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KEY WORDS:

TOLERABILITY OF HALODINE® ORAL AND NASAL ANTISEPTICS AS PART OF A SARS-COV-2 TRANSMISSION REDUCTION STRATEGY

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ABSTRACT

Background: Halodine® oral and nasal antiseptics (Halodine LLC, Miami, FL USA) have been employed for routine oral and nasal decontamination as part of SARS-CoV-2 transmission reduction protocols. These preparations designed for the mouth and nose have been developed as oral sprays (1.25% povidone-iodine solution), oral rinses (1.75% povidone-iodine solution), nasal swabsticks (2.5% povidone-iodine solution), and nasal irrigation solutions (1.25% povidone-iodine solution). ***Methods:*** In a cross-sectional survey study, individuals who used any of the Halodine nasal or oral antiseptic products as part of a SARS-CoV-2 transmission reduction protocol were consented and invited to voluntarily complete a written questionnaire based on their practice and usage. Questions were derived from the Sino-Nasal Outcome Test (SNOT-22) to capture overall comfort and nasal symptomology. ***Results:*** There were 133 individuals ages 2-86 years who used Halodine in the forms of oral sprays, oral rinse, nasal swab-sticks, and nasal irrigation solutions for oral and nasal decontamination and volunteered to complete a satisfaction survey to assess tolerability. Decontamination was well tolerated; 99.2% of respondents reported no pain and 88.0% reported no nasal symptoms. Loss of taste, loss of smell, dizziness or blocked sinuses were not reported in any individuals. Three percent of respondents reported clearing of their sinuses. Halodine oral and/or nasal antiseptics were used two or more times per day in 94.7% of respondents. ***Discussion:*** Halodine for oral and nasal decontamination appears to be well tolerated for repeated daily use, even in individuals reporting 4 months or more of use. No individuals reported severe symptoms such as loss of taste, loss of smell, or dizziness. No pain was reported in 99.2% of individuals, while the remaining <1% reported very mild/minimal discomfort. ***Conclusion:*** These findings point to high tolerability of Halodine for repeated oral and nasal decontamination.

INTRODUCTION

Halodine® oral and nasal antiseptics (Halodine LLC, Miami, FL USA) are over-the-counter (OTC) drug products specifically designed at low pH and low-concentration povidone-iodine (PVP-I) to be chemically stable[1], effective[2], safe[3], non-toxic[4,5], and non-irritating for repeated intraoral and intranasal use. Oral and nasal PVP-I antisepsis has been a part of infection control practices for decades. In Asia, oral rinses of PVP-I have been utilized to prevent/treat community acquired respiratory infections and hospital acquired pneumonia (HAP) presenting in both inpatients and healthcare workers[6,7,8,9,10,11,12,13]. They are also commonly employed to maintain oral care and treat recalcitrant dental caries in both adults and children[14,15,16]. Intranasal application of PVP-I antiseptics reduces surgical site infections and is used in the treatment of chronic inflammation/infection of the nose and sinuses[17,18,19].

The COVID-19 pandemic has led to a dramatic loss of human life worldwide and has presented an unprecedented challenge to public health. The initial dominant site of the causative SARS-CoV-2 infection is the nose and mouth with high ACE2 receptor and transmembrane serine protease 2 (TMSRSP2) expression on upper respiratory tissues and the nasal surfaces[20,21]. The highest viral loads SARS-CoV-2 in COVID-19 patients have been demonstrated in the oral cavities, oropharynx, nasal cavities, and nasopharynx,[22,23]. There is an increased interest for Halodine oral and nasal antisepsis because of demonstrated effectiveness against SARS-CoV-2 with complete inactivation within 15 seconds[24,25,26,27]. The use of Halodine oral or nasal antiseptic products help curb viral transmission[28,29,30,31,32,33,34,35,36,37,38] while definitive treatment and immunity for the global population are months away.

This survey was designed to capture the experience of those using Halodine oral or nasal antiseptic products as part of a SARS-CoV-2 transmission reduction strategy.

MATERIALS AND METHODS

The study was conducted in accordance with the ethical standards of the institutional review board and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This was a cross-sectional survey designed to collect data to make inferences about a population of interest at one point in time. Individuals who have used any of the Halodine oral or nasal antiseptic products as part of the SARS-CoV-2 transmission reduction strategy were verbally consented and invited to voluntarily complete a written questionnaire based on their practice and usage (Figure 1). In addition to demographic and product information, individuals were asked to provide input as to their experience including overall comfort (1-10 scale). Seven yes/no questions captured specific oral and nasal symptoms. These questions were derived from the Sino-Nasal Outcome Test (SNOT-22), a validated Quality of Life (QoL) instrument employed in chronic rhinosinusitis investigations and management.

A SARS-CoV-2 transmission reduction strategy for staff and patients that includes Halodine oral or nasal antiseptic products has been implemented at outpatient healthcare facilities. Four different commercial preparations of Halodine for oral and nasal decontamination are available as oral sprays (1.25% PVP-I solution), oral rinses (1.75% PVP-I solution), nasal swabsticks (2.5% PVP-I solution), and nasal irrigation solutions (1.25% PVP-I solution). Inactive ingredients in these formulations include hydroxyethylcellulose and purified water.

RESULTS

One hundred thirty-three (n=133) individuals completed the written survey; average age was 38 years. Thirty-three were younger than 18 year including 19 that were age 10 or younger. Female respondents comprised 58.6% (n=78). Demographics are summarized in Table 1.

The nasal antiseptic swabstick (PVP-I solution 2.5%) was the most frequently used Halodine product (n=72) followed by nasal antiseptic (PVP-I solution 1.25%) (n=70), oral antiseptic spray (PVP-I solution 1.25%) (n=38), and oral rinse (PVP-I solution 1.75%) (n=22). More than one Halodine product was used by 40.6% of respondents. The majority of respondents used Halodine two times per day (n=75, 56.4%) or three times per day (n=44, 33.0%). All individuals responded that the product was easy to use. There were three (n=3) who indicated that the instructions for use were not clearly written; these individuals were primarily Spanish speaking.

Halodine was very well tolerated with 99.2% of individuals reporting no pain with administration; 88% reported no symptoms. No individuals reported loss of smell, loss of taste, blocked sinuses, or dizziness with Halodine. The sensation of needing to blow the nose was experienced most frequently in 14 (10.5%) individuals. Clearing of the sinuses and sneezing were each reported by four individuals; two reported experiencing coughing. The results of the collected surveys are summarized in Table 2.

DISCUSSION

The active ingredient in Halodine, PVP-I, is a well-known, well-characterized pharmaceutical agent employed in almost every branch of human and veterinary medicine for its anti-microbial properties with no known resistance. It is listed as a World Health Organization "essential medicine" for antisepsis. Because of this extensive history, products containing PVP-I as an active ingredient are Generally Regarded as Safe and Effective (GRAS/E) for OTC use as topical antimicrobials. The findings in this satisfaction survey do not contradict such assessments.

With >99% of respondents reporting no pain, the findings with this survey suggest a greater tolerability with Halodine compared to other PVP-I products available on the market[39,40]. This is not unsurprising as Halodine was designed to have less toxicity and better tolerability with lower PVP-I concentrations. When examined in-vitro, the safety of nasal PVP-I is highly concentration dependent, with a clear threshold in toxicity that occurs at 2.5%. This is similar to the toxicity threshold seen in other mucous secreting tissues of the respiratory tract and the conjunctiva[41,42]. PVP-I solution less than 1.25% applied to air liquid interface cultures of human nasal epithelial cells from chronic rhinosinusitis patients did not cause pathological effects on paracellular permeability or cilia beat frequency.

An overall lack of symptoms was also reported through the use of a validated QoL instrument commonly used in rhinology, with modifications to only include the questions most relevant to low-concentration PVP-I oral and nasal antiseptic use in a healthy population to prevent infection. No other assessment of sinonasal PVP-I has employed such a comprehensive assessment of symptomatology. Loss of smell, loss of taste, or dizziness were not reported by any individuals, suggesting low systemic absorption and minimal risk of neurologic involvement. Lack of these particularly severe symptoms points to broad tolerability of repeated use of Halodine oral and nasal decontamination for preventative use.

Weaknesses of the study include limited number of respondents, self-selection bias, and limited duration of use in some cases. While not a small number of subjects responded (n=133), an even more robust sample size is always appreciated. Self-selection bias can occur due to subjects volunteering to fill out the survey versus requiring all participants to submit a survey response. Finally, duration of use is limited with approximately 20% of subjects using Halodine for 1 month or less compared to 24% of subjects using Halodine for 4 months of more.

The tolerability of Halodine oral and nasal antiseptics is underscored by the wide age range and consistent tolerability findings even in children and the elderly. While further quantitative and objective toxicity assessments are possible, observations of >94% of individuals using Halodine multiple times per day show that these oral and nasal decontamination products are well tolerated by the general consumer.

CONCLUSION

During the unprecedented COVID-19 pandemic, many layers of infection control were introduced as a means to mitigate the spread of the SARS-CoV-2 virus. Measures such as masks, hand washing, and social distancing have shown to be helpful but not enough to completely halt the spread of the virus. New mutations within the viral genome have even resulted in the discovery of highly infectious strains in the UK[43] and South Africa[44]. Halodine has been shown to rapidly inactivate the SARS-CoV2 virus and its active ingredient has a long, proven history of being able to kill 99.9% of pathogenic bacteria and viruses without leading to resistance. The CDC currently recommends "to continue using all the tools available to us to help stop this pandemic" even after receiving the COVID-19 vaccine. In addition to wearing a mask to cover the nose and mouth, washing hands, and social distancing, well-tolerated Halodine oral and nasal antiseptic products are available to further mitigate the COVID-19 pandemic and provide another tool in the infection control armamentarium.

Figure 1. User Satisfaction Questionnaire

Satisfaction Questionnaire					
1. Initials					
2. Age					
3. Gender	☐ F		☐ M		☐ Other
4. Were instructions for use clearly written?	☐ Yes		☐ No		
5. Was the product easy to use?	☐ Yes		☐ No		
6. How long have you used your Halodine product(s)?	0-1 months ☐	1-2 months ☐	2-3 months ☐	3-4 months ☐	>4 months ☐
7. Which Halodine product(s) are you using?	Swab ☐	Nasal Antiseptic ☐	Oral Spray ☐	Oral Rinse ☐	More than 1 product ☐
8. How many times a day do you use your Halodine product(s)?	1 ☐	2 ☐	3 ☐	4 ☐	>4 ☐
9. On a scale of 1 to 10, 1 being no discomfort and 10 being the worst pain you have ever had, how much discomfort do you experience while using your Halodine product(s)?	1 No Pain ☐	2 ☐	3 ☐	4 ☐	5 ☐
	6 ☐	7 ☐	8 ☐	9 ☐	10 Worst Pain ☐

Immediately after using Halodine products have you experienced any of the following?		
10. Need to blow your nose	☐ No	☐ Yes
11. Sneezing	☐ No	☐ Yes
12. Coughing	☐ No	☐ Yes
13. Loss of smell	☐ No	☐ Yes
14. Loss of taste	☐ No	☐ Yes
15. Blocked sinuses	☐ No	☐ Yes
16. Clearing of your sinuses	☐ No	☐ Yes
17. Dizziness	☐ No	☐ Yes

Table 1. Demographics

Demographics	
Respondents (n)	133
Average Age (years)	33 (Range: 2-86)
Gender (n)	Female: 78 (58.6%) Male: 55 (41.4%)

Table 2. Nasal Symptomatology

Usage	
Halodine Product (n)	Nasal Antiseptic Swabstick: 72 Nasal Antiseptic: 60 Oral Antiseptic Spray: 38 Oral Rinse: 22 More than one product: 54 (40.6%)
Duration (n)	0-1 month: 27 (20.3%) 1-2 months: 36 (27.1%) 2-3 months: 34 (25.6%) 3-4 months: 4 (3.0%) >4 months: 32 (24.1%)
Frequency (n)	1 time per day: 7 (5.3%) 2 times per day: 75 (56.4%) 3 times per day: 44 (33.0%) 4 times per day: 7 (5.3%) >4 times per day: 0 (0.0%)
Instructions for use clearly written? (n)	Yes: 130 (97.7%) No: 3 (2.3%)
Product easy to use? (n)	Yes: 133 (100%) No: 0 (0%)
Tolerability	
Average Pain (Scale 1 to 10; 1 is no discomfort, 10 is worst pain ever experienced)	1.01
Symptoms	
Need to blow nose	No: 119 (89.5%) Yes: 14 (10.5%)
Sneezing	No: 129 (97.0%) Yes: 4 (3.0%)
Cough	No: 131 (98.5%) Yes: 2 (1.5%)
Loss of Smell	No: 133 (100%) Yes: 0 (0%)
Loss of Taste	No: 133 (100%) Yes: 0 (0%)
Blocked Sinuses	No: 133 (100%) Yes: 0 (0%)
Clearing of Sinuses	No: 129 (97.0%) Yes: 4 (3.0%)
Dizziness	No: 133 (100%) Yes: 0 (0%)

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