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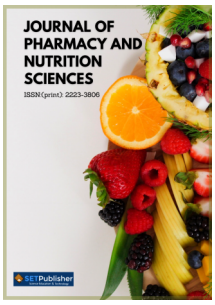

Use of Over-the-Counter Products in Lebanese Adults with Cardiovascular Disease

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Abstract:

Background: While selling over-the-counter (OTC) products in pharmacies is convenient to individuals and can be beneficial, it might potentially cause harm. We hereby describe the patterns of OTC product consumption amongst adults with cardiovascular disease (CVD) in Lebanon and the potential interactions with prescription medications and patient diseases.

Methods: This was a cross-sectional study in the setting of nine community pharmacies across different governorates of Lebanon. Data of interest were collected from adult patients with CVD history through face-to-face interviews using a short questionnaire.

Results: Out of 201 adult patients included in the study, 190 (94.5%) were using at least one OTC product, with a mean of 3.2 ± 2.4 per patient (range of 1 to 12 products). The proportion of patients taking analgesics was the greatest (81.1%), followed by those taking vitamins (48.8%), minerals (29.9%), and herbal products (13.9%). Several potentially harmful OTC product- drug or -disease interactions were identified. Only 65.3% of OTC users reported obtaining information about the used products from healthcare professionals (HCPs), and 35.3% did not disclose the use of the products to their HCPs.

Conclusion: The use of OTC products was highly prevalent among patients with CVD with potential interactions with prescription medications and patient diseases. In order to ensure optimal patient outcomes, clinicians are strongly encouraged to inquire about OTC product use and counsel patients about the risks and benefits associated with such products.

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INTRODUCTION

Cardiovascular disease (CVD) represents a leading cause of morbidity and mortality worldwide, resulting in an estimated total of 17.9 million deaths in 2015 [1]. Of these, 1.4 million CVD deaths occurred in the Eastern Mediterranean Region. This is an area with a growing CVD burden, whereby the years lived with disability caused by CVD had increased by 85.7% between 1990 and 2015 [2]. With respect to Lebanon, an Eastern Mediterranean country, scarce data exist on the local incidence and prevalence of CVDs.

Meanwhile, an increasing trend is also being observed for the consumption of over-the-counter (OTC) products comprised of nonprescription medications, vitamins, minerals, and herbal remedies. Currently, 240 million people use OTC medications in the United States, and those with CVD rank first in their use of vitamins and herbal remedies among the general population [3, 4]. In addition, two-thirds of the Canadian cardiac patient population under study reported the use of OTC products [5]. Another study in Saudi Arabia revealed that more than half of the CVD patient population regularly used OTC products [6].

This widespread behavior can be explained by the increased availability and marketing of these products, their accessibility to the public without a prescription, and the general perception that they are safe [7]. Nonetheless, unlike prescription medications, prior to their release on the market, products like dietary supplements and herbal preparations do not undergo thorough testing for efficacy and safety, nor are they obliged to receive authorization from regulatory agencies [8]. As such, clinicians cannot be confident that these products are as effective and safe as they claim to be.

While the availability of OTC products offers convenient access and choice of medications and supplements and involves people as active participants in their health, a major concern is that many of these products have the potential to inflict harm upon the CVD patient through either interacting with prescribed medications or producing relevant CV adverse effects [5, 6, 8]. Another important issue is that patients often refrain from reporting the use of OTC medications to their healthcare providers (HCPs), which limits their role in preventing severe adverse outcomes as well as significant drug-drug, supplement-drug, and herb-drug interactions [6, 8].

Accordingly, the common practice of OTC medication utilization and the potential for harm amongst CVD patients, alongside the lack of data assessing OTC use of this specific population in Lebanon, lay the grounds for conducting this study. The study's objective is to describe the patterns of OTC product consumption and identify potential interactions with prescription medications on the one hand, and with patient diseases on the other, amongst adults with CVD in Lebanon. We also assessed the source of information for the used OTC products and whether patients disclosed their use to HCPs.

MATERIALS AND METHODS

A cross-sectional study was conducted between June 1 and December 31, 2019, in the setting of nine community pharmacies across the different governorates of Lebanon (three in Mount Lebanon, two in Beirut, two in the South, one in the North and one in Bekaa). Subjects were included in the study if they were adults (≥18 years) diagnosed with at least one of the following CV conditions: hypertension (HTN), dyslipidemia, cardiac arrhythmias, heart failure (HF), coronary artery disease (CAD), cerebrovascular disease or peripheral vascular disease. The research team, composed of two pharmacy students and supervised by a clinical pharmacist, approached patients visiting the pharmacies, screened them for eligibility, and collected data of interest through face-to-face interviews using a short questionnaire. The research team developed the questionnaire, and data collection was initiated after receiving appropriate intensive training, and a pilot test was conducted on the intended population. In addition, two community pharmacists strongly agreed that the content of the questionnaire was appropriate to measure the outcome of interest. The questions in the survey addressed patient demographics, medical history, use of prescription and OTC products, the source of information for the latter, the reason for use, and disclosure to healthcare professionals. In Lebanon, OTC products can be bought directly by the consumer without any medical prescription and include nonprescription medications, vitamins, minerals, and herbs. Consent to the participation in the study was implied by the voluntary completion of the questionnaire by the patients. No identifying information was recorded during the interview, ensuring the participants' anonymity and privacy. Descriptive statistics were expressed as means and standard deviations for numerical data and as frequencies and

percentages for categorical data. The study was approved by the Lebanese American University Institutional Review Board Committee.

RESULTS

A total of 201 adult patients with a history of CVD were interviewed at nine community pharmacies and were included in the study. Patients had a mean age of 61.8 ± 11.6 years, 38.3% of whom were older adults, and 52.2% were females. The proportion of patients who agreed to participate in the study approached 84%. The largest number of recruited patients was from the governorates of Mount Lebanon (45.3%) and Beirut (28.8%). The average number of prescription products utilized by the patients was 4.5 ± 2.9. Table **1** presents the descriptive characteristics of the patients. The most common CV comorbidities were HTN (74.6%), followed by dyslipidemia (50.7%), and CAD (24.9%). Table **2** shows the number and the type of CV comorbidities present among these patients.

Table 1: Descriptive Characteristics of Patients

	N (%)
Gender	
Females	105 (52.2)
Males	96 (47.8)
Total	201 (100)
Age (years)	
<65	124 (61.7)
≥ 65	77 (38.3)
Mean ± SD	61.8 ± 11.6
Geographical distribution	
Mount Lebanon	91 (45.3)
Beirut	58 (28.8)
South	23 (11.4)
North	19 (9.5)
Bekaa	10 (5)
Number of prescription products	
Mean ±SD	4.5 ± 2.9

Among included patients, 190 (94.5%) were using at least one OTC product at the time the study was conducted; a total of 653 products were used, with a mean of 3.2 ± 2.4 per patient, and the range varied widely from 1 to 12 products. The proportion of those taking at least one or more OTC analgesics was the greatest (81.1%) among these patients, followed by vitamins (48.8%), minerals (29.9%), herbal products (13.9%), and omega-3 supplements (11.4%). The usage of acetaminophen was the most common among the analgesics, followed by ibuprofen and diclofenac. Among the vitamins, vitamin D ranked first in consumption. Next were multivitamin products and vitamin B complex. As for minerals, magnesium and calcium were the most used. The herbal remedies reported include garlic and Ginkgo Biloba, among others. Table **3** shows the number and the type of OTC products consumed. To note, the percentage of older adults out of those taking OTCs was 35.3%. Among the reported reasons for OTC use, the most recurrent was pain (70.5%), followed by vitamin and/or mineral deficiency (12.6%), and CV health, i.e., treating or preventing CVD (12.1%). Among OTC users, 124 (65.3%) reported that the source of information for the used products included HCPs (physicians, pharmacists, or nurses), while the remaining patients relied on information obtained from family, friends, personal experience and media. Finally, 35.3% of OTC users did not disclose the use of the products to HCPs.

Table 2: Patients' Cardiovascular Comorbidities

	N (%)
Number of CV* comorbidities	
1	100 (49.8)
2	58 (28.9)
3	30 (14.9)
4	11 (5.5)
5	1 (0.5)
6	1 (0.5)
Mean ± SD	1.8 ± 1
Median	2
Type of CV* Comorbidities	
Hypertension	150 (74.6)
Dyslipidemia	102 (50.7)
Coronary artery disease	50 (24.9)
Arrhythmias	21(10.4)
Heart failure	14 (7)
Stroke	14 (7)
Peripheral vascular disease	9 (4.5)

*CV: cardiovascular.

DISCUSSION

This investigation aims to depict the OTC consumption practices amongst CVD patients in Lebanon. In addition, it aims to identify potential interactions with prescription medications and patient diseases that have a local impact as well as a global impact. To our knowledge, this is the first study to describe the use of OTC products by adults with CVD in Lebanon. The results reveal largely extensive use of OTCs, whereby

Table 3: Number and Type of OTC Products Used by Patients

	N (%)
Number of OTC products	
0	11 (5.5)
1	41 (20.4)
2	43 (21.4)
3	35 (17.4)
4	21 (10.4)
5	15 (7.5)
6	12 (6.5)
7	7 (3.5)
8	8 (4)
9	1 (0.5)
10	3 (1)
11	0 (0)
12	2 (1)
Mean ± SD	3.2 ± 2.4
Median	3
Total	653
Type of OTC products	**N* (%) Δ**
Analgesics	**195 (81.1)**
APAP ¶	129
NSAIDs†	66
Ibuprofen	28
Diclofenac	22
Other NSAIDs	16
Vitamins	**124 (48.8)**
Vitamin D	51
Multivitamins	24
Vitamin B complex	14
Vitamin C	12
Vitamin B6	7
Vitamin B9	5
Vitamin B12	3
Other vitamins	8
Minerals	**74 (29.9)**
Magnesium	33
Calcium	29
Iron	9
Zinc	2
Manganese	1
Herbal products (including garlic, gingko biloba, and others)	**44 (13.9)**
Omega 3	**23 (11.4)**
Caffeine	**22 (10.9)**
Stomach acid reducers	**21 (10)**
PPIs‡	15
Antacids	5
H2 Antagonists	1
Topical analgesics	**30 (10)**
Antihistamines	**10 (5)**
Antispasmodic agents	**16 (4)**
Aspirin	**8 (4)**
Glucosamine	**8 (4)**
Cold products	**7 (3.5)**
Pseudoephedrine	4
Phenylephrine	3
Chondroitin	**4 (2)**
Miscellaneous	**37 (19.4)**

* Number of OTC products consumed.
Δ Percentage of patients taking at least one of the OTC products.
¶APAP: Acetaminophen.
†NSAIDs: Non-steroidal anti-inflammatory drugs.
‡PPIs: Proton pumps inhibitors.

about 9 out of 10 patients regularly consume at least one nonprescription product. This is in accordance with a number of studies demonstrating the prevalence of OTC use in CV patient populations. For instance, 88.8% of HF patients from the US and 92% of hypertensive patients from the Republic of Trinidad and Tobago reported regular OTC product consumption [4, 9].

In this study, the most commonly used class of OTC medications was analgesics, which is in line with findings from several other investigations [5, 9, 10]. Acetaminophen ranked first in use which can be explained by its relatively benign safety and tolerability profile [11]. However, it is important to be aware of the potential for hepatotoxicity, especially with the unmindful consumption of multiple OTC products containing acetaminophen that could result in unintentional overdose.

OTC Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) were also commonly reported. Their use, however, can be problematic, particularly for patients with CVD. These agents can cause elevated blood pressure even with short-term use [12]. This is alarming, considering the high prevalence of HTN (74.6%) in this patient population. Moreover, as cautioned by the FDA, NSAIDs increase the risk of myocardial infarction and stroke in patients with or without established CAD [13]. Their use can also result in fluid retention and is associated with a 10-fold increase in the risk of acute decompensation among HF patients [12]. Furthermore, NSAIDs are notorious for attenuating the therapeutic effects of aspirin, renin-angiotensin-aldosterone system (RAAS) inhibitors, and diuretics, in addition to enhancing the risk of adverse events linked to these prescribed medications. These include the risk of renal failure with RAAS inhibitors, which is particularly heightened with concomitant diuretic use, and the risk of hemorrhagic events with antiplatelet and/or anticoagulants [12, 14]. Therefore, the general recommendation should be to avoid NSAIDs in patients with CVD and, if deemed medically necessary, limit their use to the lowest effective dose for the shortest duration possible while closely monitoring the patient.

In the study, vitamins and minerals were among the most common OTC products. Similar trends are seen in studies conducted in the USA and Canada in patients with CVD [5, 15, 16]. Although many dietary supplements are being promoted by the industry and are often recommended by HCPs to prevent disease, including CVD, there is a lack of substantial evidence

to support the role of multivitamins and other nutrient supplements in the absence of micronutrient deficiencies [17]. In fact, when consumed in excessive amounts, mineral or vitamin consumption might even pose harm [17, 18]. Some noteworthy interactions can arise from the use of such supplements. Vitamin K, a common component of multivitamins, may antagonize the anticoagulant effects of vitamin K antagonists, such as warfarin and acenocoumarol, thus increasing the risk of thromboembolic events [19]. Moreover, a warning has been issued by the FDA concerning biotin's (vitamin B7) interference with the lab test for the cardiac biomarker troponin. This interaction may result in falsely low troponin levels, potentially leading to serious clinical implications due to the possible misdiagnosis of myocardial infarction [20]. The public's perception of dietary supplements must be addressed by HCPs who should educate their patients that they are not a substitute for a balanced, nutritious diet.

A considerable portion (12.1%) of the OTC users reported taking nonprescription products specifically to treat and prevent CVD. A surveillance study conducted in the US showed a similar frequency of 16% among nonprescription users [21]. One of the main products used for perceived CV health was omega-3 supplements consumed by almost a tenth of our patient population. However, a Cochrane review published in 2018, involving 79 randomized controlled trials, showed that omega-3 fats have little or no effect on mortality or CV health (evidence mainly from supplement trials) [22]. These findings dispute the popular upheld belief in the CV benefits of omega-3 fat intake.

A noticeable number of patients in the study used herbal products, namely garlic and Ginkgo Biloba. These agents have no documented CV benefit and are among the herbs most commonly involved in herb-drug interactions [23]. This clearly illustrates that herbal therapies may pose significant risk to certain patients while assumed to be safe.

Some patients reported independently initiating low-dose aspirin for primary prevention of CVD. The American College of Cardiology and the American Heart Association state that adults without a history of heart disease should not take the drug to prevent a first heart attack or stroke as the risk of side effects from aspirin, particularly bleeding, might outweigh the potential benefit [24]. Therefore, the use of low-dose aspirin for primary prevention of CVD should be considered only in select adults after weighing the risks and benefits assessed by the healthcare provider.

About one in ten patients used stomach acid reducers (proton pump inhibitors, H_2 antagonists, or antacids). Several clinically significant interactions may exist with prescribed CV medications. For instance, esomeprazole and omeprazole can inhibit clopidogrel's bioactivation, counteracting its antiplatelet effects and increasing the risk of negative CV-related outcomes when used concomitantly [11]. Furthermore, using the antacid calcium carbonate may diminish the antihypertensive effect of calcium channel blockers [11].

A minority of patients reported the use of common cold products containing the sympathomimetics pseudoephedrine and phenylephrine. These products have been associated with hypertensive episodes, acute myocardial ischemia, tachydysrhythmias, and stroke [11]. Of concern is the potential interaction between phenylephrine and acetaminophen, which are commonly present in combination to treat cold. Acetaminophen has been shown to increase the bioavailability of phenylephrine, enhancing the risk of deleterious CV outcomes [11].

There seem to exist numerous contributors to a patient's choice of OTC products. When asked about the source of information for OTC products used, patients more often mentioned their HCPs. While this is reassuring, a substantial ratio of patients, about one out of three, still referred to family and friends, personal experiences, as well as the media (including internet resources and advertisements), indicating the widespread practice of self-medication. Such behaviors carry potential risks, especially in CVD, which is characterized by complex disease processes and multiple drug regimens. These risks involve delays in receiving medical examination and advice, incorrect diagnosis and choice of medication, polypharmacy, in addition to serious adverse drug events and drug interactions, including those previously mentioned [25]. These issues can be averted when HCPs are made aware of any OTC product being consumed.

More than a third of the patients refrained from reporting about used OTC products to their HCPs. This follows tendencies of underreporting observed in other patient populations. A study involving HF patients revealed a 40% discrepancy rate between the OTC use reported during an interview and documented in the patient's medical records [4]. It remains the responsibility of HCPs to inquire about and provide guidance for OTC drug use consistently.

This study is not without limitations. This cross-sectional study used a short questionnaire to collect data, relying almost fully on participant reports with only a few patients presenting their used products during the interview. As such, results are subject to recall bias, especially that a portion of the patients were older adults exhibiting polypharmacy. In addition, despite trying to control for social desirability bias during the patient interview, it could have played a role in answering survey questions. Moreover, the patients recruited were confined to certain pharmacies, which could have resulted in selection bias. That being said, these pharmacies were distributed across different Lebanese areas, enhancing the representativeness of the study sample and the generalizability of the results to the Lebanese CV patient population. It is noteworthy that the higher proportion of patients from the governorates of Mount Lebanon and Beirut is justified, as these regions are considered Lebanon's main urban areas and its centers of social, economic, and cultural activities. Finally, including more participants would have led to more accurate results.

CONCLUSION

The use of OTC products in patients with CVD is quite frequent, and many patients exhibit inappropriate and potentially harmful OTC products practices. The potential interactions with prescription medications and patient diseases apply to patients with CVD worldwide and are not limited to a particular geographic area. Therefore, in order to ensure optimal patient outcomes, clinicians should question the use of OTC products during patient encounters and provide counseling regarding the risks and benefits associated with OTC product use.

CONFLICT OF INTEREST STATEMENT

Authors have no competing interests to declare.

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