ORIGINAL ARTICLE

ANALYSIS OF MARKET DATA REGARDING THE MEDICINES USED IN TREATMENT OF DYSLIPIDAEMIA

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Abstract

Dyslipidaemias are some of the most frequent metabolic diseases encountered in medical practice. Due to the increasing number of patients suffering from dyslipidaemia, its treatment is frequently on medical prescriptions presented to pharmacies. It was analysed a volume of 360 of patients and THEIR medical prescriptions provided by 12 pharmacies from Cluj-Napoca during the year 2010. The drugs most frequently prescribed in the treatment of some forms of dyslipidaemia have been the following: *Simvastatin®10, Simvastatin®20, Simvastatin®40, Rosuvastatin®5, Rosuvastatin®10, Rosuvastatin®20, Atorvastatin®10, Atorvastatin®20, Atorvastatin®40, Fenofibrat®160, Omacor®*. All patients considered, who has been administered one of these drugs, were chosen so that to respect the homogeneity on each age category, namely, the age's interval is quite symmetrically comparing to the average age. The aim of this paper was to find the most frequently prescribed drug for dyslipidaemia. Also, the median differences between the younger and older groups were tested for statistical significance using the Mann-Whitney test. In order to test the effect of medical treatment on 12 subgroups corresponding to the period of time studied, namely, on 12 months, a Kruskal-Wallis nonparametric test was used.

Rezumat

Dislipidemiile reprezintă unele dintre cele mai frecvente boli metabolice întâlnite în practica medicală. Datorită creşterii numărului de pacienţi având dislipidemie, tratamentul asociat acesteia se întâlneşte frecvent în prescripţiile medicale prezentate la farmacii. S-a analizat un volum de 360 de pacienţi, respectiv de prescripţii medicale provenite de la 12 farmacii din Cluj-Napoca, pe perioada anului 2010. Medicamentele cele mai frecvent indicate în tratarea câtorva forme de dislipidemie au fost: *Simvastatin®10, Simvastatin®20, Simvastatin®40, Rosuvastatin®5, Rosuvastatin®10, Rosuvastatin®20, Atorvastatin®10, Atorvastatin®20, Atorvastatin®40, Fenofibrat®160, Omacor®*. Pacienţii care au utilizat unul din aceste medicamente, au fost selectaţi astfel încât să respecte omogenitatea pe fiecare categorie de vârstă, şi anume, intervalul vârstei pacienţilor este aproximativ simetric comparativ cu vârsta medie. Scopul lucrării de faţă a fost de a stabili care e medicamentul cel mai prescris pentru tratarea dislipidemiei. De asemenea, s-a evaluat diferenţa medianelor (testul Mann-Whitney) între grupurile formate sub şi peste media de vârstă. Pentru a testa efectul tratamentului medicamentos pentru cele 12 eşantioane corespunzătoare celor 12 luni de studiu, s-a folosit o analiză neparametrică multifactorială.

Keywords: dyslipidaemia, cholesterol, antihyperlipidaemic drugs, pharmacies, statistical approach

Introduction

The pharmaceutical industry has had a spectacular development along the 20th century and in the beginning of the 21st century [8, 9], having new challenges. The new changes in industry lead to new strategies and portfolios. Therefore, trying to produce new scientific discoveries and to find the right strategies fitted for the new challenges, this industry become immersive and changeable at the same time. One can say that nowadays the major pharmaceutical companies spend a lot of money on pharmaceutical marketing which is aligned closer to the consumption capacity of patients. For this reason, the studies on pharmaceutical market are indispensable [2-4, 9].

The importance of dyslipidaemia results from their epidemiological, biological and economic impact. Epidemiological impact results from the fact that it has a high prevalence for all the population, therefore, dyslipidaemia may be considered a disease of population. Hypercholesterolemia plays a crucial role in the pathogenesis of coronary atherosclerosis, which is considered the first cause of morbidity and mortality in the world [10].

Dyslipidaemia represents an important cardiovascular risk factor. The parameters considered the most significant for atherogenesis are: increases of total cholesterol, increases of LDL (low density lipoproteins, also known as "bad cholesterol"), of VLDL (very low density lipoproteins), of triglycerides and decreases of HDL (high density lipoproteins, called "good cholesterol") [7, 10].

Treatment costs are significant, both for individuals and for medical system. The costs are for: treatment of cardiovascular diseases, screening and treatment of patients with risk factors.

Lipid-lowering drugs decrease plasma levels of various lipoprotein fractions, combat atherosclerosis and reduce mortality from coronary heart disease. Hyperlipidaemias are a complex group of diseases that can be: primary and secondary. Primary hyperlipidaemia results from monogenic defects or from interaction of genetic factors with those of environment. Secondary hyperlipidaemia occurs in some metabolic diseases: hyperglycaemia (diabetes mellitus), alcoholism, hypothyroidism, biliary cirrhosis [10].

This study is a pharmaceutical market research with the purpose of highlighting the most prescribed drug for treatment of dyslipidaemia. In order to find this, the study is concentrated on two non-parametric tests. The first test takes into account two groups of drugs composed by age criteria, namely, drugs corresponding to the patients under and over average age. The second test compares 12 groups of drugs corresponding to the 12 months of the study.

Materials and Methods

The data collection was a sequential well-defined time period, namely 12 months. We considered a total of 360 medical prescriptions corresponding to 360 patients given by the family and specialist physicians during 2010 year. The sample selected was a number of 30 medical prescriptions per month for each drug considered provided by a pharmacy. The database on dyslipidaemia study was collected from 12 community pharmacies from Cluj-Napoca so that the sample selected to be homogenous on each month considered. For this reason, the period of one month was divided in three equal parts. The selected medical prescriptions were taken random from the beginning, the middle, respectively, the end of the considered month using simple randomization selection.

The representativeness of this experiment composed from a sample of 360 patients provided by 12 pharmacies from Cluj-Napoca is given by the representative average error which is proportional to the variance parameter and inverse proportional to the sample volume:

$$\Delta = z_{\alpha/2}\sqrt{\frac{p(1-p)}{N}},$$

where p = m/n the frequency of the characteristic variable (*m* - the average, respectively, *n* - the size), *N* - the number of pharmacies and $z_{\alpha/2}$ - the appropriate normal deviate obtained from statistical table [5, 11].

The characteristic variable was constructed as the average of frequencies corresponding to prescribed treatment for each pharmacy. The representative average error for this is $\Delta = 0.05 \leq 5$ %. Further, we concluded that our sample of 12 pharmacies is representative.

The descriptive part of the study depicts the central and variation parameters. Demographic characteristics are summarized in Table II. We have determined the frequency, the mean, the standard deviation for each sample collected. Also, it is presented in tabular form the frequency of male patients compared with those of female. For this, we have grouped the medical prescriptions after provenience – from the family physicians, respectively, from the specialist physicians.

The analytical part of the study contains the inferential tests. Taken into account the type of data, namely categorical, nonparametric methods were considered [1, 6, 12]. In order to construct two comparable groups regarding their dimension we sort each prescription drug after the variable *Age* of patients. Computing the average of the *Age* (M) we form two groups corresponding to each drugs prescribed: the group of drugs for patients with their age less and equal with M and the group of drugs for patients with their age greater than M. A Mann–Whitney test was used to compare the distribution of each drug for the two groups formed as above. Also, the investigation on statistic hypothesis about the average of occurrence numbers of each specific product on a prescription taken separately for each month was performed using Kruskal-Wallis test. The statistical threshold of significance considered is $p < 0.05$. The mentioned statistical tests were performed using SPSS 16.

Description of research group

The characteristics of the 360 patients taken into account are: 233 females and 127 males, the mean of age is 67 years, the lower and upper age limit are 38, respectively 87 years, the average, respectively the age limits of patients who have the prescription from a specialist physician are: 64 years, respectively, 41-83 years, and the average, respectively, the age limits of patients who have the prescription from the family physician are 67 years, respectively, 38-87 years. In order to analyse the treatment of dyslipidaemia, the following data available in pharmacies were collected, i.e. age, patient' gender, type of prescriptions - coming from the family or specialist physician, drugs prescribed (*Simvastatin®10, Simvastatin®20, Simvastatin®40, Rosuvastatin®5, Rosuvastatin®10, Rosuvastatin®20, Atorvastatin®10, Atorvastatin®20, Atorvastatin®40, Fenofibrat®160, Omacor®*), cost of drugs and period of time for prescription dispensed. One month from the database analysed is briefly listed below in Table I.

Table I

Data collected from pharmacies, corresponding to one of the months studied (June 2010)

P	Age	Gender	FaD(1)/SpD(0)	S10	S20	S40	R5	R10	R20	A10	A20	A40	FN	OM	Cost(RON)	Month
1	70	1	1	0	1	0	0	0	0	0	0	0	0	0	22.65	June2010
2	62	1	1	1	0	0	0	0	0	0	0	0	0	0	12.08	
3	61	0	1	0	0	0	0	0	0	0	0	0	1	0	37.58	
4	60	0	1	1	0	0	0	0	0	0	0	0	0	0	12.08	
5	77	1	1	0	1	0	0	0	0	0	0	0	0	0	22.65	
…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…
30	80	0	1	0	1	0	0	0	0	0	0	0	0	0	25.61	

P = patients; Gender (1) = male, Gender (0) = female; FaD = family physician; SpD = specialist physician;
S10 = Simvastatin®10; S20 = Simvastatin®20; S40 = Simvastatin®40; R5 = Rosuvastatin®5; R10 = Rosuvastatin®10; R20 = Rosuvastatin®20;
A10 = Atorvastatin®10; A20 = Atorvastatin®20; A40 = Atorvastatin®40; FN = Fenofibrat®160, OM = Omacor®.

Results and Discussion

In the studied sample, were chosen an unequal distribution from the point of view of sex (35% men versus 64% women). Most patients received the medical prescriptions from family physician. The characteristics of the sample can be observed in Table II.

Figure 1 displays the distribution of patients following the treatment prescribed by the family physician (351 out of 360 patients). One can notice that dyslipidaemia appears in a maximum percentage of 21% at patients between 67-72 years old from a total number of 351 of patients. The minimum percentage about 1% is found around of 38, respectively, over 82 years old.

Table II

The risk factors of studied sample (n = 360)

The risk factors value	(Mean ± SD/Median)
Age	67 ± 10.1664
Masculine/feminine gender	35.3% ± 0.48/64.7% ± 0.48/0
Treatment indicated by family physician	97.5% ± 0.16/0
Treatment indicated by specialist physician	2.5% ± 0.16/0
Simvastatin®10	12.8% ± 0.34/0
Simvastatin®20	36.6% ± 0.48/0
Simvastatin®40	6% ± 0.24/0
Rosuvastatin®5	0.6% ± 0.07/0
Rosuvastatin®10	7.5% ± 0.26/0
Rosuvastatin®20	0.8% ± 0.09/0
Atorvastatin®10	5% ± 0.22/0
Atorvastatin®20	5.3% ± 0.22/0
Atorvastatin®40	1.7% ± 0.13/0
Fenofibrat®160	23% ± 0.44/0
Omacor®	1.4% ± 0.12/0
Months	6.5 ± 3.464

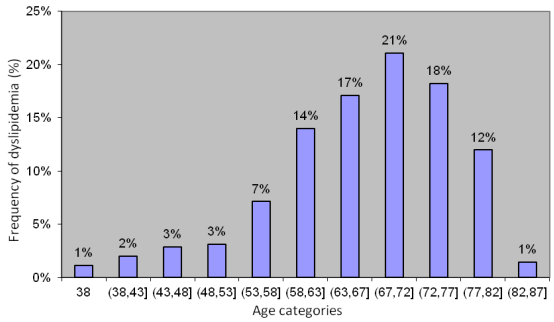

Figure 1.
Patients' distributions following the treatment prescribed by the family physician in respect with age categories

Further, other analysis illustrates the balance of distribution for medical treatment (see Figure 2).

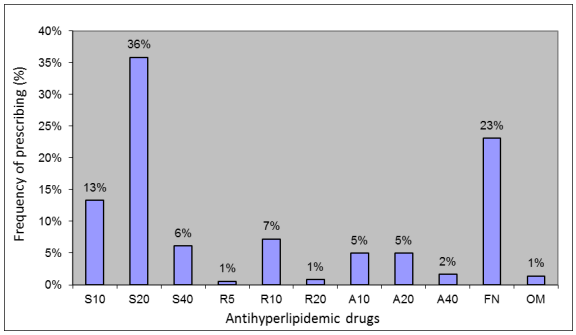

Figure 2.
Frequency of prescribing antihyperlipidaemic drugs

S10 = Simvastatin®10; S20 = Simvastatin®20; S40 = Simvastatin®40;
R5 = Rosuvastatin®5; R10 = Rosuvastatin®10; R20 = Rosuvastatin®20;
A10 = Atorvastatin®10; A20 = Atorvastatin®20; A40 = Atorvastatin®40;
FN = Fenofibrat®160, OM = Omacor®.

The most commonly prescribed drug is *Simvastatin®20* with 36% from a total of sample

360 medical prescriptions. It is followed in decrease order by 23% of *Fenofibrat®160*, 13% of *Simvastatin®10*, 7% of *Rosuvastatin®10*, 6% of *Simvastatin®40*, 5% of *Atorvastatin®10*, *Atorvastatin®20*, 2% of *Atorvastatin®40* and on the last position, the minimum percentage, 1%, is got by *Rosuvastatin®5*, *Rosuvastatin®20* and *Omacor®*.
Statistical analysis of prices corresponding to the prescribed treatment is presented in Figure 3. The average minimum price provided by pharmacies is given for *Simvastatin®10*. It is followed by most frequent drug *Simvastatin®20* which is the most prescribed drug, then by *Simvastatin®40* and *Fenofibrat®160*. Note that *Rosuvastatin®20* has the highest average current price in pharmacies. From the previous statistics, this drug is prescribed in only 1% of cases.

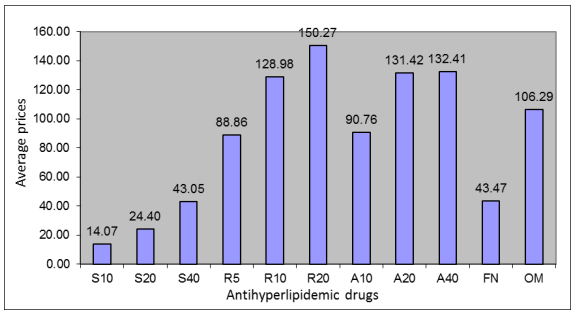

Figure 3.
Comparative chart of average prices for prescribed treatment
S10 = Simvastatin®10; S20 = Simvastatin®20; S40 = Simvastatin®40; R5 = Rosuvastatin®5; R10 = Rosuvastatin®10; R20 = Rosuvastatin®20; A10 = Atorvastatin®10; A20 = Atorvastatin®20; A40 = Atorvastatin®40; FN = Fenofibrat®160; OM = Omacor®.

Sample distribution in terms of patient's gender allow us to divide and to make a comparative analysis between subgroups composed by female and male patients. The percentage of patients who follows the treatment prescribed by specialist physician is 2.5% from which 65.2% represents female patients, respectively, 34.8% represents male patients and the remaining of 97.5% are the patients who have the treatment prescribed by family physician (see Table III).

Table III
The table of frequency by categories – family physician/ specialist physician, respectively, female/male patients

Physicians categories			Frequency
Family physician	Gender	F	44.4%
		M	55.6%
		Total	100%
Specialist physician	Gender	F	65.2%
		M	34.8%
		Total	100%

We have compared the distribution of drugs prescribed between the groups under and over average age. Mann-Whitney test was used to compare independent variable [12], (unpaired groups).
In case of treatment indicated by *Simvastatin®10, Simvastatin®20, Simvastatin®40, Rosuvastatin®5, Rosuvastatin®10, Rosuvastatin®20* it is found that the difference by age categories it is not statistically significant (p = 0.25, p = 0.21, p = 0.52, p = 0.13, p = 0.25, respectively, p = 0.62), see Tables IV and V. Therefore, we can conclude that for patients who are younger than 67 years old the prescribed treatment is not significantly different compared with the treatment for those over 67 years old, in term of drug consumption.

Table IV
Mann-Whitney test for *Simvastatin®10*, *Simvastatin®20*, *Simvastatin®40*

Test Statistics			
	Simvastatin®10	*Simvastatin®20*	*Simvastatin®40*
Mann-Whitney U	15498.000	15142.500	15898.500
Wilcoxon W	33453.000	29848.500	30604.500
Z	-1.150	-1.232	-0.638
Asymp. Sig. *p*	0.250	0.218	0.523

Table V
Mann-Whitney test for *Rosuvastatin®5*, *Rosuvastatin®10*, *Rosuvastatin®20*

Test Statistics			
	Rosuvastatin®5	*Rosuvastatin®10*	*Rosuvastatin®20*
Mann-Whitney U	15970.500	15651.000	16083.000
Wilcoxon W	33925.500	30357.000	30789.000
Z	-1.489	-1.130	-.493
Asymp. Sig. *p*	0.137	0.258	0.622

Further, for the treatment with *Atorvastatin®10* patients of two subgroups of different age administrate different amount of drugs (p = 0.028), but in case of *Atorvastatin®20* and *Atorvastatin®40* the situation is contrary (p = 0.161, respectively, p = 0.902).
The medical treatment with *Fenofibrat®160* is administrated in different amounts for both age

categories ($p < 0.05$) and for medical treatment with *Omacor®* the values of p (> 0.05) is not statistically significant.

Taking into account the confidence interval for age (67 ± 10.1664) we took, also, the cut-off points for statistical significance the age 58, respectively 78. For the first cut-off point Mann-Whiney test reports a statistical significance in case of *Simvastatin®10* ($p = 0.014$). For the second cut-off point Mann-Whiney test reports a statistical significance in case of *Rosuvastatin®10* ($p = 0.048$).

The Kruskal-Wallis test is used to test the homogeneity of prescription patterns along time (12 months) for 12 subgroups of sample [12].

Tables VI and VII display the results for Kruskal-Wallis test in case of *Simvastatin®10, Simvastatin®20, Simvastatin®40, Rosuvastatin®5, Rosuvastatin®10, Rosuvastatin®20*. As one can see from these tables only for *Simvastatin®40* we got $p < 0.05$, so, we reject the hypothesis proposed. The conclusion is that the medical treatment on 12 months is, on average, the same excepting *Simvastatin®40*.

Table VI

Kruskal-Wallis test for *Simvastatin®10*, *Simvastatin®20*, *Simvastatin®40*

Test Statistics[a,b]			
	Simvastatin®10	*Simvastatin®20*	*Simvastatin®40*
Chi-Square	5.121	15.001	31.073
Df	11	11	11
Asymp. Sig. *p*	0.925	0.182	0.001
a. Kruskal Wallis Test			
b. Grouping Variable: months			

Table VII

Kruskal-Wallis test for *Rosuvastatin®5*, *Rosuvastatin®10*, *Rosuvastatin®20*

Test Statistics[a,b]			
	Rosuvastatin®5	*Rosuvastatin®10*	*Rosuvastatin®20*
Chi-Square	10.028	17.386	9.050
Df	11	11	11
Asymp. Sig. *p*	0.528	0.097	0.617
a. Kruskal Wallis Test			
b. Grouping Variable: months			

Analogue, Kruskal-Wallis test gives for the rest of the administrated drugs: *Atorvastatin®10, Atorvastatin®20*, *Atorvastatin®40*, *Fenofibrat®160* and *Omacor®* the following values of the probabilities: $p = 0.475$, $p = 0.228$, $p = 0.524$, $p = 0.705$ and $p = 0.799$. These results lead us to accept the null hypothesis considering the level of significance of order 0.05. In these cases the distribution of drugs on each month is on average equal.

Conclusions

The study for testing the distribution of drugs administered on age categories and on periods of time is based on a total number of 11 medicines, namely, *Simvastatin®10, Simvastatin®20, Simvastatin®40, Rosuvastatin®5, Rosuvastatin®10, Rosuvastatin®20, Atorvastatin®10, Atorvastatin®20, Atorvastatin®40, Fenofibrat®160, Omacor®*.

Following the patients' distributions in respect with age categories for patients following the treatment prescribed by the family physician, it can be concluded that dyslipidaemia occurs in a maximum percentage at patients between 66 to 72 years.

The most prescribed drug for treating dyslipidaemia is *Simvastatin®20* while the least used medicines are *Rosuvastatin®5*, *Rosuvastatin®20* and *Omacor®*. Statistical analysis of average prices shows that *Simvastatin®20* is situated next to the minimum position while *Rosuvastatin®20* has in average the highest price. Therefore, we conclude that for treating dyslipidaemia the patients buy neither the cheapest nor the most expensive product from pharmacies.

Relative to statistical analysis of subgroups constructed on age categories (under and above averaged age), it is found that only for the treatment prescribed by *Atorvastatin®10* and *Fenofibrat®160* the difference on age categories is statistically significant. For the rest of the drugs, it is concluded that the treatment is the same for the both categories of ages.

The statistical analysis of drugs treatment between the subgroups formed by patients on each month during one year, confirms that for all considered drugs, except *Simvastatin®40*, patients administer the same amount of drugs.

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