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Role of Famotidine and Other Acid Reflux Medications for SARS-CoV-2: A Pilot Study

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Summary: Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the coronavirus-19 disease (COVID-19) pandemic. The H-2 blocker famotidine has been suggested as an FDA-approved drug that could potentially be repurposed for treatment of COVID-19. Famotidine has since been shown to improve patient outcomes and reduce symptom severity in patients acutely ill with COVID-19. Other studies have suggested that proton pump inhibitors (PPIs) might have an association with COVID-19.

Objective. The purpose of the present study was to determine whether famotidine or any other antireflux medications have a prophylactic or detrimental effect for SARS-CoV-2 infection when taken regularly for the management of acid reflux.

Methods. An anonymous, web-based survey was distributed via email to adult otolaryngology patients to collect demographic data, past medical history, medication history, incidence of symptoms associated with COVID-19, potential exposure to SARS-CoV-2, and results of any PCR or serological testing. Associations between reflux medications and incidence of COVID-19 cases were analyzed. Statistical analysis was performed using SPSS. Chi-square with Fisher’s exact test, Point-Biserial correlation, Kendall’s-tau-b, independent samples t test, and the Mann-Whitney U test were used as appropriate. A binary logistic regression model was fit to determine probability of COVID-19 cases after adjustment for other risk factors.

Results. There were 307 patients who responded to the survey. The average age of respondents was 52.63 ± 17.03. Famotidine use was not associated with incidence of laboratory-confirmed (P = 0.717) or symptomatically suspected (P = 0.876) COVID-19. No other reflux medications were found to be significant predictors for laboratory-confirmed or suspected COVID-19 (P > 0.05). Younger age (odds ratio [OR] = 1.043, 95% CI: 1.020–1.065, P < 0.001), high risk obesity (OR = 4.005, 95% CI: 1.449–11.069, P = 0.007), and use of a corticosteroid nasal spray (OR = 3.529, 95% CI: 1.352–9.211, P = 0.010) were significant predictors for symptomatically suspected COVID-19 cases.

Conclusions. There was no association between incidence of COVID-19 and use of reflux medications, including famotidine at doses used orally to manage reflux and high dose PPIs. Reflux medications did not protect against or increase the risk of COVID-19.

Key Words: COVID-19—SARS-CoV-2—Famotidine—Proton pump inhibitor—Intranasal corticosteroid—Age—Obesity

INTRODUCTION

Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the coronavirus-19 disease (COVID-19) pandemic, which has affected over 37 million people worldwide since January 2020.1 A potential preventative or therapeutic role for acid reflux medications such as famotidine (an H-2 blocker) and proton pump inhibitors (PPIs) for SARS-CoV-2 has been proposed.2–4 However, others have also suggested that PPIs are associated with an increased risk for severe illness from SARS-CoV-2.5,6 No group thus far has investigated whether there may be a prophylactic role for famotidine therapy. In this observational study, we tried to address these issues by distributing a survey to over 3000 patients at our center, where we treat a high volume of patients with acid reflux disease (laryngopharyngeal reflux and/or gastroesophageal reflux disease). The primary objective of this study was to determine whether famotidine, or any other antireflux medications, have a prophylactic or detrimental effect for SARS-CoV-2 infection when taken regularly for the management of acid reflux.

METHODS

This observational study was approved by the Drexel University College of Medicine Institutional Review Board. An anonymous web-based survey was distributed via email between September 2020 and October 2020. All adult otolaryngology patients seen in the practice from June 2016 to September 2020 were invited to take the survey. The survey was created and distributed using the Research Electronic Data Capture Tool7,8 hosted through Drexel University. The survey was designed to collect demographic data, past medical history, medication history including use of reflux medication, incidence of symptoms associated with COVID-19 since the start of the SARS-CoV-2 pandemic, potential exposure to SARS-CoV-2, and results of PCR or serological testing. Anonymous informed consent was obtained from

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respondents prior to their beginning the survey. Any participant who reported at least one positive COVID-19 test (either antibody or RNA testing) was considered a laboratory-confirmed COVID-19 case. A group of symptomatically suspected COVID-19 cases was created from respondents who reported three or more non-specific symptoms, because it was recently shown that self-report of three or more symptoms was a significant predictor for subsequent positive SARS-CoV-2 RNA detection. Nasal symptoms (congestion/rhinorrhea) have been shown to be a significant negative predictor for COVID-19 and therefore were not counted among the suspect symptoms. Respondents who reported chronic symptoms, or symptoms that they attributed to another illness, were excluded from this group of symptomatically suspected COVID-19 cases. High risk obesity was considered a BMI greater than 35.

Statistical analysis was performed using SPSS (Armonk NY). Means were reported as the mean ± standard deviation (SD). The appropriate statistical test was selected based on type of data and number of observations in each comparison. Significance for counts and categorical data were determined using chi-square with Fisher’s exact test. Point-Biserial correlation was used to evaluate the correlation between age and symptomatically suspected COVID-19. Differences between means of continuous variables were assessed by independent-samples t test or nonparametric Mann-Whitney U test, as appropriate for the degree of variance. Correlations between rated symptom severity (1–5), symptom duration, H-2 blocker dosage, and H-2 blocker use duration were evaluated by Kendall’s-tau-b. All statistical tests were two-sided. A binary logistic regression model was fit to determine probability of COVID-19 cases after adjustment for age, gender, SARS-CoV-2 exposure, reflux medication usage, steroid medications, and comorbid chronic disease. Covariates with an expected cell count <5 were excluded from the regression model. Regression results were provided as odds ratio (OR) and corresponding 95% confidence interval (95% CI). The Hosmer-Lemeshow test for goodness of fit was used to assess fit of the regression model. A P value <0.05 was considered statistically significant for all statistical tests.

RESULTS
The survey was delivered to 3347 patients, and 307 responded (response rate = 9.23%). The average age of respondents was 52.63 ± 17.03 (range = 19–92). Of all, 36.07% were male and 63.93% were female. Of all, 51.14% had a chronic health condition which might increase susceptibility to COVID-19, 2.61% were taking methotrexate, 1.95% were taking an immunosuppressive biologic (etanercept, adalimumab, or secukinumab), and 0.65% were receiving chemotherapy. There were 171 respondents (55.70%) who reported a history of acid reflux disease (laryngopharyngeal reflux [LPR] and/or gastroesophageal reflux disease [GERD]). Of those with reflux, 146 (85.38%) had been using reflux medications within the last 6 months, including famotidine (46.78%) and PPIs (73.68%; omeprazole, pantoprazole, esomeprazole, lansoprazole, dexlansoprazole, and rabeprazole; Table 1).

Of the 307 respondents, 20.52% reported potential exposure to SARS-CoV-2, including having had someone with whom they live test positive for COVID-19 (4.23%), having had contact with someone who tested positive (12.70%), or international travel (8.79%). Of all, 133 (43.32%) had been tested for SARS-CoV-2, either by PCR (RNA detection) or by serology (antibody detection). Of those tested, 6.02% were positive for SARS-CoV-2. There were 67 respondents (21.82%) who were symptomatically suspect for COVID-19 based on reporting of ≥3 symptoms consistent with COVID-19 within the last 6 months. Suspect symptoms included fever or chills, cough, dyspnea, fatigue, myalgia, headache, anosmia, sore throat, nausea or vomiting, and diarrhea. Symptomatically suspected COVID-19 cases were associated significantly with a positive COVID-19 test (P < 0.003), contact with someone who tested positive (P = 0.003) and having someone with whom they live test positive (P < 0.001). A significant negative correlation was found between age and symptomatically suspected COVID-19 (r_sp = −0.226, n = 269, P < 0.001). The average age of respondents with suspected COVID-19 was 45.75 ± 15.89, versus 54.78 ± 16.84 for all other respondents (P < 0.001). When stratified by age group (ages 19–30, 31–45, 46–60 and 61+), respondents aged 19–30 had the highest percent incidence of symptomatically suspected COVID-19 (incidence = 41.18%, P = 0.002). Incidence among respondents aged ≥61 (incidence = 13.08%) was significantly lower than all younger age groups (P < 0.05).

There were 163 respondents with chronic disease, including asthma, chronic obstructive pulmonary disease, high risk obesity (BMI >35), chronic kidney disease, diabetes mellitus, heart and coronary artery disease, cancer, immunodeficiency, or an autoimmune disease. Autoimmune diseases included rheumatoid arthritis, Crohn’s disease, autoimmune inner ear disease, multiple sclerosis, and ankylosing spondylitis. There were 144 respondents who did not have any chronic condition. Respondents reporting any chronic disease were an average of 8.29 years older than those who did not, which was significantly different (P < 0.001). However, chronic disease was not associated with laboratory-confirmed (P = 1.000) or symptomatically suspected (P = 0.891) COVID-19 (Table 2). Each chronic condition reported was then tested for association with COVID-19 (see Table 3). High risk obesity (BMI >35) was associated significantly with symptomatically suspected COVID-19 (P = 0.004) but not laboratory-confirmed COVID-19 (P = 0.059). High risk obesity was not associated significantly with reflux disease in this study (P = 0.560). No other conditions were associated significantly with an increased likelihood of laboratory-confirmed or suspected COVID-19 (P > 0.05).

There were 12 respondents taking methotrexate or a biologic immunosuppressive medication, and age did not differ significantly between these two groups (P = 0.921). Neither incidence of laboratory-confirmed (P = 0.320) nor
**TABLE 1.**
Respondent Demographics, Past Medical History, and Medication History

| Male/Female (%) | Total Respondents = 307 |
|-----------------|-------------------------|
| Age (Mean ± SD) | 52.63 ± 17.03           |
| History of chronic disease (%) | Immunosuppressive Medication (%) |
| Asthma          | 17.92                   | Oral corticosteroid | 0.98 |
| COPD            | 2.61                    | Methotrexate       | 2.61 |
| Hypertension    | 21.82                   | Cyclophosphamide  | 0.00 |
| High risk obesity (BMI >35) | 9.45                   | Chemotherapy       | 0.65 |
| Chronic kidney disease | 1.95                   | Radiation         | 0.33 |
| Diabetes mellitus | 7.49                  | Nasal Steroid    | 12.05 |
| Heart disease   | 7.17                    | Inhaled Steroid   | 7.17 |
| Cancer          | 5.54                    | Immunosuppressive Biologic † | 1.95 |
| Immunodeficiency| 9.45                    |                   |     |
| Autoimmune disease* |                   |                   |   2.93 |

**TABLE 2.**
Percent Incidence of Laboratory-Confirmed and Symptomatically Suspected COVID-19, Stratified by Risk Groups

| No Reflux No Medications | reflux + no famotidine | reflux + PPI | reflux + Famotidine + PPI | Sig. (Pvalue)* |
|--------------------------|------------------------|--------------|---------------------------|---------------|
| Age (mean ± SD)          | 51.63 ± 17.59          | 48.29 ± 14.26| 55.44 ± 17.25             | 53.80 ± 18.66 | 53.96 ± 16.79 | 0.635 |
| Confirmed COVID-19 (%)   | 2.22                   | 20.00        | 14.29                     | 3.85          | 4.17          | 0.227 |
| Suspected COVID-19 (%)   | 17.80                  | 40.00        | 26.67                     | 20.37         | 26.32         | 0.159 |

| No Chronic Disease       | Any Chronic Disease   | Sig. (Pvalue)* |
|--------------------------|-----------------------|---------------|
| Age (mean ± SD)          | 48.44 ± 17.79         | 56.73 ± 15.23 | <0.001 |
| Confirmed COVID-19 (%)   | 6.45                  | 5.80          | 1.000 |
| Suspected COVID-19 (%)   | 22.22                 | 21.47         | 0.891 |

| No Immunosuppressive Medications | Immunosuppressive Medications (Methotrexate or Biologic) | Sig. (Pvalue)* |
|----------------------------------|--------------------------------------------------------|---------------|
| Age (mean ± SD)                  | 52.62±17.22                                             | 52.82±12.38   | 0.921 |
| Confirmed COVID-19 (%)           | 5.60                                                   | 16.67         | 0.320 |
| Suspected COVID-19 (%)           | 22.03                                                  | 16.67         | 1.000 |

| No Steroids | Nasal Steroid | Inhaled Steroid | Nasal + Inhaled Steroid | Sig. (Pvalue)* |
|-------------|---------------|-----------------|-------------------------|---------------|
| Age (mean ± SD) | 51.78 ± 17.18 | 58.34 ± 15.48  | 52.62 ± 17.27           | 52.75 ± 16.91 | 0.277 |
| Confirmed COVID-19 (%) | 6.00           | 7.69            | 0.00                     | 25.00         | 0.264 |
| Suspected COVID-19 (%) | 19.67          | 40.00           | 25.00                    | 44.44         | 0.074 |

* Significance determined by Fisher’s exact test.

† Biologics included etanercept, adalimumab, and secukinumab
symptomatically suspected \((P = 1.000)\) COVID-19 differed significantly between respondents taking immunosuppressive medications and those who were not (Table 2). No immunosuppressive medications were associated independently with an increased likelihood of laboratory-confirmed or suspected COVID-19 \((P > 0.05,\) Table 3). Incidence of laboratory-confirmed and suspected COVID-19 was then compared between respondents based on topical corticosteroid use: 254 respondents used no corticosteroids, 28 used a nasal steroid only, 13 used an inhaled steroid only, and 9 used both an inhaled and a nasal steroid. Neither incidence of laboratory-confirmed \((P = 0.264)\) nor suspected COVID-19 \((P = 0.074)\) differed significantly between groups. Age also did not differ significantly \((P = 0.277)\) between groups (Table 2). When analyzed independently, nasal steroid use was associated significantly with symptomatically suspected COVID-19 \((P = 0.018)\), but use of an inhaled steroid was not \((P = 0.282)\). Neither nasal \((P = 0.327)\) nor inhaled steroid use \((P = 0.480)\) was associated with an increased likelihood of laboratory-confirmed COVID-19 (Table 3).

Respondents were divided into two groups, depending on reflux medication use. The first group did not have reflux and used no reflux medications \((n = 118)\). The second group did have reflux (LPR and/or GERD, \(n = 151\)) and was stratified into subgroups based on reflux medications: no reflux and medications (untreated reflux, \(n = 25\)), famotidine only \((n = 15)\), a PPI only \((n = 54)\), and famotidine plus a PPI \((n = 57)\). There were 25 respondents who reported use of ranitidine, and one who reported use of cimetidine; and they were excluded from this comparison. Age did not differ significantly \((P = 0.635)\) between groups (Table 2). A diagnosis of reflux disease in and of itself was not associated with an increased incidence of laboratory-confirmed or symptomatically suspected COVID-19 \((P = 0.141, P = 0.266;\) Table 3).

When analyzed independently, famotidine use was not associated significantly with laboratory-confirmed \((P = 0.717)\) or symptomatically suspected \((P = 0.876)\)

| TABLE 3. Association Between Reflux Medications, Comorbid Chronic Disease, and Immunosuppressive Medications With Laboratory-Confirmed and Symptomatically Suspected COVID-19 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Risk Factors | Laboratory-Confirmed COVID-19 | | | | | | | | | | |
| | Negative | Positive | Sig. \((P\text{Value})^*\) | Negative | Positive | Sig. \((P\text{Value})^*\) |
| H-2 Blocker | 93.88 | 6.12 | 1.000 | 78.72 | 21.28 | 1.000 |
| Famotidine | 93.02 | 6.98 | 0.717 | 77.50 | 22.50 | 0.876 |
| Proton pump inhibitor (PPI) | 96.72 | 3.28 | 0.283 | 76.98 | 23.02 | 0.676 |
| Omeprazole | 96.30 | 3.70 | 1.000 | 77.97 | 22.03 | 1.000 |
| Pantoprazole | 100.00 | 0.00 | 0.596 | 80.00 | 20.00 | 1.000 |
| Lansoprazole | 100.00 | 0.00 | 1.000 | 66.67 | 33.33 | 0.302 |
| Rabeprazole | 100.00 | 0.00 | 1.000 | 100.00 | 0.00 | 1.000 |
| Esomeprazole | 90.00 | 10.00 | 0.480 | 76.19 | 23.81 | 0.787 |
| Dexlansoprazole | 66.67 | 33.33 | 0.173 | 60.00 | 40.00 | 0.300 |
| Gaviscon | 88.00 | 12.00 | 0.178 | 80.77 | 19.23 | 0.715 |
| Chronic Disease: | | | | | | | | | | |
| Reflux (LPR or GERD) | 90.91 | 9.09 | 0.141 | 75.44 | 24.56 | 0.266 |
| Asthma | 91.67 | 8.33 | 0.638 | 72.73 | 27.27 | 0.284 |
| COPD | 100.00 | 0.00 | 1.000 | 87.50 | 12.50 | 1.000 |
| Hypertension | 96.15 | 3.85 | 1.000 | 76.12 | 23.88 | 0.620 |
| Heart disease | 100.00 | 0.00 | 1.000 | 81.82 | 18.18 | 0.794 |
| Chronic kidney disease | 66.67 | 33.33 | 0.173 | 50.00 | 50.00 | 0.121 |
| High risk obesity (BMI >35) | 71.43 | 28.57 | 0.059 | 55.17 | 44.83 | 0.004 |
| Diabetes mellitus | 90.00 | 10.00 | 0.480 | 78.26 | 21.74 | 1.000 |
| Cancer | 100.00 | 0.00 | 1.000 | 88.24 | 11.76 | 0.381 |
| Immunodeficiency | 88.24 | 11.76 | 0.277 | 68.97 | 31.03 | 0.237 |
| Autoimmune disease | 66.67 | 33.33 | 0.173 | 77.78 | 22.22 | 1.000 |
| Immune modulatory medications | | | | | | | | | | |
| Methotrexate | 66.67 | 33.33 | 0.173 | 87.50 | 12.50 | 1.000 |
| Immunosuppressive biologic | 100.00 | 0.00 | 1.000 | 83.33 | 16.67 | 1.000 |
| Chemotherapy | 50.00 | 50.00 | 0.119 | 50.00 | 50.00 | 0.389 |
| Oral corticosteroid | 100.00 | 0.00 | 1.000 | 100.00 | 0.00 | 1.000 |
| Nasal steroid | 89.47 | 10.53 | 0.327 | 62.16 | 37.84 | 0.018 |
| Inhaled steroid | 90.00 | 10.00 | 0.480 | 68.18 | 31.82 | 0.282 |

* Significance determined by Fisher’s exact test.
COVID-19 (Table 3). Respondents who had confirmed or suspected COVID-19 taking famotidine reported a symptom duration of 6.31 ± 6.22 days, versus 10.00 ± 20.12 days in respondents not taking famotidine, but this difference was not significant (P= 0.316). Reported symptom severity was not affected by famotidine use (2.51 ± 0.88 out of 5 in famotidine users versus 2.38 ± 0.82 in all others, P= 0.316). Respondents reported taking 33.54 ± 10.86 mg famotidine per day (range = 20–80 mg) for 14.28 ± 14.16 months. No correlation existed between symptom duration or severity and famotidine dose or duration (P> 0.05).

Use of the PPI omeprazole was not associated significantly with laboratory-confirmed (P= 1.000) or symptomatically suspected (P= 1.000) COVID-19 (Table 3). The duration of symptoms (8.69 ± 12.19 days in omeprazole users versus 8.98 ± 18.33 days in all others) and reported severity (2.46 ± 0.85 out of 5 in omeprazole users versus 2.40 ± 0.83 in all others) did not differ significantly between respondents taking omeprazole and those who were not (P= 0.732, P= 0.940, respectively). Use of the PPI pantoprazole also was not associated with laboratory-confirmed (P= 0.596) or symptomatically suspected (P= 1.000) COVID-19 (Table 3). No other PPI was associated with an increased or decreased likelihood of laboratory-confirmed or suspected COVID-19 (P> 0.05). There were insufficient numbers of respondents who reported taking other PPIs to test for differences in duration of symptoms and reported severity.

We then fit a binary logistic regression model to determine the probability of a symptomatically suspected COVID-19 case after adjusting for age, gender, exposure to SARS-CoV-2, medication use, and comorbid chronic disease. Hosmer-Lemeshow goodness of fit test did not indicate poor fit of the model (P= 0.665). The OR and 95% CI for each variable in predicting laboratory-confirmed or suspected COVID-19 are reported in Table 4. Age was a significant negative predictor for symptomatically suspected COVID-19 (adjusted OR = 0.959, 95% CI: 0.939–0.980, P< 0.001). Respondents who had reported known contact with someone, inside or outside of their home, who tested positive for SARS-CoV-2 had a significantly higher probability of symptomatically suspected COVID-19 (adjusted OR = 3.038, 95% CI: 1.352–6.827, P= 0.007). Famotidine use was not associated with a decreased probability of a symptomatically suspected COVID-19 case (adjusted OR = 0.735, 95% CI: 0.307–1.759, P= 0.489), nor was use of any other reflux medication (P> 0.05). After adjusting for other factors, high risk obesity (BMI > 35) still was associated with a significantly higher probability for symptomatically suspected COVID-19 (adjusted OR = 4.005, 95% CI: 1.449–11.069, P= 0.007). No significant association was found for any chronic disease (P> 0.05). Use of a corticosteroid nasal spray was associated with a significantly higher probability of symptomatically suspected COVID-19 (adjusted OR = 3.529, 95% CI: 1.352–9.211, P= 0.010), but use of an inhaled corticosteroid was not (adjusted OR = 1.156, 95% CI: 0.286–4.668, P= 0.838). No other significant predictors were identified (p> 0.05).

**DISCUSSION**

Acid reflux (LPR and/or GERD) is common. Management strategies include lifestyle modification and medications

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**TABLE 4. Probability of a Symptomatically Suspected COVID-19 Case, Adjusted for Demographics, Exposure to SARS-CoV-2, Reflux Medication Use, Comorbidities, and Steroid Use**

| Suspected COVID-19* (n = 269 Respondents)¹ | OR       | 95% CI          | Sig. (PValue) |
|-------------------------------------------|----------|-----------------|---------------|
| Age                                       | 0.959    | 0.939–0.980     | <0.001        |
| Gender                                    | 1.665    | 0.818–3.387     | 0.159         |
| SARS-CoV-2 exposure                       | 3.038    | 1.352–6.827     | 0.007         |
| Famotidine                                | 0.735    | 0.307–1.759     | 0.489         |
| Ranitidine                                | 0.684    | 0.210–2.229     | 0.529         |
| Omeprazole                                | 0.829    | 0.349–1.968     | 0.671         |
| Pantoprazole                              | 0.605    | 0.188–1.943     | 0.399         |
| Gaviscon                                  | 0.767    | 0.286–2.055     | 0.598         |
| Reflux disease                            | 1.905    | 0.850–4.270     | 0.117         |
| Asthma                                    | 1.045    | 0.393–2.782     | 0.930         |
| Hypertension                              | 1.481    | 0.604–3.630     | 0.391         |
| Heart disease                             | 0.999    | 0.235–4.257     | 0.999         |
| High risk obesity                         | 4.005    | 1.449–11.069    | 0.007         |
| Diabetes mellitus                         | 0.707    | 0.158–3.155     | 0.649         |
| Immunodeficiency                          | 1.788    | 0.647–4.939     | 0.262         |
| Nasal steroid                             | 3.529    | 1.352–9.211     | 0.010         |
| Inhaled steroid                           | 1.156    | 0.286–4.668     | 0.838         |

* Suspected COVID-19 cases determined by report of ≥3 symptoms.

¹ n = 269 cases included in regression model, n = 38 cases excluded due to missing data points. Significant values bolded (P<0.05).
such as H-2 blockers and PPIs. To the best of our knowledge, this was the first study to investigate a COVID-19 prophylactic role of acid reflux medications. We did not find any association between reflux disease (LPR or GERD), famotidine or PPIs and incidence of COVID-19, suggesting that there was not any prophylactic benefit. However, a therapeutic role for famotidine has been suggested previously in patients with COVID-19. Typically, patients in our center are instructed to take famotidine, 40 mg orally per day at bedtime, and/or a high dose PPI, such as 80 mg of omeprazole or pantoprazole, or the equivalent dose of another PPI. The average daily dose of famotidine reported by respondents in this study was 34 mg, but respondents did not report PPI dosage. High-dose oral famotidine, 240 mg per day, reportedly was used successfully previously to treat outpatients with COVID-19. So, it is possible that the dosage used to manage reflux in our patients was not sufficient to prevent or mitigate symptoms of COVID-19. Two inpatient studies reported improved patient outcomes when oral or intravenous (IV) famotidine was administered. Neither study stratified their outcome data by route of famotidine administration. So, it is also possible that famotidine was only effective when given IV rather than orally. Previous studies have suggested that famotidine may have unintended anti-viral properties due to binding of famotidine to the SARS-CoV-2 chymotrypsin-like protease and papain-like protease, enzymes necessary for replication and survival of the virus, respectively. Pharmacokinetic analysis of famotidine previously showed poor absorption and low volume of distribution, suggesting that IV administration would be advantageous, if not necessary, to achieve sufficient plasma levels of famotidine for the treatment of COVID-19. It is also possible that famotidine has no prophylactic effect but does have a role in limiting illness after symptom onset or preventing severe complications. There are mixed reports regarding omeprazole and other PPIs. Use of a PPI has been proposed to prevent viral replication, but PPI use also has been associated with more severe clinical outcomes from COVID-19.

In this study, we found that incidence of confirmed or symptomatically suspected COVID-19 was increased in respondents of younger age, consistent with recent findings by Boehmer et al. Although individuals in the younger population may be more likely to get COVID-19, individuals in the older population are more likely to experience severe symptoms and have a higher rate of mortality. High risk obesity (BMI ≥35) and use of a corticosteroid nasal spray were associated with increased incidence of symptomatically suspected COVID-19 cases. An association between obesity and increased susceptibility to COVID-19 has been shown previously. Obesity is well known to be associated with hindered immune function and increased susceptibility to infectious disease, including respiratory pathogens. Obesity also is known to increase the risk for reflux disease, but this was not the case in the present study. High risk obesity was found to have a four-fold increase in probability of a symptomatically suspected COVID-19 case, independent of other risk factors including comorbid reflux disease. Currently, it is not known whether there is a risk or benefit to intranasal corticosteroid use regarding susceptibility to SARS-CoV-2 infection. Arguments have been made for both a beneficial role and increased risk of infection. Of note, the criteria for a suspected COVID-19 case were independent of patient-reported nasal congestion and rhinorrhea, because nasal symptoms were shown previously to be a negative predictor for COVID-19. We found no evidence to support increased susceptibility to SARS-CoV-2 infection with inhaled corticosteroids. Corticosteroid use appears to be an important topic for further investigation.

A limitation to this study was the low rate of survey responses. Although we do not suspect any form of response bias that would favor famotidine users or non-users, the low response rate limited the total number of subjects that could be included in this study. Due to the low incidence of COVID-19 in the population, it is necessary to include a high number of subjects for sufficient study power. It therefore is possible that a prophylactic (or detrimental) effect of famotidine does exist for COVID-19, but that the effect size was too small to be detected in this study due to limited power. The challenge of low incidence of COVID-19 in the population might be overcome through a multi-institutional study design for further research.

CONCLUSIONS

When taken orally, 20–40 mg/day famotidine and/or high dose PPIs do not offer prophylaxis against SARS-CoV-2 and do not increase the risk of infection. Further research is necessary to confirm or refute these findings.

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