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The subjective assessment of causes of adverse effects of drugs in the population of Ukraine

The urgency of effective and safe pharmacotherapy is determined by a high incidence of side effects of medicines, genetic polymorphism is one of their causes. For its assessment the genetic testing is conducted on the basis of drug prescribing.

Aim. To study the subjective assessment of the causes of drug side effects among the population of Ukraine for estimating the potential consumers of genetic tests.

Materials and methods. A specially designed questionnaire was used as an analysis tool. The study involved 3143 respondents.

Results and discussion. It was shown that the most frequent subjective causes of side effects according to the respondents were the unread patient information leaflets and misunderstanding of them, possible genetic traits of a person, the simultaneous use of several drugs, drug faking, etc.

Conclusions. It is necessary to develop the algorithm for implementation of the system of measures aimed at raising awareness of the potential means of reducing the side effects of drugs, in particular carrying out a genetic testing.

***Key words**: adverse drug reactions; Ukraine; pharmacogenetics; pharmacogenetic testing; personalized medicine*

М. М. Кобець

Суб'єктивна оцінка причин виникнення побічних ефектів лікарських засобів у населення України

Актуальність ефективної та безпечної фармакотерапії обумовлена високою частотою побічних ефектів лікарських засобів (ЛЗ), однією з причин яких є генетичний поліморфізм. Для його оцінки проводять генетичне тестування, на підставі якого виконуються лікарські призначення.

Мета роботи – вивчення суб'єктивної оцінки причин виникнення побічних ефектів ЛЗ у населення України для приблизної оцінки потенційних споживачів генетичних тестів.

Матеріали та методи. Як інструмент аналізу була використана спеціально розроблена анкета. У дослідженні взяли участь 3143 респонденти.

Результати та їх обговорення. Показано, що найчастіше суб'єктивними причинами розвитку побічних ефектів, на думку респондентів, було: неознайомлення і нерозуміння вивчення інструкції по застосуванню ЛЗ, можливі генетичні особливості, застосування декількох препаратів одночасно, фальсифікація препаратів.

Висновки. Необхідна розробка алгоритму з впровадження системи заходів, спрямованих на підвищення інформованості про потенційні засоби зниження побічних ефектів ЛЗ, зокрема, проведення генетичного тестування.

***Ключові слова**: побічні реакції; Україна; фармакогенетика; фармакогенетичне тестування; персоналізована медицина*

М. Н. Кобец

Субъективная оценка причин возникновения побочных эффектов лекарственных средств у населения Украины

Актуальность эффективной и безопасной фармакотерапии обусловлена высокой встречаемостью побочных эффектов лекарственных средств (ЛС), одной из причин которых является генетический полиморфизм. Для его оценки проводят генетическое тестирование, на основании которого выполняются лекарственные назначения.

Цель работы – изучение субъективной оценки причин возникновения побочных эффектов ЛС у населения Украины для примерной оценки потенциальных потребителей генетических тестов.

Материалы и методы. В качестве инструмента анализа была использована специально разработанная анкета. В исследовании приняли участие 3143 респондента.

Результаты и их обсуждение. Показано, что чаще всего субъективными причинами развития побочных эффектов, по мнению респондентов, являлось: неознакомление и непонимание изучения инструкции по применению ЛС, возможные генетические особенности, применение нескольких препаратов одновременно, фальсифицирование препаратов.

Выводы. Необходима разработка алгоритма по внедрению системы мероприятий, направленных на повышение информированности о потенциальных средствах снижения побочных эффектов ЛС, в частности, проведение генетического тестирования.

***Ключевые слова**: побочные реакции; Украина; фармакогенетика; фармакогенетическое тестирование; персонализированная медицина*

The urgency of effective and safe pharmacotherapy is determined by a high incidence of side effects of medicines across the world, some effects may be fatal [1]. As a rule, side effects are associated with the increased length of staying in the patient care institutions, increase of treatment costs, and decrease in the quality of life of patients [2].

There are state organizations involved in the analysis of the dynamics of side effects in different countries. Ukraine is no exception: there is a special structure of pharmacovigilance – the State Expert Centre at the Ministry of Health of Ukraine. In particular, only in 2015 four proven deaths arising as a result of drug therapy were registered in Ukraine according to the official data. There are reports of dozens of drugs, which administration either is not associated with the expected effect, or accompanied with the unexpected adverse reactions [3]. In addition, it is shown that in 2015 more than 17.000 reports of side effects and/or the absence of efficacy of drugs were in database of adverse reactions. These figures were 18 % higher than the data of the previous period. Apparently, these figures were understated and incomplete due to the lack of such information from the Crimea [4]. In 2015 the integral index considering the number of reports of adverse reactions and the absence of efficacy per 1 million of the Ukrainian population exceeded the boundary indicators recommended by the World Health Organization by 55 % and was equal to 400 [4].

At the same time, all over the world more and more importance is given to genetic polymorphism as a cause of drug side effects [5]. For its assessment the genetic testing is conducted on the basis of drug prescribing [6-13]. In Ukraine, this approach is also used, but in a much smaller scale [14-16]. Despite the possibility of a significant reduction in side effects for genotyping such a personalized approach is not yet a universal and widespread. It is impeded by financial difficulties among the population all over the world, in some cases the uncertainty of the interpretation of the results of genetic tests, the absence of the action plan of the patient and the physician when obtaining the appropriate results, etc. [5, 6].

A phenomenon that often occurs is the low awareness of the population, the medical personnel and pharmacy professionals concerning the possibility of individual approach based on genetic testing [17-20]. In particular, there is no information on the subjective assessment of the causes of drug side effects in the population of Ukraine. It may be of interest in assessing the potential target audience for conducting genetic tests in prescribing drugs in the near future.

The aim of this work is to study the subjective assessment of the causes of drug side effects among the population of Ukraine for estimating the potential consumers of genetic tests.

Materials and Methods

A specially designed questionnaire containing questions of the socio-demographic and research character was used as an analysis tool. Only a fragment of the questionnaire with questions, which were aimed at understanding of pharmacogenetics, determining the source of awareness in this area and a subjective assessment of side effects during treatment, was used for the current analysis.

The study involved 3143 respondents. More than 80 % of the respondents were the young population aged 15-25 years. The vast majority of the respondents were students of the Ukrainian universities and faculties of the medical, pharmaceutical and biological profile. In the sample the sex bias (83 % of males and 17 % of females) was observed due to the specificity of the pharmaceutical and healthcare industry. A small part (less than 10 % of the respondents) was not related to these specialties and was included in the study in a random order.

Collection of personal information was conducted taking into account the ethical requirements when dealing with a person in accordance with the Helsinki Declaration [5]. All participants gave their informed consent to the anonymous survey. The relationship between the quality characteristics was assessed by $\chi 2$ test. The conclusion regarding the statistical hypotheses was made at the significance level of $p \leq 0.05$. The calculations were performed in Microsoft Excel and Statistica 6 software.

Results and Discussion

The analysis of the causes of side effects implied the choice of the following variants by the respondents: the unread patient information leaflet, or improper familiarization and its misunderstanding, the possible genetic traits affected the drug effectiveness, the simultaneous use of several drugs, drug faking, as well as the purchase of cheaper generic drugs.

Since in our previous studies [19] the sexual specificity was revealed, the analysis of the data in different sexes was carried out separately. As is known [9], not only the results of the survey, but the actual consequences of drug intake by males and females can be sex specific [21].

The results of the study (Fig.) showed that approximately one third of the respondents (32 % of males and 30 % of females) thought that the side effects might occur as a result of the unread patient information leaflet, and approximately the fifth part of the respondents (18 % of males and 20 % of females) – because of misunderstanding of this information leaflet.

Approximately one third of the subjects (27 % of males and 29 % of females) also considered that the cause of

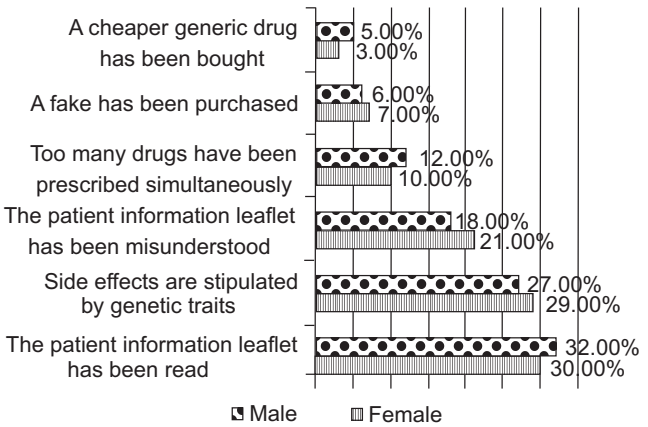

Fig. Distribution of subjective causes of common side effects among the respondents

Table

The essence of the concept of pharmacogenetics according to the respondents

Possible answers	1	2	3	4	5	6
I do not know	6.9	11	4.7	5.6	6	34.7
I heard, but can not say exactly	26.6	33	19.7	12.4	19	26.5
Hereditary diseases	6.9	2.2	15	23.6	12.9	3.1
The effect of drugs on human	4.8	5.7	2.4	3.7	5.1	8.2
The impact of genes on drugs	3.2	4.9	3.1	3.1	2.6	2
The possibility of mutations due to drug intake	6.9	7.9	7.9	5	7.8	–
The reaction of the body to drugs depending on the genetic traits	44.7	35.3	47.2	46.6	46.6	25.5

Note. $\chi^2 = 83.8$, $\nu = 28$, $p \leq 0.001$. 1 – the 1st year students of the NUPh; 2 – the 2nd year students of the NUPh; 3 – the 3d year students of the NUPh; 4 – the 4th year students of the NUPh; 5 – the 5th year students of the NUPh; 6 – Persons who have no relation to the field of medicine or pharmacy.

unexpected reactions to drugs was the genetic traits of individuals taking drugs. Currently, a special attention is paid in the world to the problem of side-effects occurrence as a result of the potential of genetic differences. Earlier we considered the question of understanding of the pharmacogenetics essence directly by the students of the National University of Pharmacy (NUPh) as a contingent that studied this issue (Table).

When analyzing the understanding of the pharmacogenetics essence by students of different years of study of the specialized higher school (National University of Pharmacy) and persons unrelated to medicine or pharmacy there was a relationship between the interpretation of pharmacogenetics and professional affiliation of the respondent ($\chi 2 = 83.8$, $\nu = 28$, $r \leq 0.001$). In our study we were guided by the fact that undergraduates could be considered as patients, and senior students – as professionals.

As can be seen from Table, the correct understanding of pharmacogenetics was present in 35-47 % of students of different years of study. At the same time, only a quarter of the respondents who did not face with medical and pharmaceutical aspects in their professional activities had the correct understanding of pharmacogenetics.

When analyzing the sources of information about pharmacogenetics it was shown that most of the students first received information about this discipline in a higher school (66 % – the 5th year students, 70 % – the 1st year students of the NUPh). In fact, this information is fragmentary studied in the NUPh within the discipline "Biology with Fundamentals of Genetics" (the 1st year) and "Pharmacology" (the 3rd year) by students of specialty "Pharmacy", and these students actually participated in the current study.

Approximately 10 % of the respondents suggested that a possible cause of side effects was the simultaneous use of several drugs. It should be noted that when dispensing medicines in pharmacies patients are not always warned about the risk of development of side effects. Moreover, when prescribing the combined treatment regimens the risk of simultaneous intake of drugs can be underestimated without taking into account the genetic factor.

It was found in the studies that a small proportion of the population (6 % of males and 7 % of females) thought that the side effects were the consequence of the purchase of counterfeit drugs or buying cheaper generic products (6 % of males and 3 % of females).

CONCLUSIONS

1. It has been shown that the most frequent subjective causes of side effects are considered to be the unread patient information leaflets (one third of the cases), as well as possible genetic traits of a person (one third of the cases).

2. The more prepared segment of potential consumers of genetic testing comprises approximately 30 % of the population.

3. Training in specialized institutions is an effective basis for acquisition of innovative knowledge in the field of pharmacogenetics. For other groups of the population without access to such professional information it is necessary to develop the algorithm for implementation of the system of measures aimed at raising awareness of the potential means of reducing the side effects of drugs, in particular carrying out a genetic testing.

Conflicts of Interest: authors have no conflict of interest to declare.

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