

Research Article

Open Access

Eye Drop Self-medication: Comparative Questionnaire-based Study of Two Latin American Cities

Gabriel E. Marquez¹, Hildegard Piñeros-Heilbron², Victoria M. Sanchez¹, Victor E. Torres³, Ana L. Gramajo¹, Claudio P. Juarez¹, Fernando Y. Peña² and Jose D. Luna^{1*}

¹Centro Privado de Ojos Romagosa-Fundación VER, Córdoba, Argentina

²Fundación Universitaria San Martín - Fundación Oftalmológica del Caribe, Barranquilla, Colombia

³CEA-CONICET y Facultad de Ciencias Económicas, UNC, Córdoba, Argentina

Corresponding author: José D. Luna, M.D., Departamento de Oftalmología, Centro Privado de Ojos Romagosa-Fundacion VER, Deán Funes 432, (5000) Córdoba, Argentina, Tel: 54-351-4211334; Fax: 54-351-4234848; E-mail: fundacionver@gmail.com

Received date: Feb 09, 2014, Accepted date: Mar 17, 2014, Published date: Mar 24, 2014

Copyright: © 2014 Marquez GE, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Background: A broad spectrum of ocular symptoms are treated by self-medication with commercial eye-drops. This behavior threatens individuals' visual health. In Latin America, evidence is poor.

Objective: To detect, characterize and compare patterns of ophthalmic self-medication between Córdoba (Argentina) and Barranquilla (Colombia).

Design: Analytic, cross-sectional and comparative population-based study. Setting: Two private tertiary care ophthalmology centers from Córdoba, Argentina, and Barranquilla, Colombia.

Participants: Patients 18 years of age or older who consulted for the first time in this two institutions during August-November 2009, were included. A number of 570 patients were enrrolled.

Methods: Data collected through a semi-structured questionnaire. Main outcome measure: To determine the frequency of self-medication with eyedrops on a specific population of two cities in Latin America.

Results: Comparable rates of ocular self-medication were found (25.6% and 25.7% for Cordoba and Barranquilla, respectively). The percentage of men and women who self-medicated was not significantly different between both samples. The major source of eye drops recommendation in the Argentineans patients was the pharmacist (31%); while the social source was predominant in Colombian individuals (53%). In Cordoba, the most frequently used product was a non-steroidal anti-inflammatory drop in combination with a vasoconstrictive agent (32%); while in Barranquilla, antibiotic eye drops were preferred (33%). Self-medication was higher between the ages of 31 and 50 years old in Argentinean citizens (28%) and between 18 to 31 years old in the Colombian community (39%). This habit was found mostly in patients who completed university studies in Cordoba (33%); in Barranquilla, individuals with lower educational level practice more this behavior (36%).

Conclusion: In both populations, patients commonly treat ocular conditions by self-medicating. Currently, an increasing number of eye drops are obtainable without prescription and a high percentage of self-medicated patients in both samples ignore the possible side effects of the used medication.

Keywords: Self-medication; Eye drops; Latin America; Ocular deseases; OTC drugs; Questionnaire-based study

Introduction

Self-medication is defined by the World Health Organization as the selection and use of medicines by individuals to treat self-recognized illnesses or symptoms [1]. This behavior includes purchasing drugs without a prescription, using leftover doses from previous prescriptions, sharing drugs with other family members or social groups, or misusing the medical prescription either by prolonging,

interrupting or modifying the dosage and the administration period [2-4].

A wide spectrum of symptoms and pathologies are lessened by this practice, with eye conditions being no exception. It is well known that this kind of attitude and practice carries pharmacological and toxicological risks [5], not only related to the potential severe side-effects of the topical drug itself, but also dangerous as a result of inappropriate treatment or failure to seek prompt medical care, thus leading to a postponement in diagnosis and, in turn to unintended consequences.

Several over-the-counter (OTC) drugs are available to the public without prescription, which include traditional pharmacy preparations

and medications that have been deregulated from their previous status as prescription medicines. Policies regarding these OTC medicaments vary around the world. Nevertheless, these substances are accessible for routine use and commonly sold without a medical prescription in pharmacies or even in supermarkets. Not only OTC medications can be used as a resource for self medication but also non-prescribed drugs achieved without a prescription can be another common supply for patients self medication in many countries around the world. There have been consistently high rates of use of non-prescribed drugs found in different developed countries, ranging from 22% to 67% for all ages [6-8]. In Latin America, this practice has been widely supported [2-4,9,10]. This population has a tendency to purchase and use a large variety of chemotherapeutic agents, which has also been confirmed in a study about antibiotic misuse in a Latin American population in the Unites States of America [11].

Regarding self medication in ophthalmic practice, the evidence is scarce in Latin American population. Our research group, as well as some other South American investigators, have studied eye drop misuse in ophthalmological patients recently [10,12], nevertheless, up to date, there are no comparative studies between different ophthalmic private practice populations with similar cultural background and analogous cities trying to determine some pattern of self-medication in ophthalmology.

In our study, we performed an analytic, cross-sectional and comparative population-based study on patients seen at two private tertiary care ophthalmology clinics, one of which was located in Cordoba (Argentina) and the other in Barranquilla (Colombia).

Methods

We performed a comparative questionnaire-based study of patients seen at two private tertiary care ophthalmology clinics, the Centro Privado de Ojos Romagosa, in the city of Cordoba, Argentina, and the Fundación Oftalmológica del Caribe, in Barranquilla, Colombia. The city of Cordoba is one of the largest and most important cities of Argentina. According to the data from the National Census of and Population, Housing Households 2010 (http:// www.censo2010.indec.gov.ar/index.asp), the city's estimated population is 1,329,604 (the second most populous metropolis in the country). Barranquilla, on the other hand, is the fourth largest city of Colombia, and according to projections based on the 2005 General Census the National Bureau of Statistics (http://www.dane.gov.co/ index.php?option=com_content&view=article&id=307&Itemid=124), 1,186,640 people are currently living in this urban area. These two regions have comparable demographic characteristics, with each being important historical, educational, cultural, economic and financial centers of their respective countries and having appreciable industrial and tourist development.

In this survey, we included every patients 18 years of age or older who had been seen for the first time at these institutions between August and November 2009.

All patients underwent a short semi-structured questionnaire specially prepared by the authors. The questionnaire, conducted simultaneously at both institutions, collected demographic data such as patient's age, gender and level of education and also details concerning the use of medication in the form of eye drops over the last 12 months. Self-medication was defined as the use of eye drops without a medical prescription, with participants who admitted "selfmedicating" also being asked about the type of medication used, the reasons which led to this practice, their knowledge about the components of the product or its adverse reactions, whether they had read the patient information leaflet, and the reasons for not consulting a specialist prior to using the medication.

All participants were informed about the scope and purpose of the study and told that it was voluntary to participate, without any compensation, and that their medical assistance would not be compromised if they refused or decided to participate in the survey. An informed consent was obtained in every case prior to being given the questionnaire, and no patient refused to participate. This study received Institutional Review Board approval from the Oulton-Romagosa Joint Committee on Clinical Investigation (C.I.E.I.S OULTON-Romagosa) in Argentina and also from the Comité de Investigaciones de la Fundacion Oftalmologica del Caribe (FOCA) and the Clínica Oftalmológica del Caribe in Colombia.

The interview was conducted by five medical doctors (three from Argentina and two from Colombia) who were previously trained during a pilot trial that served to improve the interrogation technique and refine the questionnaire. Interviewers in both countries remained in contact during the preparatory phase to unify criteria.

The types of medication used were classified into the following groups: antibiotics, anti-allergic drugs, steroids (STR), non-steroidal anti-inflammatory drugs (NSAIDs), vasoconstrictors, saline solution and other drug not included in the previous classifications. When the patient used preparations that included two or more drugs, each of these associations were considered separately. When the interviewed subject failed to remember the drug used, the answer was included under the category of "undetermined drugs". Homemade topical medications were not include in the survey, because patients do not usually recognize the use of these substances, either by prejudice, shame or simply because they do not considered this practice as important information for the doctor, and this could influence the results of the investigation.

Regarding educational level, 5 divisions were established: 1. illiterate and incomplete elementary school; 2. completed elementary school; 3. completed high school; 4. completion of University or college and 5. no data available.

The four age groups were arbitrarily assigned: 18-30 years old, 31-50, 51-70, and older than 71.

All results were analyzed using a descriptive analysis. The investigator who performed the statistical analysis of the data (VET) does not belong to any of the centers in which the survey was conducted, nor had contact with the interviewers or patients. The data was entered into a database and analyzed using MS Excel (2003) and SPSS version 11.5 with the level of significance in the statistical analysis being $p \le 0.05$.

Regarding the statistical methods, we first performed an exploratory analysis of the data in both countries in order to present the main features of each population separately. Then, for the second stage, in order to compare the Argentina vs. Colombia data, a test similar to the T Test was performed on the two percentages (p1 and p1, for example) to reveal whether there were any significant differences.

To carry out this test a null hypothesis was applied stating that both percentages were equal, whit the alternative claim being that they were different. The test stadistic used, z, is given by:

Page 2 of 6

$$z = \frac{(p_1 - p_2) - (\pi_1 - \pi_2)}{\sqrt{\frac{\pi_1(1 - \pi_1)}{n_1} + \frac{\pi_2(1 - \pi_2)}{n_2}}}$$

where (in terms of what sustains the null hypothesis) $p_1 - p_2 = 0$ and π_1 and π_2 represent the percentages of each group. In this way, the *z* value obtained was compared with the critical value specified in the statistical table to determine if the null hypothesis was accepted or rejected, using a confidence level of 95% [13].

Results

Five hundred and seventy subjects were interviewed in both cities. All accepted to answer the survey and did this in a complete form. In Cordoba city (Argentina), the sample included 379 patients distributed in 162 males (43%) and 217 females (57%) while in Barranquilla city (Colombia) 191 participants were enrolled, with 114 being males (60%) and 77 females (40%). The average age of the interviewed population was 46.8 years old (range: 18-85) and 44.9 years old (range: 18-92) for Argentinean and Colombian inhabitants, respectively.

Comparable rates of ocular self-medication were found in both studied samples (25.6% for Argentina and 25.7% for Colombia correspondingly (Table 1).

In relation to gender, 20% of Argentinean women and 22% of Colombian females admitted self-medicating with eye drops within the last year. Among men, this rate was 33% and 28% for Argentineans and Colombians respectively. Both these cases the differences were not statistically significant. However, when each population was analyzed separately, it was revealed that self-medication in Argentina was significantly affected by gender (p=0.004), with males being more likely to use eye drop medications than females.

When studied the age factor, both communities when pooled together showed a greater tendency to self-medication in younger patients, although no significant differences were found between the groups themselves for each population.

When asked about the major source of recommendation (Figure 1), in Argentina it was stated to be a pharmacist (31% of the interviewed patients), followed by 25% of the self-medicated individuals who used drugs at their own discretion, without any external advice. A further 24% of the consulted people in Argentina accepted suggestions from their social environment. The largest fraction of Colombians patients, however, preferred the counseling of a relative or friend (53%), followed by a pharmacist's advice (29%).

When asked about the type of drug used to self-medicate in both groups of interviewed people, there was a substantial amount of individuals who could not recall the medication employed in the last year, with this answer occurring almost at the same percentage for the two groups (Argentinean 14.4%; Colombian 18.4%; p=0.55) (Figure 2).

In Córdoba, Argentina, the most frequently used topical product was a NSAID in combination with a vasoconstrictive agent (32%), with this eye drop being significantly more utilized than in the Colombian group (2.04%; p< 0.0001). Conversely, the most common eye medication employed by the Colombians was topical antibiotics (32.6%), with this difference being significant when compared to the Argentinean population (4%; p< 0.0001).

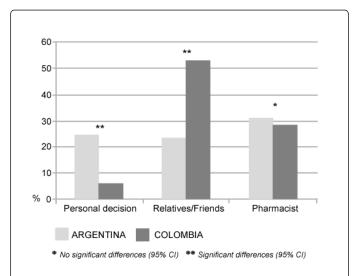
Taking into account educational levels, self-medication habits were found mostly in patients from Argentina who had completed university studies (33%), in contrast to patients from Colombia, where individuals with lower educational levels practiced this behavior more (36.4%; Table 1).

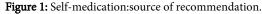
Characteriastics	Argentina					Colom	Colombia				
											Arg vs Col
	n	No Self	Self	%	Р	n	No Self	Self	%	Р	
Gender	379	282	97	25.6		191	142	49	25.7		
Male	162	108	54	33.3	0.004	114	82	32	28.1	0.404	0.37
Female	217	174	43	19.8		77	60	17	22.1		0.6
Age group	379					190					
18-30	106	76	30	28.3	0.535	41	25	16	39	0.156	
31-50	116	83	33	28.4		86	66	20	23.2		
51-70	100	78	22	22		44	34	10	22.7		
70 or older	57	45	12	21		19	16	3	15.8		
Education	343					171					
Elementary School	92	73	19	20.6	0.146	33	21	12	36.4	0.247	
High School	157	118	39	24.8		96	69	27	28.1		
University/College	94	63	31	33		42	34	8	19		

Table 1: Self-medication according to socio-demographic characteristics.

Page 3 of 6

In both group of patients, we observed a considerable lack of knowledge about the medications used to self-medicate (Figure 3), with 87.6% of individuals from Argentina and 96% from Colombia not being able to identify any of the eye drops they have employed at the moment they answered the questionnaire and with no significant differences found between these two groups (p=0.062). In addition, 97% of the people from Cordoba (Argentina) and 98% from Barranquilla (Colombia) were unaware of the possible adverse reactions of any of the drugs that they had used. Moreover, the percentage of patients who had read the information leaflet was only 25% and 4% in Cordoba and Barranquilla, repectively, but with the Argentinean inhabitants being more likely to do this (p<0001).





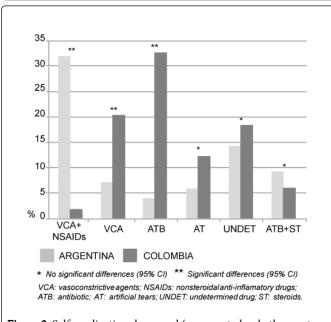


Figure 2: Self-medication:drug used (represented only the most frequent drugs utilized).

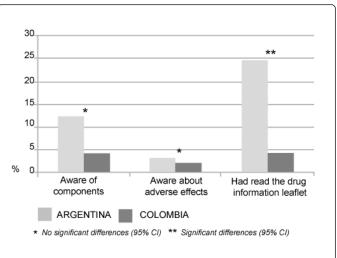


Figure 3: Self-medication: know ledge of the used drug.

Discussion

Several studies conducted in many populations around the globe have demonstrated that self-medication is a common practice, even in populations with very different characteristics. Is known that the use of non-prescribed drugs by an individual, results from a genuine or apparent need to mitigate or attenuate discomfort, with this behavior having been related to various sociodemographic, sociocultural and socioeconomic factors, including age, sex and education, among others [11,12,14,15].

Our study reveals comparable rates of ocular self-medication in the Argentinean and Colombian groups confirming that this practice is equally common in both countries taking into account ophthalmic patients. One out of every four patients used eye drops without prescription in both studied populations. This practice, however, is not exclusive to these two Latin American countries, as shown by the study of Santos et al which described approximately the same percentage of self-medication in a larger population of elders from Goiana, Brazil [16]. Nevertheless, these rates are fairly low when compared to frequencies published by Carvalho et al. [10], who reported a prevalence of eye self-medication as high as 40.5%. This discrepancy may be explained on the basis of the study design, with the main difference being that the paper by Carvalho et al. only sought to identify the practice of self-medication in the treatment of ocular emergencies, whereas in our study the questionnaire was carried out on patients presenting and requesting ophthalmic attention at two private tertiary care ophthalmology clinics, and who were not necessarily on emergency visits. We also observed another difference between these two investigations, which was that ours only contemplated patients who had self-medicated during the previous year and who had only taken into consideration the use of commercial eye drops, rather than the homemade topical medications considered in Carvalho's study [10]. These substances were likely to be used by the people in our sample, but we decided not to count them at stated in the methods section. These kind of medicines are preparations usually made by the patient with products often easily found at home, like lemon juice, milk of lactating woman, salt water and different types of teas and beverages, among others. Including them could increased the

Page 4 of 6

percentage of people who self-medicated in our populations to be more comparable to the 40% of Carvallo.

Ophthalmic self-medication seemed to be independent of gender in the Colombian population, as well as in the Brazilian cohort [10]. However in the Argentinean population a higher tendency to use this approach was found in men. Regarding age, all these three Latin American studies demonstrated that the misuse of ophthalmic topical preparations was independent of age, despite there being a nonsignificant tendency toward people from 18 to 50 years old to selfmedicate in all three countries.

In our study, the major source of recommendation, with respect to which eye drop to buy for self-medication, was markedly different for each of the studied populations. In the Argentinean residents, the pharmacist, the patient's personal decision and counseling from friends or family were the main reasons for drug misuse, with roughly the same percentages occurring for each of the three responses. In contrast, in Colombian patients, a friend or family suggestion seemed to be the most important motive in the election of which eye drop to obtain. On performing a comparative analysis between the variable "sources of recommendation" from the two studied groups, it could appreciated that Argentineans were significantly more likely to consider themselves qualified to decide which medication to use (p=0.001). In contrast, Colombian residents were significantly more accustomed to accepting the recommendation of a friend or a family member as the decisive influence for using a non-prescribed eye drop (p=0.001). Regarding the pharmacist as the source of reference, this was a common indicator in both populations (30.9% and 28.6% for Cordoba and Barranquilla, correspondingly) with a non-significant difference occurring between them (p=0.77).

The influence of the pharmacist's opinions on patients in deciding which drug is useful for their complaint is well known all over the world, especially in Latin American countries [17,18], with Pereira et al reporting in a population of Brazilian university students that 24.5% of the medicine used for self-medication was acquired by pharmacist's advice [18]. Related to this, it is worth noting that the recommendation of drugs by the pharmacies is not permitted by law either in Brazil, in Colombia or in Argentina. Therefore, better control in drug selling may rationalize the utilization of ophthalmic medicines.

Johnson et al. [19] stated that the practice of self-medication was frequent in a highly educated population of Oregon in the United States, thereby indicating that educational level could be a significant factor in the context of self-medication. However, in the present report, we studied people of different levels of education and did not find any statistical significant differences between dissimilar levels of instruction or between the same educational rank and different cities. In fact, we observed an opposite tendency in this matter, as despite showing that in the Argentinean population the most educated people tended to self-medicate, in the Colombian population less educated people practiced this method more often. These different trends could be due to many different causes such as greater or lesser access to ophthalmologists in different countries, differences in health coverage in each population or any other reason for which this study was not designed to investigate.

An important fact is that there are 489 ophthalmologists per million inhabitants in the city of Cordoba, while in Barranquilla this number drops to 51. Whereas the rate of self-medication found by us in these two populations was similar, maybe the number of ophthalmologists per million inhabitants is not a determining factor for this practice, at least in the studied populations.

In a study carried out in India by Rajani Kadri et al. about selfmedication with OTC ophthalmic preparations, they found that different kinds of antibiotics were the drugs most frequently acquired by the study group, followed by unknown drugs at 35% and decongestant eye drops at 29% [20]. This figure is very similar to the Colombian population, where antibiotics were the most commonly used medication, followed by a large population (18%) who did not remember the medication applied, with this last percentage of individuals who could not determine the type of drug utilized, being similar to that found among the Argentinean sample (14%). However, the most popularly used eye drop among the self-medicated people from Argentina at 32% was a decongestant in combination with a NSAID. It is noteworthy that in Argentina and Colombia there are few OTC eye preparations available, including some lubricants (artificial tears) and a decongestants in combination with NSAIDs eye drop.

A limitation of our study was the relative small number of patients in each group as well as the fact that the questionnaire was performed in patients that were visiting private eye clinics. As these were normally individuals with health insurance, as they were visiting private ophthalmology institutions, then the results might not be representative of all social strata. Future studies should include a more heterogeneous sample in order to reduce such bias. Another aspect to be considered is that, notably, there was a significantly lower recruitment in the Colombian group. This was due to the different number of patients attending this two institutions being almost twice in Argentinean clinic. Thus, by including in the sample only those patients attending for the first time to seek care, the Argentinean sample was larger than the Colombian one.

The safety of any drug is determined by two attributes: the intrinsic capacity of the drug to do harm and the quality of the information provided to the public about its use. Our study has demonstrated that not only are there 25% of people in both groups that self-medicated with eye drops, but also that there was a very low percentage of people who actually read the drug information leaflet. Consequently, a high percentage of self-medicated patients in both countries were not aware of the components present in used drops, and were therefore ignorant about all their possible ocular side-effects, thus making all these eye drops potentially unsafe for patient use.

Several factors in Latin Amercia, such as easy accessibility to a large number of drugs, the lack of official control over the marketing of these substances, the inherent weaknesses of health systems, the absence of the state as a source of information instructing about the risks of this custom, the influence of social environment and even cultural standards, contribute to the magnification and perpetuation of this manner. While it was not the purpose of this paper to investigate these aspects, there is no doubt that each of these factors influences the prevalence and the characteristics of self-medication in each of the studied populations. Further investigations oriented to explore these areas will be needed.

Conclusions

In conclusion, in both populations patients commonly attempt to treat conditions that probably require ophthalmologic care by using self-medication with non-prescribed eye drops. Self-medicated patient from Cordoba (Argentina) would be more probably a man between 18 to 50 years old, with a University or college degree. In addition, his source of recommendation would often be a pharmacist and he would probably seek a combination of a vasoconstrictive agent plus a NSAID. On the other hand, the Colombian patient would most likely be either a man or a young woman (18 to 30 years old) with a poor educational level. Moreover, his or her source of recommendation would probably be a friend or a family member, with an antibiotic eye drop being the most likely medication. The unawareness of the chemotherapeutic agents properties and ocular-induced side effects that could be caused by the employed OTC medication reached high levels in both groups. Further studies to determine if factors such as the educational level of the patient or the rol of the pharmacist are determinant in the phenomenon of self-medication are needed.

Acknowledgements

We thank Dr. Paul Hobson, native speaker, for revision of the manuscript.

References

- Hardon A, Hodgkin C, Fresle D (2004) How to investigate the use of medicines by consumers. World Health Organization and University of Amsterdam, Geneva.
- Paulo LG, Zanini AC (1988) [Self-medication in Brazil]. AMB Rev Assoc Med Bras 34: 69-75.
- Arrais PS, Coelho HL, Batista Mdo C, Carvalho ML, Righi RE, et al. (1997) [Profile of self-medication in Brazil]. Rev Saude Publica 31: 71-77.
- Loyola Filho AI, Lima-Costa MF, Uchôa E (2004) Bambuí Project: a qualitative approach to self-medication. Cad Saude Publica 20: 1661-1669.
- 5. Fraunfelder FT, Meyer SM (1984) Ocular toxicology update. Aust J Ophthalmol 12: 391-394.
- Haggerty RJ, Roghmann KJ (1972) Noncompliance and self medication. Two neglected aspects of pediatric pharmacology. Pediatr Clin North Am 19: 101-115.
- Du Y, Knopf H (2009) Self-medication among children and adolescents in Germany: results of the National Health Survey for Children and Adolescents (KiGGS). Br J Clin Pharmacol 68: 599-608.

- Schmidt CS, Schulte B2, Wickert C2, Thane K2, Kuhn S2, et al. (2013) Non-prescribed use of substitution medication among German drug users--prevalence, motives and availability. Int J Drug Policy 24: e111-114.
- [No authors listed] (1997) Multicenter study on self-medication and selfprescription in six Latin American countries. Drug Utilization Research Group, Latin America. Clin Pharmacol Ther 61: 488-493.
- Carvalho RS, Kara-José N, Temporini ER, Kara-Junior N, Noma-Campos R (2009) Self-medication: initial treatments used by patients seen in an ophthalmologic emergency room. Clinics (Sao Paulo) 64: 735-741.
- 11. Larson EL, Dilone J, Garcia M, Smolowitz J (2006) Factors which influence Latino community members to self-prescribe antibiotics. Nurs Res 55: 94-102.
- 12. Marquez GE, Torres VE, Sanchez VM, Gramajo AL, Zelaya N, et al. (2012) Self-medication in ophthalmology: a questionnaire-based study in an Argentinean population. Ophthalmic Epidemiol 19: 236-241.
- 13. Taro Y (1967) Statistics: An introductory analysis. (2nd edn). Harper and Row, New York.
- Bortolon PC, de Medeiros EF, Naves JO, Karnikowski MG, Nóbrega Ode T (2008) [Analysis of the self-medication pattern among Brazilian elderly women]. Cien Saude Colet 13: 1219-1226.
- 15. Bush PJ, Rabin DL (1976) Who's using nonprescribed medicines? Med Care 14: 1014-1023.
- Santos TR, Lima DM, Nakatani AY, Pereira LV, Leal GS, et al. (2013) Medicine use by the elderly in Goiania, Midwestern Brazil. Rev Saude Publica 47: 94-103.
- 17. Kamat VR, Nichter M (1998) Pharmacies, self-medication and pharmaceutical marketing in Bombay, India. Soc Sci Med 47: 779-794.
- Galato D, Madalena J, Pereira GB (2012) [Self-medication among university students: the influence of the field of study]. Cien Saude Colet 17: 3323-3330.
- 19. Johnson RE, Pope CR (1983) Health status and social factors in nonprescribed drug use. Med Care 21: 225-233.
- Kadri R, Hegde S, Kudva A, Achar A, Shenoy S (2011) Selfmedication with over-the-counter ophthalmic preparations: is it safe? Int J Biol Med Res 2: 528-530.

Page 6 of 6