

KNOWLEDGE AND ATTITUDE TOWARDS PHARMACOVIGILANCE AND ADVERSE DRUG REACTION REPORTING AMONG DENTAL MEDICINE STUDENTS IN THE REPUBLIC OF MACEDONIA

ЗНАЕЊАТА И СТАВОВИТЕ НА СТУДЕНТИТЕ ПО ДЕНТАЛНА МЕДИЦИНА ОД РЕПУБЛИКА МАКЕДОНИЈА ЗА ФАРМАКОВИГИЛАНЦАТА И ПРИЈАВУВАЊЕТО НА НЕСАКАНИ РЕАКЦИИ НА ЛЕКОВИ

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Abstract

The aim of this Study is to evaluate the knowledge and attitude towards pharmacovigilance and adverse drug reactions reporting among the dental medicine students in Macedonia. **Material and method.** This study was carried out by using a Survey Questionnaire among the pre-final and final year dental medicine students of Faculty of Dentistry in Skopje, University „Ss Cyril and Methodius“ in Skopje. The questionnaire was adapted from the previously published article of Shivadasan and Sellappan and modified according to the needs of the present study. The Questionnaire was distributed in November 2017. The Questionnaire questions related to the students demographic data, consisting of total of 28 survey items organized into two sections. The data was analyzed by using Statistica 7.1 for Windows and SPSS 17.0. Descriptive statistical analyses such as frequencies and percentages were used. **Results.** The Questionnaire was administered to 93 participants of whom 44 were from pre-final year and 49 were from final year. Out of the 93 participants, about 20.43% of participants answered correctly for the definition of pharmacovigilance. It was found that 32.25% of the participants answered correctly for the question on the important purpose of pharmacovigilance. 26.88% of the participants answered correctly that pharmacovigilance system is established in the Republic of Macedonia. Among the pre-final and final year students, 18.18% and 34.69% respectively answered correctly. About 90.91% of students from pre-final year either strongly agreed or agreed that pharmacovigilance should be taught to all health care students during their curriculum. Only 31.82% and 22.45% of pre-final and final year students respectively either strongly agreed or agreed that with their present knowledge, they are very well prepared to report any ADRs in their future practice. **Conclusion.** In the present study, the attitude of the students were positive, however their knowledge has to be increased in some aspects referring to ADR reporting. Creating awareness and carrying out educational intervention or training among these health care students would help these students to gain knowledge, which is very essential for their future practice. **Key words:** pharmacovigilance, students, knowledge, attitude, adverse drug reaction.

Апстракт

Целта на оваа студија е да се проценат знаењето и ставовите на студентите по дентална медицина од Република Македонија за фармаковигиланцата и несаканите реакции на лековите. **Материјал и метод.** Студијата беше спроведена со користење на анкетен прашалник наменет за студентите по дентална медицина од претпоследна и последна година на студирање на Стоматолошкиот факултет во Скопје при Универзитетот „Св. Кирил и Методиј“ во Скопје. Беше користен прашалник од претходно објавениот труд на Sivadasan и Sellappan, кој беше модифициран според потребите на оваа студија. Прашалникот беше дистрибуиран до студентите во ноември 2017 година. Анкетниот прашалник содржеше прашања за демографските податоци на студентите и вкупно 28 прашања организирани во два дела. Податоците беа анализирани со користење на програмат Statistica 7.1 за Windows и SPSS 17.0. Беа користени дескриптивни статистички анализи, како што се фреквенции и проценти. **Резултати.** Прашалникот беше спроведен кај 93 студенти, од кои 44 беа од претпоследната година, а 49 беа од последната година на студирање. Од 93 учесници, 20,43% од испитаниците правилно одговориле на прашањето за дефинирањето на фармаковигиланцата. Утврдивме дека 32,25% од учесниците правилно одговориле на прашањето за целта на фармаковигиланцата. 26,88% од испитаниците точно одговориле дека во Република Македонија е воспоставен систем за фармаковигиланца. Студентите од претпоследната и последна година, 18,18% и 34,69%, правилно одговориле на ова прашање. Околу 90,91% од студентите од претпоследната година, многу се согласуваат или се согласуваат дека фармаковигиланцата треба да ја изучуваат сите здравствени работници во рамки на наставната програма. Само 31,82% од студентите од претпоследната и 22,45% од последната година, многу се согласуваат или се согласуваат дека со сегашното знаење тие се добро подготвени да ги пријават несаканите реакции на лековите во своја идната практика. **Заклучок.** Во оваа студија, ставовите на студентите се позитивни, но нивното знаење треба да се зголеми во некои аспекти поврзани со пријавувањето на несаканите реакции на лековите. Преку едукативна интервенција или обука и создавањето на свест помеѓу студентите ќе се придонесе за да истите стекнат поголеми знаења, што е многу важно за нивната идна практика. **Клучни зборови:** фармаковигиланца, студенти, знаења, ставови, несакана реакција на лек.

Introduction

Safety and efficacy are the two major concerns regarding a particular drug. The efficacy of a drug can be quantified with relative ease, but the same cannot be said about safety. This is because the adverse effect of a drug may be uncommon (but very serious) and many patients may be affected or exposed to a potential risk before the causality of the drug is established¹⁻². According to Barker, there are three possible actions of drug: the one you want, the one you don't want, and the one you don't know about³.

Adverse drug reaction (ADR) is defined by the World Health Organization (WHO) as "a response to a drug which is noxious and unintended, and which occurs at doses normally used for prophylactic, diagnostic, or therapeutic purposes or for the modification of physiologic function"⁴.

Adverse Drug Reactions (ADRs) are an imperative weakness in public health sector as they represent a substantial fiscal burden on the society and health-care systems. It is one of the significant causes resulting with hospitalization, varying between 5-20%⁵⁻⁷. Furthermore, according to Uppsala Monitoring Centre, which maintains the international database of adverse drug reaction reports, only 6-10% of all the ADRs are reported. Hence, the detection, recording and reporting of adverse drug reactions becomes vital and health experts should be encouraged to execute this appropriately to ensure safer usage of medicines. For this purpose, the concept of pharmacovigilance has been established⁶.

The etymological roots for the word "pharmacovigilance" are: *pharmakon* (Greek word for 'drug') and *vigilare* (Latin word for 'monitoring')⁸. According to WHO, pharmacovigilance is defined as "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problem, particularly long term and short term adverse effects of medicines."⁹ It has been recommended for every country to set up their own pharmacovigilance programs and in the recent past several countries have initiated pharmacovigilance programs to identify the drugs causing ADRs⁸⁻⁹.

The definition that is accepted in the national legislation is similar to the WHO definition. According to the Law on medicines and medical devices¹⁰, pharmacovigilance is a system applied for the purpose of detecting, gathering, monitoring, assessing and responding to new data on safety of medicinal product and risk-benefit balance related to the use of medicinal product or its interaction with other medicinal products. The pharma-

covigilance system is further regulated with Regulations on the manner of reporting, contents of the reporting form for adverse reactions to medicinal products and the manner of organisation of pharmacovigilance system¹¹. According to this Regulation, adverse reactions to a medicinal product are all unintended reactions to medicinal products which appear during the application of the medicinal product according to the prescribing instructions or in application of any dose of the medicinal product in clinical trials¹¹.

Several studies have been conducted to evaluate the knowledge, attitude and practice towards pharmacovigilance activity among doctors, pharmacists or nurses in various countries¹³⁻¹⁶, wherefrom conclusion was made that the resident doctors and nurses had good knowledge and awareness on ADR reporting. However, there is need for improvement in their practices¹⁴. Many factors, particularly the one related to knowledge and attitudes are responsible for ADR reporting by doctors. These factors have been described as "seven deadly sins" and are related to financial incentives, legal aspects, complacency (serious ADRs well documented by the time of marketing), diffidence (ADR reporting be done if it is certain), indifference (single ADR could not contribute to medical knowledge), ignorance (it is necessary to report only serious or unexpected ADR), and lethargy (lack of time and concern for extra work). Some studies have been carried out to reveal the factors influencing on ADR reporting among medical professionals. These factors have not been investigated especially among dental professionals in Macedonia.

Dental doctors are also involved in prescribing many medicines, including local and systemic anesthetics, antibiotics, analgesic and anti-inflammatory drugs etc.

Antibiotics and analgesics are among the leading causes of ADRs. Hence the risk of ADRs cannot be ignored in dentistry and the contribution of dentists in improving spontaneous reporting cannot be underestimated¹⁷.

In spite of studies conducted among different health care professionals and students, there is a lack of information among dental students and dentists in Republic of Macedonia on knowledge, attitude and practice towards pharmacovigilance and ADR reporting. So there is a need to study the awareness among the dental students and dentists as they are also part of the health care team who are responsible to report ADR during their practice, if any. Hence, this study was designed to examine the knowledge and attitude among pre-final and final year dental students towards pharmacovigilance and ADR reporting.

Material and methods

This study was carried out using a survey questionnaire among the pre-final and final year dental students of Faculty of Dental Medicine in Skopje, within the University „Ss Cyril and Methodius“ in Skopje. The questionnaire was adapted from the previously published article of Shivadasan and Sellappan⁸ and modified according to the need of the present study

The questionnaire was distributed in November 2017, after briefing them on the study objective in their respective classrooms and the participants' informed consent was obtained. The confidentiality of their response was ensured.

The questionnaire included the demographic issues and was consisted of total of 28 survey items organized into two sections. The first section included 14 questions to evaluate the participants' knowledge and the second section included 14 elements to study the attitude and attitude of the participants. The data was analyzed using Statistica 7.1 for Windows and SPSS 17.0. Descriptive statistical analyses such as frequencies and percentages were used.

Results

The questionnaire was administered to 93 participants of whom 44 were from pre-final year and 49 were from final year. 14 (31,82%) of the participants from pre-final year were male, while 30 (68,18%) were female. 17 (34,69%) of participants from final year were male, while 32 (65,31%) were female (table 1).

Table 1. Gender distribution of the participants

	Pre-final year	Final year
Male	14 (31,82%)	17 (34,69%)
Female	30 (68,18%)	32 (65,31%)
Total	44 (100%)	49 (100%)

Knowledge analysis and comparison on knowledge of pre-final and final year dental students

The results for knowledge on pharmacovigilance and ADRs reporting based questions are presented in Table 2. Out of the 93 participants, about 20,43% of participants answered correctly for the definition of pharmacovigilance. About 38,78% of students among

final year students answered correctly and none of the pre-final year students answered correctly. It was found that 32,25% of participants answered correctly the question on the important purpose of pharmacovigilance. Among the pre-final year and final year students, 18,18% and 44,90% respectively answered correctly. For the definition of adverse drug reaction, 75,26% of participants answered correctly. It was found that 63,64% of participants among the pre-final year and 85,71% of participants among the final year answered correctly. Only 13,97% of participants answered correctly on the question on which of the phase in clinical trial, the rare ADRs can be identified. It was found that that none of the participants answered correctly among the pre-final year and 26,53% of participants answered correctly among the final year. Overall 23,65% of participants answered correctly on the question on the location of the international centre for adverse drug reaction monitoring.

It was found that only 7,52% of participants answered correctly on the 'WHO online database' for reporting ADR. Among those who answered correctly, it was observed that none of participants were among pre-final year and 14,29% of participants were among final year students. About 9,67% of the participants answered correctly for the method employed by pharmaceutical companies to monitor ADR of new drugs after launching them into the market. Among the pre-final and final year students, 18,18% and 2,04% respectively answered correctly.

Regarding the most commonly used scales to establish the causality of an ADR, only 3,22% of participants answered correctly and it was found that none of the participants among final year answered this question correctly. However, 4,55% of participants answered correctly among the pre-final year. About 23,65% of the participants answered correctly on the factor causing ADR under-reporting. Among the pre-final and final year students, 22,73% and 24,49% respectively answered correctly.

26,88% of participants answered correctly that in the Republic of Macedonia is established pharmacovigilance system. Among pre-final and final year students, 18,18% and 34,69% respectively answered correctly. It was established that 19,35% of participants answered correctly on the question referring to the regulatory body in Macedonia that is in charge for regulating ADR reporting, it was found that 19,35% of participants answered correctly.

Regarding the next question on what serious event is considered adverse, 39,78% students answered correctly. It was found that 40,91% and 38,78% of participants among the pre-final year and final year respectively

answered correctly. However, 4,3% of the students answered correctly on the question on within how many days a serious adverse event should be reported to the regulatory body in Macedonia. For the last question on

the most important health care professions for reporting ADR, about 32,25% of participants answered correctly, that is 18,18% of participants among the pre-final year and 44,90% of participants among the final year.

Table 2: Knowledge assessment on pharmacovigilance and ADRs reporting among pre-final and final year dental students

Question	Correct response		Overall
	Pre-final year	Final year	
Pharmacovigilance is	0 (0%)	19 (38,78%)	19 (20,43%)
The important purpose of Pharmacovigilance is	8 (18,18%)	22 (44,90%)	30 (32,25%)
Which one of the following best describes the 'Adverse drug reaction'?	28 (63,64%)	42 (85,71%)	70 (75,26%)
Rare ADRs can be identified during which of the following phase of a clinical trial	0 (0%)	13 (26,53%)	13 (13,97%)
The international centre for adverse drug reaction monitoring is located in	6 (13,64%)	16 (32,65%)	22 (23,65%)
Which one of the following is the "WHO online database" for reporting adverse drug reaction?	0 (0%)	7 (14,29%)	7 (7,52%)
Which of the following methods is commonly employed by the pharmaceutical companies to monitor adverse drug reactions of new drugs once they are launched into the market?	8 (18,18%)	1 (2,04%)	9 (9,67%)
Which of the following scales is most commonly used to establish the causality of an ADR?	2 (4,55%)	1 (2,04%)	3 (3,22%)
Which factor will be the cause of ADR under-reporting?	10 (22,73%)	12 (24,49%)	22 (23,65%)
Is a pharmacovigilance system established in the Republic of Macedonia?	8 (18,18%)	17 (34,69%)	25 (26,88%)
Which of the following regulatory body in Republic of Macedonia regulates ADR reporting?	6 (13,64%)	12 (24,49%)	18 (19,35%)
A serious adverse event is	18 (40,91%)	19 (38,78%)	37 (39,78%)
A serious adverse event in Republic of Macedonia should be reported to the Regulatory body within	2 (4,55%)	2 (4,08%)	4 (4,3%)
The most important healthcare professional(s) responsible for reporting ADR is/are	8 (18,18%)	22 (44,90%)	30 (32,25%)

Attitude analysis and comparison of attitude of pre-final and final year dental students

The results on the attitude towards pharmacovigilance and adverse drug reaction reporting among the pre-final and final year dental students are presented in Table 3. 100% of participants among the pre-final year and 97,96% of participants among the final year participants either strongly agreed or agreed that ADR reporting is

necessary. For the attitude towards reporting adverse drug reaction as a professional obligation, 100% and 95,92% of participants among the pre-final and final year either strongly agreed or agreed respectively. The attitude of the respondents is identical regarding the necessity of confirming ADR before its' issuance on the market is identical.

The participants were asked whether they think ADR reporting should be voluntary for which 81,82% of

participants among the pre-final year either strongly agreed or agreed. However, 69,39% of participants among the final year either disagreed or strongly disagreed. Similarly, the participants were asked whether they think ADR reporting should be compulsory for which, 95,45% and 85,72% participants among the pre-final and final year either strongly agreed or agreed respectively.

For the question on whether it is necessary to report only serious and unexpected reactions, 72,73% of participants among the pre-final year either strongly

agreed or agreed. However, 61,22% of participants among the final year either disagreed or strongly disagreed. About 90,91% of students from pre-final year either strongly agreed or agreed that pharmacovigilance should be taught to all health care students during their curriculum. Among final year students, 85,71% had the same perception. About 4,55% of pre-final year and 16,33% of final year participants either strongly agreed or agreed that the topic on pharmacovigilance is well covered in their curriculum.

Table 3: Attitude towards pharmacovigilance and adverse drug reaction reporting among pre-final and final year dental students

Question	Pre-final					Final				
	Strongly agree	Agree	Neutral	Disagree	Strongly disagree	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
Do you think adverse drug reaction reporting is necessary?	44 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	32 (65,31%)	16 (32,65%)	0 (0%)	1 (2,04%)	0 (0%)
Do you think reporting adverse drug reaction is a medical staff's professional obligation?	34 (77,27%)	10 (22,73%)	0 (0%)	0 (0%)	0 (0%)	31 (63,27%)	16 (32,65%)	1 (2,04%)	1 (2,04%)	0 (0%)
Do you think it is necessary to confirm ADR of a particular drug before its issuance?	38 (86,36%)	6 (13,64%)	0 (0%)	0 (0%)	0 (0%)	36 (73,47%)	11 (22,45%)	2 (4,08%)	0 (0%)	0 (0%)
Do you think pharmacovigilance reporting should be exclusively on voluntary basis?	14 (31,82%)	22 (50,0%)	0 (0%)	4 (9,09%)	4 (9,09%)	6 (12,24%)	7 (14,29%)	2 (4,08%)	27 (55,10%)	7 (14,29%)
Do you think pharmacovigilance reporting should be compulsory?	20 (45,45%)	22 (50,0%)	0 (0%)	2 (4,55%)	0 (0%)	22 (44,90%)	20 (40,82%)	2 (4,08%)	3 (6,12%)	2 (4,08%)
Do you think that it is necessary to report only serious and unexpected reactions?	4 (9,09%)	28 (63,64%)	0 (0%)	12 (27,27%)	0 (0%)	2 (4,08%)	10 (20,41%)	7 (14,29%)	22 (44,90%)	8 (16,33%)
Pharmacovigilance should be taught to all health care students during their curriculum.	16 (36,36%)	24 (54,55%)	4 (9,09%)	0 (0%)	0 (0%)	18 (36,73%)	24 (48,98%)	1 (2,04%)	4 (8,16%)	2 (4,08%)
I believe that the topic of pharmacovigilance is well covered in my curriculum.	2 (4,55%)	0 (0%)	4 (9,09%)	14 (31,82%)	24 (54,55%)	1 (2,04%)	7 (14,29%)	2 (4,08%)	13 (26,53%)	26 (53,06%)
I do not have any idea on how to report ADRs	16 (36,36%)	26 (59,09%)	0 (0%)	2 (4,55%)	0 (0%)	6 (12,24%)	28 (57,14%)	8 (16,33%)	5 (10,20%)	2 (4,08%)
Information on reporting ADRs should be presented to all health care students in their curriculum.	16 (36,36%)	22 (50,0%)	0 (0%)	6 (13,64%)	0 (0%)	16 (32,65%)	26 (53,06%)	3 (6,12%)	4 (8,16%)	0 (0%)
Information on reporting ADRs shall be better learnt during additional seminars/training/student exchange programs	10 (22,73%)	34 (77,27%)	0 (0%)	0 (0%)	0 (0%)	11 (22,45%)	27 (55,10%)	2 (4,08%)	8 (16,33%)	1 (2,04%)
A pharmacist is one of the most important health care professional to report ADRs.	10 (22,73%)	18 (40,91%)	2 (4,55%)	14 (31,82%)	0 (0%)	7 (14,29%)	17 (34,69%)	5 (10,20%)	16 (32,65%)	4 (8,16%)
In my opinion, reporting of already established ADRs will make no significant contribution to the reporting system.	2 (4,55%)	8 (18,18%)	6 (13,64%)	20 (45,45%)	8 (18,18%)	2 (4,08%)	12 (24,49%)	3 (6,12%)	20 (40,82%)	12 (24,49%)
With my present knowledge, I am very well prepared to report any ADRs notice in my future practice.	10 (22,73%)	4 (9,09%)	2 (4,55%)	22 (50,0%)	6 (13,64%)	2 (4,08%)	9 (18,36%)	3 (6,12%)	25 (51,02%)	10 (20,41%)

The results found that 95,45% of pre-final students either strongly agreed or agreed that do not have idea on how to report ADRs to the relevant authorities in Republic of Macedonia. Among the final year students, about 69% of participants had the same perception. 86,36% of pre-final year participants either agreed or strongly agreed that information on reporting of ADRs should be taught to all health care students during their curriculum, whereas, 85,71% of final year participants had the same perception.

100% of pre-final students have agreed that the information on ADR reporting shall be better learnt during internships, additional seminars, training and student exchange, while, 77,55% of final year students agreed to the same. It was found that 63,64% of pre-final students admitted that pharmacist is one of the most important health care personnel to report ADR whereas, among the final 48,98% of the participants have the same perception. For the students' perception on whether reporting of known ADRs will make any significant contribution to the reporting system, about 22,73% of pre-final students participants and 28,57% of participants from final year agree. Only 31,82% and 22,45% of pre-final and final year students respectively either strongly agreed or agreed that with their present knowledge, they are very well prepared to report any ADRs in their future practice.

Discussion

Adverse drug reactions results in unnecessary health care expenditures through augmented patient morbidity and mortality. Awareness about ADRs among the health care professionals can minimize the factor contributing to adverse drug reaction reporting. Knowledge is a very important factor that influences attitude and practice. Various studies had been carried out in different countries to assess the knowledge of pharmacovigilance among the medical, pharmacy, dental students and practitioners¹⁸⁻²¹.

The present study was conducted among the pre-final and final year dental students and 93 students participated. From the results, it was noticed that the overall knowledge on the definition of pharmacovigilance was poor among these students. Namely, only 10,43% of them were familiar with the definition on pharmacovigilance (table no. 2) On comparison, final year dental students had better knowledge than pre-final year students. However, a low percentage of students knew the purpose of pharmacovigilance.

The definition of adverse drug reaction was known better by the final year students. The student's knowl-

edge was poor for the question on the phase which rare ADRs can be identified, the location of the international centre for ADR monitoring, 'WHO online database' for reporting ADR, the most commonly used scales to establish the causality of an ADR and cause of ADR under-reporting. Our results are similar to the results of other surveys^{8,22-24}.

Final year students were better aware that the regulatory body that regulates reporting in the Republic of is the Macedonian Agency for Drugs and Medical device (MALMED). However, the overall knowledge was poor. The results show that knowledge among students on what a serious event is poor. Unfortunately, only 4,3% of the students were aware on which stage of the process a serious adverse event should be reported to the Macedonian Agency for Drugs and Medical device (MALMED).

Small percent of students were aware that dentists are also important health care professionals to report ADR. This suggests that pharmacovigilance topic is either not incorporated sufficiently or not incorporated in the curriculum and there is need of information regarding the topic among these students. Educational training programs on the topic can enhance their knowledge and perception as recommended by different researchers^{25,26}. Pharmacovigilance modules taught to the undergraduate students must be associated to modules on the rational use of medicines²⁷.

The results of the present study showed that most of the students had positive perception on ADR reporting. Most of the students agreed that ADR reporting is a professional obligation. ADR reporting, as a professional obligation, is subject to moral binding to healthcare professionals and ethical issues. Previous studies have also reported that ADR reporting should be a professional obligation²⁷⁻²⁹.

About 90,91% of students from pre-final year either strongly agreed or agreed that pharmacovigilance should be taught to all health care students during their curriculum. Among final year students, 85,71% had the same perception. This indicated their positive perception for importance of pharmacovigilance. This finding is similar to others studies involving healthcare professionals^{25,30}. Three fourth of the students also agreed that the information on ADR reporting shall be better learnt during additional seminars, trainings and student exchange. One-half of the participants perception was that pharmacist is one of the most important health care personnel to report ADR. These findings are similar to the results of healthcare professionals in other studies^{8,20,31,32}.

Under-reporting of ADRs is a common problem in pharmacovigilance program. The reasons for under-reporting are due to inadequate funds, lack of trained

staff and lack of awareness about the detection, communication and spontaneous monitoring of ADRs. The effectiveness and success of any pharmacovigilance system depends highly on the participation of all health care professionals and thus, dentists are also important healthcare professionals responsible for the pharmacovigilance activities and ADR reporting during their practice¹⁷.

Conclusion

It is essential that ADRs are to be reported and their significance is communicated effectively to the public who is under strong influence of the knowledge and attitude of health care professionals. The lack of knowledge and negative perceptions about pharmacovigilance and ADR reporting would lead to ADR under-reporting. Overall, the final year dental students had better knowledge than pre-final year students. Fortunately, in the present study, the attitude of the students were positive, however their knowledge has to be increased in some of the aspects of ADR reporting. Creating awareness through educational intervention or training among these health care profession students would help these students to gain knowledge, which is very essential for their future practice.

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