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Changes in inpatient medicine prescribing during COVID-19 lockdown

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Abstract

Background: New Zealand went into lockdown March 2020 successfully eliminating the circulation of the coronavirus disease 2019 (COVID-19) virus. During lockdown there were reduced rates of respiratory infections and hospital admission numbers were low. At the time, rumours of benefit and harm of medicines for COVID-19 were widespread in the lay and medical media.

Aim: To describe changes in inpatient prescribing in an acute general medicine service during the New Zealand COVID-19 lockdown in 2020.

Methods: Rates of prescribing of medicines during the 33 days of lockdown were compared with a 33-day control period before lockdown. Prescriptions, patients and bed days were calculated from the hospital patient administration and electronic prescribing and administration systems.

Results: In the general medicine service, acute admissions were 20% lower during lockdown (from 1216 pre-lockdown to 974). There was a small decrease in the rate of prescriptions per patient (10.1 vs 10.4, $P = 0.01$) during lockdown, and the average length of stay was shorter (3.2 vs 3.6 days). Nebulised administration decreased by 75% (1.3% vs 5.3% of admissions) but unexpectedly there was no change in the prescribing rates of antibacterial medicines, e.g. amoxicillin (26% vs 26%). There were no changes in rates of prescribing of medicines being rumoured to potentially improve (e.g. hydroxychloroquine) or worsen (e.g. angiotensin-converting enzyme inhibitors) COVID-19 outcomes.

Conclusions: Acute medical admissions decreased 20% during lockdown for COVID-19, with a proportional decrease in prescriptions. Reduced rates of respiratory tract infections did not lead to decreased prescribing of antibacterial medicines. Rumour-based prescribing did not eventuate.

Introduction

On 28 February 2020, New Zealand (NZ) reported its first case of coronavirus disease 2019 (COVID-19) infection.[1] On 21 March, the NZ government introduced a four-tiered alert level system designating a series of measures to be taken against COVID-19.[2] On 25 March, NZ entered Alert Level 4 (lockdown) at 11:59 pm. This lasted 33 days and ended on 27 April 2020 at 11:59 pm.

During Alert Level 4, New Zealanders were advised to stay at home. All gatherings were prohibited, and all public venues were closed. All businesses were closed except for essential services. Educational facilities were closed. Travel and recreational activities were severely restricted.

Relative to comparable countries, NZ was spared the worst impact of COVID-19. Only 10 patients were hospitalised with probable or confirmed COVID-19 in Canterbury District Health Board (CDHB) hospitals during lockdown.[3] Acute hospital services were maintained at usual levels and most elective admissions were cancelled during lockdown. The unique circumstances of lockdown and low rates of COVID-19 provided a natural experiment into the effects of lockdown on acute hospital care.

Conflict of interest: None.

There was evidence of a reduction in the total number of hospital admissions during lockdown across NZ.[4–6] Some of this was due to the cancellation of day cases and elective surgery.[7] However, there was also a reduction in acute medical admissions (see Fig. 1).

With the COVID-19 pandemic, there were widespread reports in the medical and lay media of increased benefits or harms of several medicines. At CDHB, measures were put in place to inform rational prescribing and protect against rumour-driven changes in prescribing. These included a constantly updated regional/national COVID-19 Medicines Information website linked to by local guidelines[8] and close monitoring of prescribing using near real-time prescribing data (to midnight of the previous day). Local guidance provided included recommending to continue regular angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs) and nonsteroidal anti-inflammatory drugs (NSAIDs) because of insufficient evidence that they were detrimental in the setting of COVID-19.[8] During lockdown, a precautionary alert was introduced in the electronic prescribing system advising against the use of nebulisers because of concerns about aerosol-generating procedures increasing transmission of COVID-19 (subsequently shown to be unfounded). There was close engagement with clinical leaders and systematic screening of emerging literature. We were prepared to provide specific messaging, but general prophylactic measures were sufficient. Close monitoring of real-time data helped the service resist pressures to respond more vigorously to rumours.

These unique circumstances provided an opportunity to describe the changes in medicine use in acute care during lockdown (in the absence of widespread infection), and to examine the effect of medical and lay media reports on prescribing.

Methods

Our null hypothesis was that in acute hospital services, there would be no change in patterns of prescribing during the COVID-19 lockdown. Our alternative hypothesis was that there would be significant changes in prescribing in the following classes of medications: (i) antimicrobials (exemplified by amoxicillin and piperacillin, including combinations with clavulanic acid and tazobactam) were expected to decrease, given an expectation of less transmissible diseases and anecdotes of lower rates of respiratory tract infection; (ii) hydroxychloroquine was expected to increase, given reports that it may be effective in preventing or treating COVID-19[9]; (iii) ACEIs and ARBs (including combination treatments) were expected to decrease, given reports that these medications could detrimentally increase ACE2 levels, a receptor for COVID-19[10]; (iv) NSAIDs were expected to decrease, given reports that patients who received them early in the course of infection experienced more severe disease[11]; and (v) salbutamol by the nebulised route was expected to decrease, given concerns at the time that nebulised medicines might increase the risk of virus transmission.

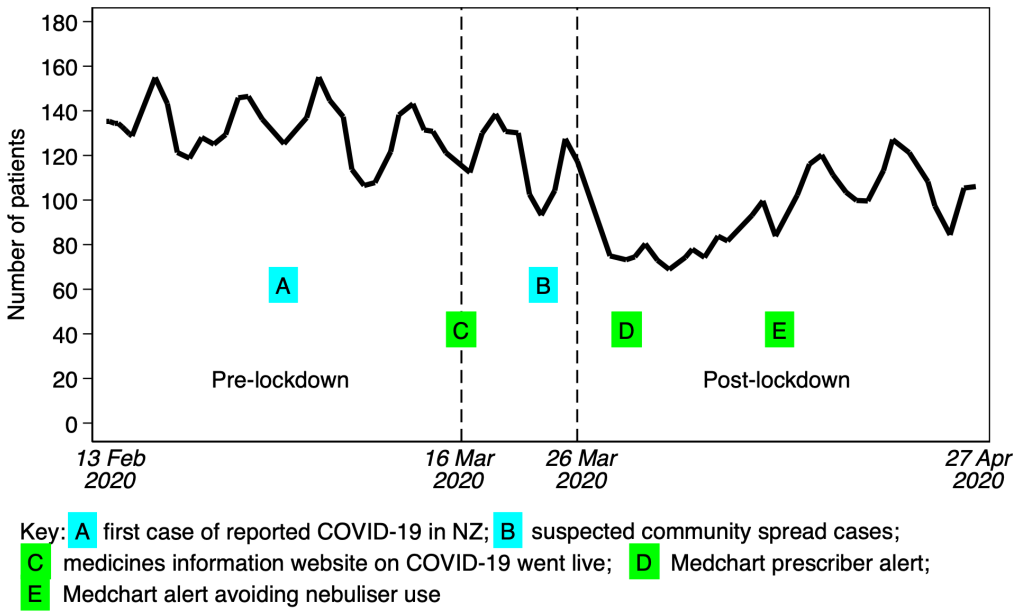

Figure 1 Bed occupancy at 1 pm in general medicine service pre-lockdown and during lockdown. COVID-19, coraonavirus 2019; NZ, New Zealand.

We analysed prescribing data from the electronic prescribing and administration system at CDHB hospitals (Medchart version 8.1.1), which serves more than 1300 hospital beds. This did not include the emergency department and intensive care units, which utilised a paper-based prescribing system.

We analysed a period of 33 days pre-lockdown (13 February 2020 to 16 March 2020), followed by 33 days of lockdown (26 March 2020 to 27 April 2020). The pre-lockdown dates were chosen to reflect the same number of weekdays and weekends as lockdown.

We then restricted the analysis to patients admitted to the general medicine service at Christchurch Hospital as this service only takes acute admissions and was unaffected by cancellation of elective admissions.

This study was approved by the CDHB research office as a locally approved audit (RO# 20311) and assessed as exempt from review by the Health and Disability Ethics Committees NZ.

The number of patients was defined as the number of unique patients over each 33-day period. If a patient was admitted to the hospital more than once during this period, this was counted as one unique patient. The NZ national health identification number was used to identify each patient. Bed occupancy was defined as the number of patients in the hospital at 1 pm of each day. This was tallied over 33 days to give us the number of patient bed days.

The number of prescriptions of each medicine was defined as the number of unique patients prescribed each medicine over each 33-day period. These data were obtained from the Medchart Events Data Cube from the CDHB data warehouse. If a patient's prescription was edited, or ceased and re-prescribed, during a 33-day period, this was counted as one unique prescription. This would include any prescription ceased the day after admission, following consultant review or medicines reconciliation by a pharmacist.

Absolute numbers and prescription rates were analysed using inferential statistics and described graphically over time. χ^2 test of independence was used to compare absolute numbers of prescriptions during the lockdown relative to the pre-lockdown period, and to compare incident rate differences during these periods. Cohen *d* was used to estimate effect size from the mean and standard deviation of each rate distribution (pre-lockdown vs lockdown).

The medicines of interest were compared with paracetamol (the most prescribed medicine) and atorvastatin (the most prescribed statin in NZ) as control medicines. These were selected as medicines widely prescribed in our patient population and, based on information circulating at the time of the study, no change in prescribing due to COVID-19 was expected.

Results

For all CDHB hospitals, the total unique patients admitted decreased by 35.6%, 4276 during lockdown and 6644 pre-lockdown. Bed occupancy was reduced by 30.4% during the 33 days of lockdown, to 25 550 bed days from 36 703 bed days in the 33 days pre-lockdown. Total unique prescriptions were reduced by 34.7% during lockdown, with 45 099 compared with 69 107 in the pre-lockdown period. Of note, most elective admissions were cancelled during lockdown.

In the general medicine service there was a 20% decrease in acute admissions during lockdown, to 974 unique patients compared with 1216 pre-lockdown. Acute bed days decreased by 28%, with 3107 bed days during lockdown and 4318 pre-lockdown with a corresponding decrease in average length of stay. During lockdown there was a 22.6% reduction in unique prescriptions, with 9826 compared with 12 698 (Table 1). There was a small (Cohen *d* 0.11) but statistically significant reduction in number of unique medicines prescribed per patient in the lockdown period, at 10.1 versus 10.4 (ratio, 0.97 [95% confidence interval (CI), 0.94–0.99], $P=0.01$).

There was a small (Cohen *d* 0.22) but statistically significant reduction in average length of stay during lockdown of 3.2 days versus 3.6 days pre-lockdown (ratio, 0.90 [95% CI, 0.86–0.94], $P<0.0001$).

There was a marked decrease in the rate of nebulisers prescribed during lockdown of 1.3%. versus 5.3% pre-lockdown ($P<0.001$) (Fig. 2). There was no observed

Table 1 Summary of data for general medicine service pre-lockdown and during lockdown

	Pre-lockdown	Lockdown	Incidence rate difference (95% CI)	*P*-value
Unique prescriptions	12 698	9826		
Unique patients	1216	974		
Bed occupancy	4318	3107		
Medicines per patient	10.4	10.1	−0.35 (−0.08 to −0.62)	0.01
Average length of stay	3.6	3.2	−0.36 (−0.21 to −0.52)	<0.0001

CI, confidence interval.

change in prescribing rates of antimicrobials, nor was there evidence of rumour-based prescribing (e.g. ACEIs/ARBs or NSAIDs) during lockdown (Table 2).

Discussion

During lockdown there was a 20% reduction in acute medical admissions and a proportional change in prescriptions. This was attributable to fewer referrals from primary care and was not constrained by hospital capacity. The small reduction in medicines per patient was not attributable to reduced prescribing of antibacterials or of medicines featured in media reports. The small reduction may be consequent to the shorter length of stay and/or reflect a change in case mix. Nebuliser prescribing decreased, consistent with advice at the time, with metered-dose inhalers using spacers substituted.

There were widespread reports in the medical and lay media of possible effects of hydroxychloroquine, ACEIs/ARBs and NSAIDs on COVID-19. Despite this, lockdown was not associated with changes in prescribing rates of these medicines in the general medicine service at CDHB. While the protective factors cannot be quantified, this supports the active measures taken to support local prescribers. Keeping local guidelines updated in near real time to maintain credibility and near real-time monitoring of prescribing to inform policy and guide decisions based on data were identified as key measures.

An Australian study of nationwide dispensing claims data found an increase in dispensing of nonevidence-based medicines repurposed for the COVID-19 pandemic, which mostly seemed to be related to stockpiling amongst existing users.[12] Subsequently, regulatory measures were introduced to restrict prescribing of hydroxychloroquine to specific specialists, resulting in an overall reduction in the frequency of their prescription.

The NZ experience contrasts with countries such as the United States, where new prescriptions for hydroxychloroquine or chloroquine were more than seven times higher in March 2020 compared with the previous year, across both primary and secondary care settings.[13] Widespread off-label use of unproven drugs for COVID-19 was rampant in many other countries across the world.[14,15] This may in part be because COVID-19 arrived later in NZ as well as differences in characteristics of the health systems.

Of note, the very small numbers of patients prescribed hydroxychloroquine regularly increased the sensitivity of this as a maker of rumour-based prescribing as a small absolute change is easier to detect with a low background rate than with a high background rate.

Surprisingly, there was no decrease in the rates of prescription of amoxicillin or piperacillin. We expected a reduction as there was a reduction in respiratory tract infections associated with lockdown. An NZ study of antimicrobial prescribing in the community found a marked reduction in antibiotic use during COVID alert level 3–4.[16] Prior to lockdown, influenza was circulating in Canterbury (120 multiplex polymerese chain reaction positive samples during February and March 2020).[17] After lockdown, no further cases of influenza were detected at CDHB in 2020.[17]

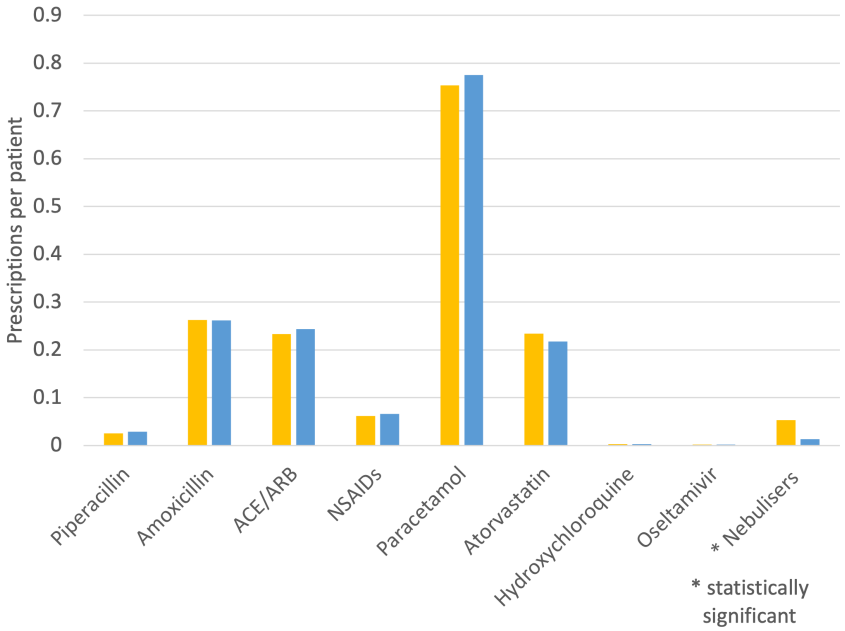

Figure 2 Number of prescriptions per patient for selected medicines pre-lockdown and during lockdown in general medicine service. ■ pre-lockdown; ■ lockdown. ACE, angiotensin-converting enzyme;)ARB, angiotensin receptor blocker; NSAID, nonsteroidal anti-inflammatory drug.

Table 2 Absolute numbers of pre-lockdown and lockdown prescriptions (% patients prescribed the medicine)

	Pre-lockdown, *n* (%)	Lockdown, *n* (%)	Incident rate difference (95% CI)	*P*-value
Total prescribed medicines	12 698	9826		
Piperacillin	31 (2.5)	28 (2.9)		0.6
Amoxicillin	319 (26)	255 (26)		1
ACEI/ARB	284 (23)	237 (24)		0.6
NSAID	75 (6.1)	64 (6.6)		0.7
Paracetamol	916 (75)	755 (76)		0.2
Atorvastatin	285 (23)	212 (22)		0.4
Hydroxychloroquine	3 (0.3)	3 (0.3)		1
Oseltamivir	2 (0.2)	2 (0.2)		1
Nebulisers	65 (5.3)	13 (1.3)	0.004 (0.002–0.005)	<0.0001
Patients	1216	974		
Bed days	4318	3107		

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CI, confidence interval; NSAID, nonsteroidal anti-inflammatory drug.

Prescription of nebulised salbutamol during lockdown was a quarter of the pre-lockdown rates, based on guidance at the time. Measures to facilitate this reduction included introduction of a prescribing alert in the CDHB electronic prescribing system (MedChart). In CDHB MedChart, a systematic approach to clinical decision support is used to minimise alert fatigue, which may help with uptake of the advice by prescribers.[18]

A limitation of this study is that it is observational from a single site. A second limitation is that it is confined to hospital prescribing data and does not examine community prescribing or other hospital data sets. To reduce bias, the study was restricted to patients admitted acutely to the general medicine service as these are unplanned. All of the hospital data were not used as these were influenced by cancelled day cases and elective procedures during lockdown. However, the reduction in acute admissions shows that there were other factors affecting acute referrals during lockdown. The hypothesised reduction in acute respiratory illnesses during lockdown was not found in reduced prescribing of antibacterial medicines. For this study, prescribing data were used, rather than dispensing or administration data.

The pre-lockdown timeframe was chosen, as it immediately preceded the lockdown period, to fully examine the effects of lockdown on acute hospital care. Of note, it also preceded community spread of COVID-19 in NZ, a time when changes in prescribing might be expected. While it is possible that some rumour-based prescribing was occurring prior to community spread of COVID-19, the very low rate of hydroxychloroquine prescribing suggests that it was not occurring prior to COVID-19 circulating in NZ.

The number of unique patients admitted to the hospital was based on CDHB electronic prescribing data and only captured patients who had at least one medicine prescribed in the electronic prescribing system, which we assume is likely to be all or close to all patients. There was some crossover of data between lockdown and pre-lockdown due to long-stay patients. For example, if a patient was admitted to the hospital in the pre-lockdown period and discharged during lockdown, they were included in both groups. There were 93 cases where this occurred.

Because of the reduction in the total number of hospital admissions, there was speculation that the patients admitted acutely to general medicine during lockdown may have been more unwell. This was not reflected in the prescribing patterns of piperacillin, nor in the length of stay.

The low rate of COVID-19 infections allowed us to examine the effects of lockdown in a natural experiment without contamination by COVID-19. The focus on hospitalised patients complements previously published research on the impact of NZ's COVID-19 response on community prescribing.[16]

Conclusion

Lockdown for COVID-19 reduced hospital admissions by 20%, with a proportional decrease in prescriptions. Reduced rates of respiratory tract infections did not lead to decreased prescribing of penicillin antibiotics. Rumour-based prescribing did not occur, despite widespread lay and medical media reports of medicines affecting COVID-19–related outcomes.

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