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Outpatient prescription patterns of COVID-19 drugs in the metropolitan area of Mexico City

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Abstract

Background: We aimed to describe the use of drugs with apparent efficacy in ambulatory patients with confirmed COVID-19 and the relationship of Google Trends searches with prescriptions and the total number of COVID-19 cases in Mexico City.

Methods: Between March 2020 and February 2021, we surveyed 350 patients confirmed to have COVID-19 across 3 hospitals in Mexico City for their ambulatory prescriptions. We analysed the correlation between prescription patterns of 4 drugs with apparent efficacy against COVID-19, Google Trends searches for these drugs, and the overall number of confirmed COVID-19 cases in Mexico City.

Results: We included 350 patients, of whom 59% were women with a median age of 38 years (interquartile range, 29–51), and 72% had a bachelor's degree or higher. There were ambulatory medical prescriptions in 172 (49%) patients, and self-prescriptions were reported in 99 (28%) patients. The prescription rate was high for hydroxychloroquine/azithromycin (19%) and dexamethasone (25%). There was a decrease in the prescription of hydroxychloroquine ($P < 0.001$) and a strong positive correlation between hydroxychloroquine ($r = 0.66$; 95% confidence interval, 0.11–0.90; $P = 0.02$) prescription and online searches for hydroxychloroquine. There was a strong positive correlation between online searches for azithromycin, dexamethasone, ivermectin, and vitamin D and the number of confirmed COVID-19 cases.

Conclusions: During the COVID-19 pandemic, there was a high proportion of prescriptions for hydroxychloroquine/azithromycin and dexamethasone despite their unproven efficacy. Analysis of Google Trends showed a strong correlation between the overall number of confirmed COVID-19 cases and searches for such drugs, suggesting a higher rate of prescriptions. Analysis of online searches could thus help to actively survey public health behaviours in the future.

Key words: COVID-19, health information, infectious diseases, medical errors/patient safety, prescription drug monitoring programs, SARS-CoV-2, self-management

Introduction

The COVID-19 pandemic has prompted healthcare providers to offer treatments that were suggested but not rigorously proven to be efficacious. Therefore, prescription patterns and sale of off-label medications have varied throughout the pandemic as hypotheses were being tested, myths being clarified, and new evidence continually emerged.[1,2] The pandemic has had a deep psychosocial impact on the population, who made panic purchases[3] and sought information about COVID-19 through search engines and social media.[4,5] In the setting of a pandemic, such as the most recent COVID-19 pandemic, it is important to track the behaviours of the general population (consumption) and primary care physicians (prescriptions) with respect to drugs that seem to have a therapeutic effect; this information might allow effective public health interventions to improve those behaviours in the case of catastrophic settings such as a pandemic. Therefore, we aimed to describe the relationship between ambulatory prescriptions of COVID-19 patients diagnosed in our centres for a period of approximately 1 year of the COVID-19 pandemic and Google Trends for the same drugs.

Methods

Study population and data collection

We performed a retrospective multicentre study from March 2020 to February 2021, which included patients with COVID-19 who visited Hospital Gea González, Hospital La Raza, and Hospital General No. 27 in the South and North of Mexico City. The study subjects were consecutive adult patients who visited these medical centres for a SARS-CoV-2 RT-PCR test and had a positive result and complete medical records. We collected clinical and demographic data from the patients' medical records. Drug prescriptions were obtained after requiring outpatient medical prescription forms. Given that some drugs with apparent efficacy against COVID-19

Key messages

- A high rate of purchasing medications with no efficacy for COVID-19 was noted.
- Dexamethasone prescriptions peaked after the RECOVERY trial results in June 2020.
- Hydroxychloroquine searches decreased after the WHO announcement regarding its lack of efficacy.
- Google Trends is a useful tool as a complement to surveys of health behaviours.

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are sold without medical prescription (except antibiotics), self-prescription (i.e. medications that did not require a physician's prescription for their purchase) was reported by the patient in-person by phone. Each drug reported by the patient was accounted for once. Google Trends is an online tool that shows the trend of searches on a scale of 0–100 in a time period. After setting 'Mexico City' and the period from 'March 2020 to February 2021' as filters on Google Trends, we searched for drugs such as azithromycin,[6,7] dexamethasone,[8] ivermectin,[9] hydroxychloroquine,[6,7] and vitamin D.[10] The drug trends were compared with the prescriptions of our patients and confirmed COVID-19 cases in Mexico City. The monthly number of confirmed cases was obtained from the Mexican Minister of Health's official website during the same time period (March 2020 to February 2021). The hospital ethics committee approved this study (Registry numbers R-2020-3501-104 and 2162418). Oral or written informed consent was obtained from all participants.

Statistical analysis

The categorical variables are expressed as percentages and the numerical values are expressed as medians. The analysis of trends was performed using the Cochran–Armitage χ^2 test. The correlation between the patients' prescriptions, Google Trends, and Mexico's total number of confirmed cases was determined using Pearson's correlation coefficient.

The statistical tests were performed using R software version 4.1.0 (R Core Team).

Results

Overall, 400 patients with confirmed COVID-19 were considered, of whom 50 were excluded because of incomplete reports or inability to be reached. Finally, we included 350 patients, of whom 208 (59%) were female with a median age of 38 years (interquartile range [IQR], 29–51), 252 (72%) had a bachelor's degree or higher, and 213 (60%) were healthcare workers. Diabetes (4%) or hypertension (11%) were present in 53/350 patients. The median time elapsed since symptom onset and evaluation was 4 days (IQR, 2-7). A total of 196 (56%) patients received an ambulatory assessment, of whom 55% (108/196) were treated by public health services, and 136/350 (38%) required further hospitalization.

Ambulatory medical prescriptions were reported for 172 (49%) patients, and use of medications that did not require a prescription was reported in 99 (28%) patients. Of note, the health care workers included in the study reported that 68/213 (32%) had self-prescribed drugs, this proportion was lower among patients who were not health care workers (31/137 [23%]), without a significant difference between the 2 groups (P = 0.07). Among the 350 patients evaluated, the overall rate of azithromycin prescription between March
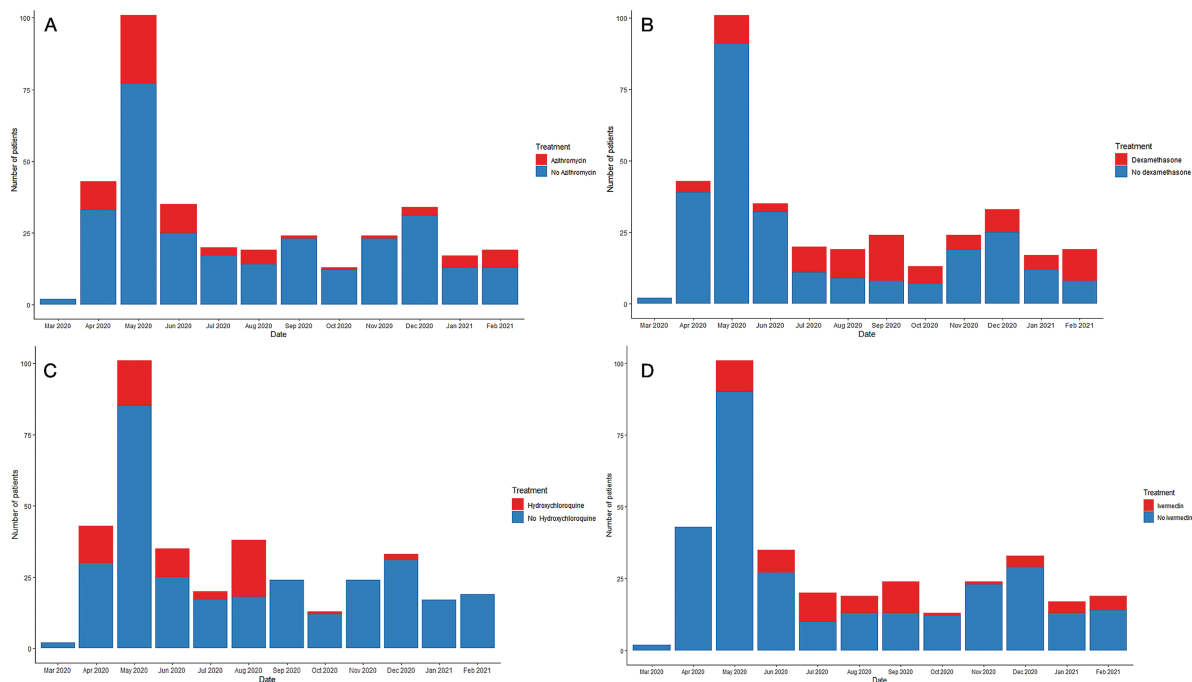

Fig. 1. Number of patients who had medical and self-prescriptions compared with those who had neither each month from March 2020 to February 2021. A) Azithromycin; B) dexamethasone; C) hydroxychloroquine; D) ivermectin.

2020 to February 2021 was 19%, with a higher monthly proportion between April and June 2020 (Fig. 1A). The overall rate of dexamethasone prescription was 25%, with a higher monthly proportion between August and October 2020 (Fig. 1B). Hydroxychloroquine was consumed by 19%, with a high prescription rate in only the first 6 months of the pandemic in Mexico (Fig. 1C). Ivermectin had an overall rate of 17%, with a sustained proportion between May and September 2020 (Fig. 1D). Vitamin D prescription was lower (6%) compared with the prescription of the drugs discussed above. Additionally, we evaluated the prescription of antibiotics such as ceftriaxone (25%) and clarithromycin (12%), which was sustained throughout the year. There was a significant decrease only in hydroxychloroquine prescription ($P < 0.001$) and a moderate but no significant decrease in azithromycin consumption ($P = 0.07$), while the rest of the drugs did not show a significant change in prescriptions over time.

There was a strong positive correlation between hydroxychloroquine prescription and searches for 'hydroxychloroquine' recorded on Google Trends for the same time period ($r = 0.66$; 95% confidence interval [CI], 0.11 to 0.90; $P = 0.02$) (Fig. 2C); there was no such correlation between prescriptions and search trends of azithromycin, dexamethasone, and ivermectin (Fig. 2A, B, D). However, there was a strong correlation between the searches for all 4 drugs on Google Trends and the COVID-19 case load in Mexico City (Fig. 2A–D): azithromycin ($r = 0.73$; 95% CI, 0.27 to 0.92; $P = 0.01$), dexamethasone ($r = 0.66$; 95% CI, 0.15 to 0.89; $P = 0.01$), ivermectin ($r = 0.71$; 95% CI, 0.23 to 0.91; $P = 0.01$), and vitamin D ($r = 0.85$; 95% CI, 0.54 to 0.95; $P = 0.01$). For hydroxychloroquine, the correlation was moderately negative ($r = -0.46$; 95% CI, -0.81 to 0.14; $P = 0.12$) but did not reach statistical significance.

Discussion

Our findings show a high rate of ambulatory prescription of treatments without documented efficacy or indications for early COVID-19. The increasing prescription of off-label drugs with unproven efficacy has been documented since the first months of the pandemic in countries such as Italy[1] and the United States,[2] where the prescription of azithromycin and hydroxychloroquine increased up to 195%[1] and 1977%,[2] respectively. Our study showed that since April 2020, an increase in prescriptions and searches for both drugs occurred after the publication of the study by Gautret et al.[6] However, there was a clear trend of decrease in the number of prescriptions and searches for hydroxychloroquine starting from July 2020, which might be related to the announcement of the World Health Organization regarding the drug's lack of efficacy.[7]

The prescription of dexamethasone in the studied outpatients had no specific trends, which might be because its efficacy was mainly for severe COVID-19.[8] The online searches had 2 peaks: the first in concordance with the statement about dexamethasone's efficacy,[8] and the second occurred at the same time as the higher peak of confirmed cases. The latter could suggest a higher dexamethasone prescription in both ambulatory and hospitalized patients.

The prescription of ivermectin in the studied patients and the online searches started in April 2020, which corresponded with the first report of *in vitro* efficacy[9]; there was a sustained proportion of online searches in concordance with COVID-19 cases, showing a higher peak in January 2021. These findings suggest that ivermectin prescriptions are sustained despite unclear evidence of clinical efficacy.[10]
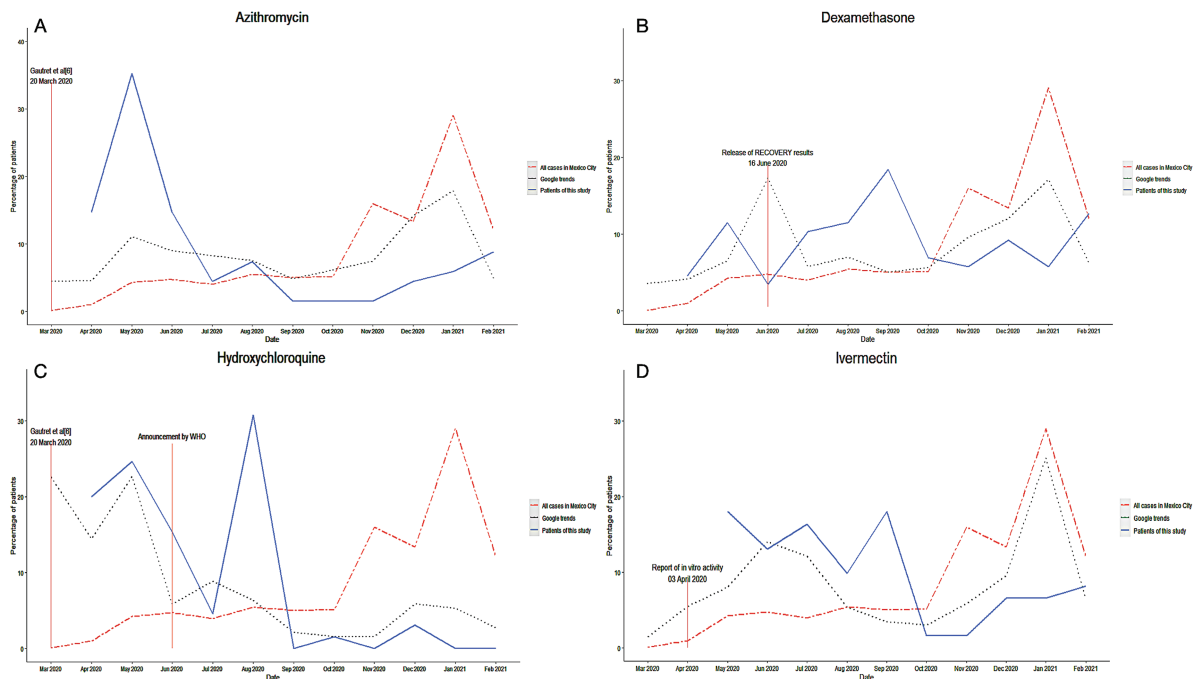

Fig. 2. Temporal patterns of patients who received medication, Google Trends searches for each medication, and confirmed COVID-19 cases in Mexico City, all expressed as percentages of total number between May 2020 and February 2021. A) Azithromycin with a vertical line pointing toward the report of apparent efficacy in combination with hydroxychloroquine in March 2020; B) dexamethasone with a vertical line marking the release of a report about dexamethasone efficacy in June 2020; C) hydroxychloroquine with the vertical lines marking the release of a report of apparent efficacy in March 2020 and a publication that hydroxychloroquine does not improve mortality in June 2020; D) ivermectin with a vertical line marking the month of publication of the study by Kaly et al.[7] in April 2020.

The vitamin D3 prescription, as well as the searches, started in May 2020, in concordance with the first opinions about its role in mitigating COVID-19 outcomes.[11] The trend of searches for vitamin D3 was similar to that of confirmed COVID-19 cases, both reaching a peak in January 2021. This could be explained by the high prescription rate of vitamin D3 despite the lack of reported efficacy.[12]

Remarkably, the ambulatory prescription of antibiotics such as clarithromycin and ceftriaxone was higher despite several reports in the early pandemic of a low proportion of bacterial coinfection of only 3.5%.[13]

Limitations

Despite the study's limitations, such as the sample size or inability to monitor the status of the prescription patterns prospectively, our study suggests that the prescription of drugs with unproven efficacy against COVID-19 was prevalent in Mexico City.

In conclusion, the number of prescriptions decreased only for hydroxychloroquine and azithromycin following a clear public statement about their lack of effectiveness. The online tool Google Trends might help survey the changing epidemiology and public health measures that would require focussed strategies to improve health behaviours.

Funding

Conflict of interest

Ethical approval

The hospital's ethics committee approved this study. Registry numbers R-2020-3501-104 and 2162418.

Data availability

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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