further investigate preventive measures such as those proposed in this publication. We have no certainty about how successful these measures could be, but we consider it logical to propose them. In the next stages, while a vaccine is being developed, it is necessary to take measures to adapt in the best possible way to the changes that this pandemic requires. Further investigation and resolution of the following issues are required:

1. Determine the usefulness and effectiveness of spray/inhalers for the administration of a substance that reaches all the desired anatomical areas .

2. Determine the existence of a substance that can inactivate the virus effectively, that is bio-tolerated and with sufficient substantivity to be adsorbed in the anatomical sites described.

3. Once the answers to the above problems have been determined, it is advisable to carry out multi-center evaluations, which would determine the effectiveness of the proposed measures.

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RESUMEN: La pandemia de COVID-19 propone desafíos que han sido manejados con medidas como distanciamiento social prologado o intermitente, el cual podría ser necesario hasta 2022. Se ha descrito que la ruta de contagio de SARS-CoV-2 corresponde a la inhalación del virus. La medicación a través de un spray nasal/ocular podría cumplir la función de inactivar SARS-CoV-2. Por las razones antes presentadas, los autores sugerimos la siguiente hipótesis: El uso de un spray ocultar/nasal/oral previene la infección y replicación de SARS-CoV-2.

PALABRAS CLAVE: COVID-19, SARS-CoV-2, sprays, infección.

REFERENCES

Amesty, M. A.; Alió del Barrio, J. L. & Alió, J. L. COVID-19 disease and ophthalmology: an update. *Ophthalmol. Ther., 9(3)*:1-12, 2020.

Cheng, S.; Kourmatzis, A.; Mekonnen, T.; Gholizadeh, H.; Raco, J.; Chen, L.; Tang, P. & Chan, H. K. Does upper airway deformation affect drug deposition? *Int. J. Pharm., 572*:118773, 2019.

Coroneo, M. T. The eye as the discrete but defensible portal of coronavirus infection. *Ocul. Surf.*, 2020. DOI: https://www.doi.org/10.1016/j.jtos.2020.05.011

Fleck, J. D.; Betti, A. H.; da Silva, F. P.; Troian, E. A.; Olivaro, C.; Ferreira, F. & Verza, S. G. Saponins from Quillaja saponaria and Quillaja brasiliensis: particular chemical characteristics and biological activities. *Molecules, 24(1)*:171, 2019.

Hui, K. P. Y.; Cheung, M. C.; Perera, R. A. P. M.; Ng, K. C.; Bui, C. H. T.; Ho, J. C. W.; Ng, M. M. T.; Kuok, D. I. T.; Shih, K. C.; Tsao, S. W.; et al. Tropism, replication competence, and innate immune responses of the coronavirus SARS-CoV-2 in human respiratory tract and conjunctiva: an analysis in ex-vivo and *in-vitro* cultures. *Lancet Respir. Med., 8(7)*:687-95, 2020.

Kissler, S. M.; Tedijanto, C.; Goldstein, E.; Grad, Y. H. & Lipsitch, M. Projecting the transmission dynamics of SARS-CoV-2 through the postpandemic period. *Science, 368(6493)*:860-8, 2020.

Lauer, S. A.; Grantz, K. H.; Bi, Q.; Jones, F. K.; Zheng, Q.; Meredith, H. R.; Azman, A. S.; Reich, N. G. & Lessler, J. The incubation period of Coronavirus Disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. *Ann. Intern. Med., 172(9)*:577-82, 2020.

Pervushin, K.; Tan, E.; Parthasarathy, K.; Lin, X.; Jiang, F. L.; Yu, D.; Vararattanavech, A.; Soong, T. W.; Liu, D. X. & Torres, J. Structure and inhibition of the SARS coronavirus envelope protein ion channel. *PLoS Pathog., 5(7)*:e1000511, 2009.

Rau, J. L. The inhalation of drugs: advantages and problems. *Respir. Care, 50(3)*:367-82, 2005.

Rogliani, P.; Calzetta, L.; Coppola, A.; Cavalli, F.; Ora, J.; Puxeddu, E.; Matera, M. G. & Cazzola, M. Optimizing drug delivery in COPD: The role of inhaler devices. *Respir. Med., 124*:6-14, 2017.

Scheller, C.; Krebs, F.; Minkner, R.; Astner, I.; Gil-Moles, M. & Wätzig, H. Physicochemical properties of SARS-CoV-2 for drug targeting, virus inactivation and attenuation, vaccine formulation and quality control. *Electrophoresis, 41(13-14)*:1137-51, 2020.

Seah, I. & Agrawal, R. Can the Coronavirus Disease 2019 (COVID-19) affect the eyes? A review of coronaviruses and ocular implications in humans and animals. *Ocul. Immunol. Inflamm., 2020*:1-5, 2020. DOI: https://www.doi.org/10.1080/09273948.2020.1738501

Wu, P.; Duan, F.; Luo, C.; Liu, Q.; Qu, X.; Liang, L. & Wu, K. Characteristics of ocular findings of patients with Coronavirus Disease 2019 (COVID-19) in Hubei Province, China. *JAMA Ophthalmol., 138(5)*:575-8, 2020.

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Received: 27-06-2020
Accepted: 04-07-2020