Povidone Iodine Mouthwash, Gargle, and Nasal Spray to Reduce Nasopharyngeal Viral Load in Patients With COVID-19: A Randomized Clinical Trial

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is primarily transmitted person-to-person through the aerosolization of droplets containing contaminated nasopharyngeal secretions.[1] Povidone iodine (PI) solutions at concentrations as low as 0.5% rapidly inactivate SARS-CoV-2 in vitro with contact times as short as 15 seconds.[2] We investigated whether nasopharyngeal application of PI could reduce the viral load of patients with nonsevere coronavirus disease 2019 (COVID-19) symptoms.

Supplemental content

Methods | We included adult outpatients (≥18 years old) having tested highly positive (cycle threshold ≤20) for SARS-CoV-2 ribonucleic acid (RNA) by reverse transcription-polymerase chain reaction (RT-PCR) in nasopharyngeal swabs within the previous 48 hours. Patients with a history of thyroid disease were excluded. The study was approved by the South Mediterranean Institutional Review Board, and written informed consent was obtained from all participants. The trial protocol is included in Supplement 1.

Patients underwent an additional nasopharyngeal swab for viral quantification at baseline before being randomly assigned (1:1) to a control group (no intervention, n = 12) or an intervention group (n = 12). Intervention consisted of 4 successive mouthwashes and gargles with 25 mL of 1% aqueous PI solution each (Mylan, Merignac, France), followed by one 2.5-mL nasal pulverization of the same solution into each nostril using an intranasal mucosal atomization device (MAD Nasal, Teleflex, Morrisville, North Carolina) connected to a 5-mL syringe while sniffing and 1 application on each nasal mucosa of a dab of 10% PI ointment followed by a massage of the

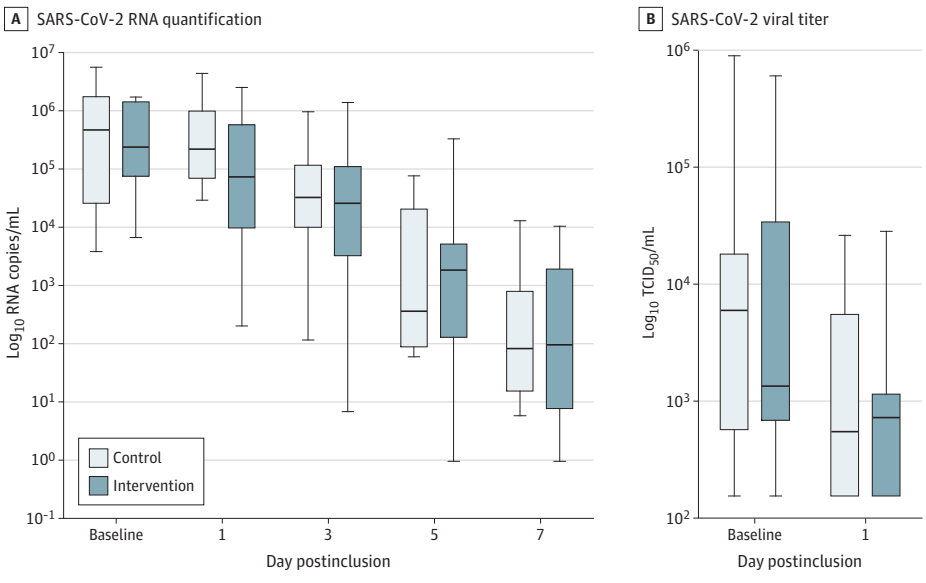
Table. Patient Demographics and Baseline Clinical Characteristics

Characteristic	Intervention group (n = 12)	Control group (n = 12)
Age, median (IQR), y	33 (23-46)	57 (45-68)
Male, No. (%)	4 (33)	4 (33)
BMI,[a] median (IQR)	22.5 (20.3-24.3)	24.7 (19.9-27.4)
Body temperature, median (IQR), °C	37.3 (36.5-37.5)	36.9 (36.2-37.6)
Respiratory rate, median (IQR), cycles/min	16 (14-16)	16 (14-20)
Pulse oxygen rate, median (IQR), %	98 (97-99)	98 (97-99)
Medical history, No. (%)		
Diabetes	1 (8)	0
Dyslipidemia	0	4 (33)
Chronic obstructive pulmonary disease	0	0
Hypertension	0	3 (25)
Smoker, No. (%)	2 (17)	0
Clinical signs, No. (%)		
Dyspnea	2 (17)	1 (8)
Chest pain	2 (17)	0
Anosmia	4 (33)	5 (42)
Ageusia	2 (17)	5 (42)
Tiredness	10 (83)	10 (83)
Cough	4 (33)	6 (50)
Body aches	4 (33)	6 (50)
Diarrhea	0	2 (17)
Nasal congestion	7 (58)	7 (58)
Dysphagia	2 (17)	1 (8)

Abbreviation: IQR, interquartile range.

[a] BMI indicates body mass index, calculated as weight in kilograms divided by height in meters squared

Figure. Box Plots Indicating Median, Interquartile Range, and 5th and 95th Percentiles, by Treatment Group



RNA indicates ribonucleic acid; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; $TCID_{50}$, tissue culture infectious dose.

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nostril to help spread the ointment. Patients were trained during the first decolonization session, and received the necessary materials and a guide to help them perform the following sessions 4 times a day for 5 days.

Follow-up was done on day 1 and then every 2 days until day 7 to assess the efficacy (viral quantification) and safety of the decolonization. Almost all (>95%) of the nasopharyngeal swabs were taken by the same skilled nurse at least 3 hours after the last PI application for quantification of viral RNA using RT-PCR,[3] and viral titer using the dilution limit method on Vero cells and the Spearman-Karber approach with a limit of detection of $10^{2.5}$ tissue culture infectious dose ($TCID_{50}$) per mL.[4] Changes in viral load over time were compared between study groups using a linear mixed model for repeated measures.

Results | All patients completed the study, and none required hospital admission. Compared with the control group, patients in the intervention group were younger (**Table**). Median (IQR) age of patients in the control group was 57 (45-68) years and in the intervention group was 33 (23-46) years. A total of 4 patients (33%) in each group were male. All patients but 1 had negative viral titer by day 3. Use of PI had no influence on changes of viral RNA quantification over time (**Figure**). Mean relative difference in viral titers between baseline and day 1 was 75% (95% CI, 43%-95%) in the intervention group and 32% (95% CI, 10%-65%) in the control group (Figure). All patients exposed to PI experienced unpleasant nasal tingling but completed the study. Thyroid stimulating hormone elevation (median [IQR], 3.4 [2.6-4.3] mIU/L vs 2.1 [1.4-3.1] mIU/L at baseline) was observed in all patients after 5 days of PI exposure, exceeding the upper normal value in 5 patients, with a return to baseline values 7 to 12 days later. No modification in thyroid hormone (T3, T4) or creatinine levels was observed.

Discussion | Nasopharyngeal decolonization may reduce the carriage of infectious SARS-CoV-2 in adults with mild to moderate COVID-19.[5] Thyroid dysfunction occurred in 42% of the patients exposed to PI, with spontaneous resolution upon treatment discontinuation, as previously reported.[6] Strengths of this study include assessment of viral titer to determine whether the virus was viable and thus potentially transmissible. Limitations include the small number of patients and the single-center design. These data call for a larger clinical trial to confirm the benefit of PI in limiting the excretion and resulting human-to-human transmission of SARS-CoV-2, using lower PI concentrations to minimize adverse effects.

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OBSERVATION

Adolescent Presentation of Nasal Chondromesenchymal Hamartoma: A Case Report and Literature Review

Nasal chondromesenchymal hamartoma (NCMH) is a very rare benign tumor of the nasal cavity and paranasal sinuses that usually presents in infancy. These tumors may be expansile and locally destructive. The etiology has remained unclear, but it has been linked in the past to pleuropulmonary blastoma as

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