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RESEARCH ARTICLES

Stockpiling on Off-Label Medicines in Anticipation of COVID-19 in Belize: A Qualitative Study

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ABSTRACT

Introduction: Needless stockpiling of approved medications for the treatment of other diseases cause undue shortages of approved drugs. This study was conducted to assess stockpiling on off-label pharmaceutical products in anticipation of COVID-19 in the country of Belize. The results of the study provide evidence on needless and wasteful stockpiling on medications, with the aim to discourage artificial shortages while reducing the risks of inappropriate medication use.

Methods: The study utilized a qualitative phenomenological approach. Interviews using semi-structured questions were conducted with 15 community pharmacists in the country of Belize. The emerged themes and sub-themes were extracted and exported to Excel 2010® for integration, narration, and presented as summary findings.

Results: Data analysis yielded three salient and inter-related themes: stockpiled products, motives for stockpiling, and pharmacist response.

Conclusion: Panic stockpiling on pharmaceutical products in anticipation of COVID-19 was reported in this study. The World Health Organization advised against the needless stockpiling of approved medications for the treatment of other diseases, thereby causing undue shortages of approved drugs. Observing personal hygiene and social distancing is encouraged as a measure to curb the spread of COVID-19.

KEYWORDS: COVID-19; Stockpiling on Medications; Off-Labelled Medications; Community Pharmacists; Belize.

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INTRODUCTION

The country of Belize was the last to report the novel coronavirus disease (COVID-19) in Central and North America. Presently, over 112 million confirmed cases of COVID-19, including over 2 million deaths, have been reported globally [1]. COVID-19 is considered a newly emergent virus declared an outbreak and a public health emergency by the World Health Organization (WHO) on the 30th January 2020, and later, upgraded to a pandemic [2].

COVID-19 is generally reported to produce mild or uncomplicated sicknesses that do not require hospitalization; however, about 14% of individuals usually progress to more serious diseases leading to hospitalization in the intensive care unit [3]. Acute respiratory disease syndrome (ARDs), cardiac and kidney injuries, sepsis, and septic shock have been reported in severe cases of COVID-19. Patients with comorbidities and the elderly (60 years and above) are reported to be at higher risk of severe complications and death [4,5].

Presently, WHO is coordinating the development of many guidelines to aid clinicians, the entire healthcare personnel, and the general public on how to navigate, curb, and hopefully bring an end to this pandemic. The lack of sufficient and inadequate supporting evidence, environmental factors, and the mutating nature of the virus

make the development of guidelines a slow process [6]. While many countries desperately await a breakthrough with the COVID-19, governments, pharmaceutical industries, and the entire healthcare system is putting public safety measures in place to curb the spread of the virus.

In anticipation of COVID-19 Belize, the government, through the Belize Ministry of Health (MOH) provided some safety guidelines for COVID-19 [7-9]. Furthermore, the ministry advised the public against the use of off-labelled medications citing Nigeria and the USA where cases of poisoning related to electrocardiogram, liver, and eye damage were reported with chloroquine and hydroxychloroquine [7,8,10,11]. Despite concerted efforts by the Ministry of Health to provide detailed and accurate information on COVID-19 to the Belizean population, panic buying of many products, including pharmaceuticals, was observed and reported all over the country [12].

Off-label use of medications encompasses the prescription of medications for purposes that have not yet been approved by regulatory drug bodies [13]. The practice takes place in virtually all aspects of medicine, even though commonly reported in target populations not likely included in clinical trials during drug development [13]. Pharmaceutical industries and physicians usually endorse or prescribe medications for the purposes for which they have been approved to reduce or avoid legal liabilities and huge settlements [14-16].

This qualitative study was conducted to assess stockpiling on off-label pharmaceutical products in anticipation of COVID-19 in the country of Belize. The results of the study will provide evidence of the needless and wasteful stockpiling on medications, discouraging artificial shortages while reducing the risks of inappropriate medication use.

MATERIALS AND METHODS

A qualitative research design was used for this study utilizing a phenomenological approach. All registered community pharmacists and pharmacists in drug distribution were conveniently selected and included in the study. Study participants were selected from 3 major districts (Belize, Cayo, and Corozal) of the country of Belize. A convenient sampling technique was used for sample selection. Fifteen registered community pharmacists in Belize were conveniently selected for the study. All selected pharmacists participated in the study.

DATA COLLECTION

Data were collected from community pharmacists using semi-structured interview guidelines via telephone. The semi-structured interview guidelines were designed in line with the study objectives. The interview guide was tested with 4 community pharmacists to provide the face validity of the instrument. Examples of potential scenarios and probing questions were utilized to further test the instrument. The interview instrument explored the experiences of pharmacists towards public stockpiling on off-label medications in anticipation of COVID-19. Data collection was done until saturation was achieved. All interviews and responses from the 15 community pharmacists were noted and thematically analyzed. The study was conducted in the month of March 2020. The study began before the first COVID-19 case in Belize and concluded shortly after the second COVID-19 case was confirmed on March 25th 2020.

DATA ANALYSIS

Data were analyzed and managed as described by Creswell [17]. Responses from the pharmacist were independently read several times by the researchers to identify patterns and to generate codes based on the outlined framework. The data collected were transcribed and analysed thematically using the Qualitative Data Analysis software Miner Lite version 2.0.6. The integrated themes and sub-themes generated were presented in narrative passages and used to summarize study findings on stockpiling on off-labelled medicines in Belize. Since the emphasis for this study was to explore an understanding on stockpiling of off-labelled medications in Belize as a result of COVID-19, only the themes and sub-themes that address these issues were presented.

The analysis was conducted in a proportionate manner until saturation was achieved. The themes and sub-themes that emerged were extracted and exported to Excel 2010® for integration, narration, and presentation of summary findings.

ETHICS

The study was approved by Faculty of Health Science, University of Belize as part of faculty work plan for 2019-2020 academic year. All ethical issues related to the conduct of the study were strictly observed throughout the entire study. Informed consent was obtained from the participants before they were included in the study. Participation was voluntary with the full right to withdraw at any point in the study without penalty. Assurance of confidentiality and anonymity of the data was provided and ensured throughout the study period. The research was strictly conducted in accordance with the ethical standards as laid down in the 2013 Declaration of Helsinki ethical standards.

RESULTS

A total of 15 interviews were analyzed after the data was considered saturated. The respondents comprised of 10 females and five males. Five participants were from Cayo district, seven from Belize district, and three from the Orange Walk district. The mean year for pharmacy practice was 8.87±3.18. The thematic analysis conducted yielded three major themes, stockpiled products, motives for stockpiling pharmaceutical products, and pharmacist's response to stockpiling pharmaceutical products.

Stockpiled products

Stockpile products were the first theme that emerged in this study, along with two of its sub-themes. Pharmaceutical products and Personal care products. The pharmaceutical and personal products. The pharmaceutical products demanded from the pharmacist were evidenced by the following quotations from the pharmacists:

"Yes, medications and products that we sold on a daily basis included; Isopropyl alcohol 50%, 70% or higher; alcohol gel; hand sanitizer but none available; masks (surgical or dust); latex gloves (Sm, Med, Lg); Vicks vaporub; Vitamins or multivitamins/minerals such as (Vitamin C's, Seven seas cod liver oil, others such as vitamin D, Zinc, B-complex, multivitamins and minerals

syrups for infants and adults). Also, I sold and stock out on antihistamines, Flu, and cough medications, almost of all kinds available; common brands sold were (Viro grip soft gels, tea power, syrups, Suda grip capsules, tea power, syrups, Fluibron, Trimetose, Ambroxol, Benadryl, loratadine [syrups, tablets], Tylenol tablets and suspensions). Additionally, antiasthmatic of almost all kinds such as Salbutamol or Buto Asma inhaler, syrups, and related products, tropium, albugenol, and TR nebulizer solution. Demands were made for prescription meds such as chloroquine and azithromycin, but we only sold those based on prescription." (P4)

I have had people coming to ask for tylenol, ibuprofen, sanitizers, hand gloves, chloroquine, hydroxychloroquine, antiviral drugs, antibacterial such as azithromycin, antidiabetics, antihistamines, and antihypertensive. Those with chronic diseases will ask majorly for antihypertensive and antidiabetic. Some will request anti-asthmatics for children who suffer from asthma. Yeah many people also asked to buy vitamins. I ran out on all the vitamins including zinc sulphate and gluconate, seven seals, vitamins C, D, B, and vitamin B complex. I have also sold out on thermometers, nebulizers, and nebulizer solution." (P8)

Motives for stockpiling pharmaceutical products

The following quotations by the community pharmacists revealed the motives behind stockpiling on pharmaceutical products in Belize

"I would say there was some kind of panic due to the covid-19 virus. I can say, many people are not taking the coronavirus lightly, so all purchases including prescription and non-prescription medications were to prepare and not to be caught unaware." (P1)

"Most customers came to buy these medications or products to prepare themselves for the coming coronavirus or simply corona… they bought Flu and cough medications in case any of them would have signs of flu and coughs." (P3)

"Oh certainly it is in preparation for coronavirus. People bought vitamins and minerals they say to strengthen the immune system and their healthy well-being." (P13)

"The stockpiling for anti-asthmatics medications was to equip or have these meds ready in case of any attacks from COVID-19, especially for their kids who suffer asthma. Tylenol, they say it is the medicine of choice for the coronavirus in the event of any fever or pain." (P15)

"I have never experienced something like this in my entire years of practice. Our entire stock on some products keeps running out because people will just come and buy them. It is definitely panic buying because of the Coronavirus." (P2)

Yes people are coming in to buy so many things because they want to prepare for the virus. Some were panic buying, but some with chronic diseases have been advised to get a stock of at least two months. So, some are buying out of panic while others are buying because they need to stock." (P12)

Pharmacists responses to stockpiling of pharmaceutical products

The sub-themes that emerged under this theme were demand for prescription drugs and subsequent patient counselling.

"People were asking to buy chloroquine and azithromycin without a prescription. I did not sell the medications to them, and I counsel some of them that medications have not yet been approved for the treatment of coronavirus." (P5)

"Well, you know despite the fact that business was good, I still had to be professional and maintain ethics in how I conduct myself. I advised people against buying ibuprofen because I have read it worsen the symptoms of coronavirus, so I did not sell to the public. I also did not sell prescription drugs without prescriptions." (P10)

"We had a number of American tourists visiting the country that came to purchase chloroquine, hydroxychloroquine, and azithromycin because according to them they were the medications for COVID-19. But they did not have a prescription, so I denied them the medications." (P11)

DISCUSSION

Inappropriate and excessive accumulation of non-prescription or prescription medications for later use is referred to as medication stockpiling [18]. People stockpile medications for a number of reasons. Fear of shortages on medications, unintentional abuse or misuse, terrorists' attacks, and imminent dangers are some of the reasons the public goes into panic and stockpiling on medications. With the forthcoming threat of the COVID-19 pandemic, few reports indicated that people stockpiled on medications not necessary for diagnosed diseases but in anticipation and readiness for COVID-19 [18,19]. Inappropriate and unnecessary stockpiling of medications has been reported to create unintentional and unplanned scarcity for patients who need these medications, thereby putting them in an undue risks [18]. Presently, no pharmaceutical product has shown proven efficacy and safety for the treatment of COVID-19. Even though a number of medicinal agents have been identified, these are still under investigation as possible treatment options [1].

In the current study, most community pharmacists reported increased public demand for off-labeled drugs like azithromycin, chloroquine, and hydroxychloroquine. None of the participating pharmacists reported selling these drugs to the public without a prescription. The off-labeled drugs demanded by the public required prescription, and the Belize Ministry of Health has issued a warning against the practice of selling these drugs without a prescription. Most of the pharmacists reported counseling the public against stockpiling these drugs for COVID-19 in line with the Ministry of Health's guidelines. Reported chloroquine and hydroxychloroquine poisoning might have added to the restrictions made by MOH in obtaining these products for the prevention of COVID-19 by the public [10,11]. Recent opinion on the use of chloroquine, hydroxychloroquine, and azithromycin for COVID-19 treatment indicated that these therapies might have no in vitro activity against COVID-19 and no clinical evidence currently supports the use of these drugs for such therapy [20,21]. Furthermore, the report added that chloroquine, hydroxychloroquine, and azithromycin have the potential to increase cardiac death as a result of their diverse adverse effects such as neutropenia, anaphylaxis, QT prolongation, hepatitis, torsade's de pointes, and acute pancreatitis [20]. This study revealed

that in anticipation for COVID-19, the demand for chloroquine, hydroxychloroquine, and azithromycin was made by the public without prescription, but the pharmacists did not dispense these medications except with a prescription.

Public stockpiling on vitamins (especially vitamin C) to boost immunity was not without credible scientific justification. For instance, for many years, vitamin C has been reported to be an immune-boosting agent [22-24], aiding in disease prevention [25,26], and effective against exercise-induced bronchospasm [27]. The presentation of vitamin C as an immune booster has held sway for many years until the scientist challenged Pauling's position in this regard. Presently, a number of studies have shown that vitamin C is not effective in common colds [28,29] and may be of little or no help in COVID-19 [29-31]. Based on the lack of concreate evidence that vitamin C supplementation can lower the incidence of colds [28] or COVID-19, the public rush to stockpile vitamin C or other vitamins for the management of COVID-19 may not be justifiable. However, the use of vitamin C supplements in daily allowable doses enhances the intestinal absorption of iron, thereby increasing its availability [32]. The use of vitamin C, therefore, in the recommended doses causes no harm to the individual but offers a wide range of benefits to the individual [33].

The reported increased demand for paracetamol (acetaminophen) by the public in anticipation for COVID-19 could be justified without available guidelines. Fever has been one of the common signs of COVID-19. Several infectious processes trigger the immune system, resulting in pyrexia or fever as a response to the infectious disease [34]. Viral infections such as COVID-19 present such an opportunity for the body to raise the temperature in response to immune defense. Although no evidence exists for the use of NSAIDs for either cardiovascular, septic, or respiratory complications in the management of COVID-19, acetaminophen has been suggested for the management of pyrexia and sore throat symptoms as opposed to ibuprofen [35]. In this study, the pharmacists reported public demand for ibuprofen. However, none of the pharmacists indicated supplying ibuprofen as a measure to prevent COVID-19 complications. The public was counselled and discouraged against such purchases.

The upsurge in the stockpiling of cough medications reported by the pharmacists in this study was not unrelated to the fact that cough has been reported as a symptom of COVID-19 [1]. Mucolytics such as ambroxol and N-acetylcysteine have been reportedly prescribed in the management of acute cough [36,37]. The use of cough preparations in the management of COVID-19 might be best described as supportive therapy.

Acute respiratory disease syndrome (ARDs), cardiac and kidney injuries, sepsis, and septic shock have been reported in severe cases of COVID-19 [3]. A recent review listed a number of pharmacological agents suggested for the management of ARD's [38]. Agents such as corticosteroids, beta-agonists, surfactants, statins, and N-acetylcysteine have been suggested for ARDS; however, as at the time of this report, sufficient evidence is currently lacking to ascertain whether such claims reduce mortality in patients with ARDS. Severely infected patients with COVID-19 present with ARD's and are in need of supportive or pharmacological therapies. In the absence of standard management guidelines for COVID-19, critically ill adults have benefited from hemodynamic and ventilator support and low-dose corticosteroids [39]. Interim guidelines have been provided by the WHO for the clinical management of severe acute respiratory infections when COVID-19 infections are suspected [40]. Notwithstanding that few pharmacological agents have been approved for the management of COVID-19, national laws and regulatory authorities must comply with the use of off-label medications for COVID-19 management [1]. The World Health Organization advised against the needless stockpiling of approved medications for the treatment of other diseases such as COVID-19 thereby causing undue shortages of the approved drugs [1]. The initiation of an experimental therapy for emergency purposes must be ethically and legally weighed by both the medical team and the patient. Benefits, safety, risks, and efficacy of an off-label agent must always be established within formal clinical trials.

The rest of the items reported by the pharmacists in this study were personal care products mainly for the prevention or spread of infections. The increased demand for the purchase of nebulizers was probably related to asthma patients or in anticipation of COVID-19. As at the time of this study, the country had no sufficient ventilators even though some were expected. In all these, the panic stockpiling purchases of many of the items reported in this study could be best described as reactionary. The advice given by the Ministry of Health in terms of personal hygiene, washing of hands, social distancing, wearing of facemask, and avoiding overcrowding as means of preventing the spread of COVID-19 were perhaps more effective than panic stockpiling of off-labelled medication [9]. Overcrowded supermarkets and pharmacy stores for panic stockpiling of pharmaceutical products might have aided the risks for the spread of COVID-19 in the long run. To this end therefore, panic purchases of off-label pharmaceutical products reported in this study was unnecessary since guidelines for pharmacological products for the management of COVID-19 are still being developed [41]. To date, abiding by the guidelines from WHO [1] and the Belize Ministry of Health [7-9] is still a beneficial and useful advice.

CONCLUSION

Stockpiling on prescription, non-prescription, and personal items were reported in this study. Panic stockpiling on off-label medications if allowed unchecked has the capacity to cause a shortage of approved medications for the diseases they were intended to treat. The panic attempt to stockpile on azithromycin, chloroquine, and hydroxychloroquine was reported by pharmacists, but such medications were only supplied with prescriptions after patients were counselled against their use for COVID-19 management. The World Health Organization advised against the needless stockpiling of approved medications for the treatment of other diseases, thereby causing undue shortages of approved drugs. Patients' and buyers of off-labeled medications may suffer unnecessary costs while causing artificial shortages. Observing personal hygiene and social distancing is still encouraged as a measure to curb the community spread of COVID-19 in Belize.

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AUTHORS' CONTRIBUTIONS
The participation of each author corresponds to the criteria of authorship and contributorship emphasized in the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals of the International Committee of Medical Journal Editors. Indeed, all the authors have actively participated in the redaction, the revision of the manuscript, and provided approval for this final revised version.

COMPETING INTERESTS
The authors declare no competing interests with this case.

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