PATTERN AND ECONOMIC ASSESSMENT OF UNUSED MEDICATIONS FOR CARDIOVASCULAR DISEASE TREATMENT IN METROPOLITAN MONTERREY, MEXICO

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SUMMARY

Underutilization and inadequate disposition of expired medicinal drugs represent an important problem. The objective of this study was describing the pattern and amount of unused cardiovascular drugs in Metropolitan area of Monterrey, in the Nuevo León state, Mexico. Through several dissemination ways, inhabitants were invited to deposit their unused medication at several collection centers distributed across the metropolitan area, the period of collection was of 12 months. Individual drugs were identified, counted, and classified according to the Anatomical Therapeutic Chemical (ATC) system. The difference among the grouped drugs was tested with ANOVA or Chi square as correspond. The cost of each drug identified was obtained through the consultation of price in at least three pharmacies. During the time of collection, a total of 207963 units were collected, of which lipid modifying agents were the more abundant, the estimated cost of all cardiovascular drugs was of 0.03 USD per inhabitant. These results shown that an important quantity of cardiovascular drugs is wasted and represent an important cost.

Introduction

The underutilization of drugs results in a loss of economic resources and reflects poor treatment compliance, in addition to representing a risk of accidental poisoning in children, environmental contamination and self-medication (Narvaez y Jimenez, 2012; Kozak *et al*., 2016; Paut Kusturica *et al*., 2016; Makki *et al*., 2019). Regarding the economic aspect, the World Health Organization reported that health spending is increasing faster than the rest of the world economy; In 2016, the world spent $ 7.5 trillion USD on health, representing close to 10% of the world's gross domestic product (GDP) (Xu *et al*., no date). It is estimated that across Organization for Economic Co-operation and Development countries in 2013 spending on drugs corresponded to 20% of the health budget (OECD, 2015). Therefore, one of the main challenges faced by health systems is finding the most efficient way to use the budget. This involves reducing losses due to the underutilization of pharmaceuticals. To design resource optimization strategies, it is necessary to know the causes of drug underuse, as well as the main types of unused drugs and the costs they represent (West *et al*., 2014; Bekker *et al*., 2018), mainly for the most prevalent diseases and the most expensive ones. Among these are cardiovascular diseases, as reported by Gracia-Vásquez and co-workers. They reported that cardiovascular drugs were the second group of pharmaceuticals with the highest underutilization in their study (Gracia-Vásquez *et al*., 2015).

Cardiovascular diseases are the most prevalent medical conditions with the highest mortality rate. They caused 32% of deaths worldwide in 2019 (World Health Organization, 2021) and 20% of deaths in Mexico in 2017 (Instituto Nacional de Estadística y Geografia, 2019). According to The Global Economic Burden of Non-communicable Diseases, in 2010, heart diseases cost 863 billion USD worldwide. This is estimated to increase by 22% by 2030 (Bloom *et al*., 2011). In Mexico, cardiovascular diseases, in conjunction with mental health conditions, are the dominant contributors to the global economic burden of noncommunicable diseases (Rosas-Peralta, *et al*., 2017).

The objective of this study was to determine the pattern of unused/expired cardiovascular drugs and estimate their cost in a sample of unused drugs collected in the Metropolitan area of Monterrey, Mexico (MMM).

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PATRÓN DE SUBUTILIZACIÓN Y EVALUACIÓN ECONÓMICA DE MEDICAMENTOS PARA EL TRATAMIENTO DE ENFERMEDADES CARDIOVASCULARES EN EL ÁREA METROPOLITANA DE MONTERREY, MÉXICO

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RESUMEN

La subutilización e inadecuada disposición de medicamentos caducos representa un importante problema. El objetivo de este estudio fue describir el patrón y la cantidad de medicamentos cardiovasculares no utilizados en el área Metropolitana de Monterrey, en el estado de Nuevo León, México. A través de varias vías de difusión, se invitó a los habitantes a depositar los medicamentos que no utilizan en diversos centros de acopio distribuidos en el área metropolitana, el período de acopio fue de 12 meses. Los medicamentos individuales fueron identificados, contabilizados y clasificados de acuerdo con el sistema Anatómica, Tera-péutica y Química (ATC, por sus siglas en inglés). La diferencia entre los fármacos agrupados se probó con ANOVA o Chi cuadrado según corresponda. El costo de cada medicamento identificado se obtuvo a través de la consulta de precio en al menos tres farmacias. Durante el tiempo de estudio se recolectaron un total de 207963 unidades, de las cuales los hipolipemiantes fueron los más abundantes, el costo estimado de todos los medicamentos cardiovasculares fue de 0,03 USD por habitante. Los resultados muestran que una gran cantidad de medicamentos cardiovasculares se desperdician y esto representa un costo importante.

PADRÃO DE SUBUTILIZAÇÃO E AVALIAÇÃO ECONÔMICA DE MEDICAMENTOS PARA O TRATAMENTO DE DOENÇAS CARDIOVASCULARES NA ÁREA METROPOLITANA DE MONTERREY, MÉXICO

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RESUMO

A subutilização e inadequado descarte de medicamentos vencidos representa um importante problema. O objetivo deste estudo foi descrever o padrão e a quantidade de medicamentos cardiovasculares não utilizados na área Metropolitana de Monterrey, no estado de Novo Leão, no México. Através de vários meios de divulgação, os moradores foram convidados a depositar os medicamentos que não utilizam em diversos centros de coleta distribuídos na região metropolitana, o período de coleta foi de 12 meses. Os medicamentos individuais foram identificados, contabilizados e classificados de acordo com o sistema Anatômico, Terapêutico e Químico (código ATC, segundo suas siglas em inglês). A diferença entre os medicamentos agrupados foi testada com ANOVA ou Chi quadrado, segundo corresponda. O custo de cada medicamento identificado foi obtido através da consulta de preços em pelo menos três farmácias. Durante o tempo de estudo foram coletadas 207.963 unidades, sendo os hipolipemiantes os mais abundantes. O custo estimado de todos os medicamentos cardiovasculares foi de US$ 0,03 por habitante. Os resultados mostram que grande quantidade de medicamentos cardiovasculares é desperdiçado, o que representa um custo importante.

Materials and Methods

The study was conducted in northeast Mexico, in the MMM in Nuevo Leon state. During 12 months, a group of professors and students from the School of Chemical Sciences of the *Universidad Autónoma de Nuevo León*, in collaboration with the State Ministry of Health, collected and classified medical drugs from several collection centers. The overall process included six different stages: (1) "Final disposal of non-utilized and/or expired medication" program dissemination, (2) drug collection from homes in Monterrey's metropolitan area (Nuevo Leon, Mexico), (3) random sampling of 30% of collected medication, (4) medication classification under the Anatomic Therapeutic Chemistry (ATC) system, (5) accounting and registration of solid drugs (tablets and capsules) from the cardiovascular group, and (6) cost estimation of non-utilized and/or expired medication and analysis of the results.

Program dissemination consisted of news bulletins that invited the public to deliver unnecessary, expired, or non-utilized medication to collection centers. The collection was conducted with containers specifically designed for the study; these were gathered at 28 different collection centers across several pharmacies in the region.

The collected medication was transported to the state delegation of the Ministry of Health for classification and registration based on stratified random sampling with proportional allotment. Once classified, the medicines were separated from their primary and secondary packages and kept stored under the custody of the Ministry of Health until final disposal. The packaging materials were treated according to the Official Mexican Standard (*Norma Oficial Mexicana*) NOM-161 that establishes the criteria to classify the special handling of waste (SEMARNAT, 2013). Upon final disposal, the medication was incinerated, according to the provisions of the Official Mexican Standard NOM-098-SEMARNAT 2002 (SEMARNAT, 2004).

The cardiovascular drugs were classified according to the ATC System; in addition, the following information was included: brand, generic name, potency, pharmaceutical formulation, administration route, origin, expiration date, and unit quantity.

The medications' cost was estimated by averaging the commercial cost of three medicines containing the active ingredient (patented and generic); the latter information was consulted by telephone call or through the web pages of different Mexican pharmacies. The medicine's unit cost was obtained by dividing the cost of the commercial package by the number of units (tablets/capsules) contained in the commercial package. The commercial value of the total sample (expired and/or unused

medications) was determined by multiplying the unit cost by the total number of tablets or capsules.

Results were grouped according to the ATC system and expressed as the number of units, percentages, and unit cost. The difference between groups was analyzed with chi-square or ANOVA as corresponded. The correlation between the unit cost and the number of units unused/expired was analyzed with Spearman′s correlation, and a cost estimation at the state and national levels was performed. For this, first, the cost of all samples was divided by the total population of municipalities where the sample was collected, obtaining the cost per inhabitant. The next step was to multiply the state or national population by the cost per inhabitant.

Ethics approval

Due to the descriptive nature of the study and considering that there was no human participation, we did not seek an ethics committee approval.

Results

The amount of expired and unused medications in the sample was 1,463,499 units, of which 207,963 units (14.2%) corresponded to medications to treat cardiovascular diseases (ATC-C). The number of units and the respective cost of each group of cardiovascular drugs are presented in Figure 1. A significant difference was found among the groups (p < 0.05).

Among cardiovascular drugs, lipid modifying agents (ATC-C10) were the more abundant, followed by drugs that act on the renin-angiotensin system (ATC-C09) with a total of 57,593 (27.7%) and 44,816 (21.5%) units, respectively. The C04 group was the least frequent. The three most abundant drugs of each subclass are presented in Table I.

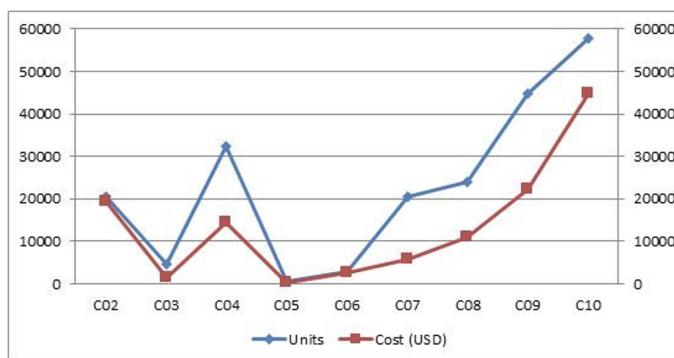The estimated cost for the total sample of all cardiovascular drugs in MMM was

Figure 1. Units and cost of underused cardiovascular drugs classified by the ATC system. C01: Cardiac therapy, C02: Antihypertensives, C03: Diuretics, C04: Peripheral vasodilators, C05: Vasoprotective, C07: Beta-blocking agents, C08: Calcium channel blockers, C09: Agents acting on the renin-angiotensin system, C10: Lipid modifying agents.

121,836 USD. This corresponds to 0.03 USD/per inhabitant. Considering the state and national population, the cost of wasted cardiovascular drugs could be 135,000 and 3,810,000 USD, respectively. The unit cost for each group of Cardiovascular Disease (CVD) is presented in Figure 1. The group with the lowest cost was C04, while the group with the highest cost was C01 (p< 0.05). According to the active principle, pravastatin was the most economic drug while the most expensive drugs were the combinations amlodipine/atorvastatin, and verapamil/trandolapril.

A correlation between unit cost and the number of unused units was not found (p>0.05), so the price seems to not affect the wasted drugs.

Discussion

In this study, a description of the pattern and estimated costs of unused cardiovascular drugs in MMM, the second most important metropolis of Mexico, is presented. According the literature, the most frequently underused drugs are analgesics (23.3%), antibiotics (18%), and those used for chronic conditions (17%) and mental health issues (8.3%). Although causes of medicine non-utilization can vary greatly, the most prevalent are related to the patient's health improvement (42.4%), adverse effects (0.5%), and forgetfulness (5.8%) (Law *et al.*, 2015).

Knowing the degree of underutilization of prescribed drugs can be useful for several reasons; mainly to define

programs that reduce economic loss, reduce the risk of self-medication, and avoid environmental contamination associated with inappropriate disposal. The cost of drug waste is high, in the United States, one of the world's top medical waste-producing nations, annually produce over 3.5 million tons of medical waste with an average disposal cost of $790 per ton (Bakiu and Durmishaj, 2018).

The results showed that among CVD, the drugs that reduce serum lipids (ATC-C10) were the most wasted followed by drugs that act on the renin-angiotensin system (ATC-C09). Both drug types are included in some combined regimens to prevent or treat cardiovascular diseases in which they have been demonstrated to be cost-effective (Yusuf *et al.*, 2014). This finding could be explained by the high prevalence of hypertension and dyslipemia in Mexico and probably the poor adherence to treatment by this patients. Similar results have been reported by Schuh and Hewuse (2015), where antihypertensive and lipid-lowering drugs occupied the second and fourth positions of the most underutilized drugs (Schuh and Hewuse, 2015).

While the estimated cost of unused CVD in MMM was 121,836 USD, the real cost could be much higher, since the amount of collected drugs is likely a fraction of what remains in patients' homes (Schuh and Hewuse, 2015).

TABLE I
MAIN DRUGS UNDERUSED PER ATC GROUP

Group	Protein	Total amino acids	Total phenols
C01	isosorbide dinitrate (7,692)	glyceryl trinitrate (4,026)	digoxin (3,380)
C02	prazosin (4,005)	methyldopa (433)	clonidine (40)
C03	hydrochlorothiazide (9,893)	furosemide (9,717)	chlorthalidone (7,889)
C04	bufenin (666)		
C05	diosmin (872)	diosmin/hesperidin (809)	calcium dobesilate (340)
C07	metoprolol (18,188)	propranolol (3,619)	atenolol (1,808)
C08	nifedipine (15,804)	amlodipine (3,373)	verapamil (2,284)
C09	enalapril (18,854)	captopril (10,442)	losartan (8,085)
C10	pravastatin (27,902)	bezafibrate (23,976)	atorvastatin (1,222)

C01: Cardiac therapy, C02: Antihypertensives, C03: Diuretics, C04: Peripheral vasodilators, C05: Vasoprotective, C07: Beta-blocking agents, C08: Calcium channel blockers, C09: Agents acting on the renin-angiotensin system, C10: Lipid modifying agents.

Furthermore, probably not all patients have the habit of taking them to collection centers; also, the final disposal price should be added to the total cost. With the previous considerations, the estimated cost of unused CV drugs per inhabitant was 0.03 USD, a low value compared with other studies, however, these studies have focused in overall drugs not a specific group as CVD. For example, a report in Austria extrapolated the cost of expired drugs from the local to the country level and the result was 21 € per inhabitant (Vogler and de Rooij, 2018). The cost per inhabitant of all wasted drugs is probably much higher in Mexico, so more studies of this respect are needed.

It was found that the unit cost did not correlate with the number of wasted units; the reason for this is unknown, although it could be due to the fact that most patients, do not know the cost of drugs, so that, they have the same consideration and treat to this drugs. In Mexico, a great majority of patients receive CVD without cost by mean of social security.

The problem related to drug underutilization could be reduced by enforcing the rol of community pharmacist, specially in developing countries, like Mexico. The advice of the pharmacist is a strategy to ensure that the patient becomes more aware of the importance of therapeutic adherence and consequently encourages the rational use of drugs, including the adequate disposal of unused drugs. This has been demonstrated in some countries, where pharmaceutical advice on the adequate disposal of unused medications has been effective since a higher percentage of the patients who received this advice did not store medications in their homes, contrary to those who were not advised in this respect (Chien *et al.*, 2013; Vogler *et al.*, 2014). The joint effort between different stakeholders, such as government institutions, the manufacturer, organizations, the public, and healthcare professionals can help minimize drug waste by implementing policies and increasing public and healthcare provider awareness (Makki *et al.*, 2019).

Conclusions

The estimated costs of wasted drugs to treat cardiovascular diseases in MMA are considerable high and represent an important loss of economical resources and health care spending. This could be reduced with the design of more efficient distribution and dispensing systems, and a rational use in patients. Implementing awareness programs in the general population, with the participation of pharmacists, also could contribute to this respect.

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