Spontaneous adverse drug reaction reporting: attitudes and practice of health care professionals and distributors in South East European region

Spontano poročanje neželenih učinkov: odnos in praksa zdravstvenih delavcev in distributerjev v Jugovzhodni Evropi

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Abstract: *Study objectives:* The study was conducted to determine current pharmacovigilance practice, knowledge and attitude of health care professionals and employees working for Baxter distributors in selected countries (Croatia, Serbia, Macedonia, Bosnia and Herzegovina, Romania) of South East European (SEE) region and to determine what further steps might be effective to increase the reporting culture from the company perspective. *Method:* Pre-notification letters and 115 questionnaires were prepared and distributed via e-mail to the distributors in the selected countries of SEE region. Distributors then submitted the questionnaires to health care professionals. Completed questionnaires were analysed in a descriptive way. *Results:* 44% (24) of distributors and 33% (20) of health care professionals returned the questionnaires. Responders were in majority sales representatives and medical specialists from hospitals. Results showed low ADR reporting rate for both responder types. Major obstacles and important factors to motivate reporting were identified. *Conclusion:* Reporting form availability, intensive education about ADR reporting importance and providing a feedback about ADRs to reporter should be an important focus of the company in order to improve reporting rate in the SEE region. Further steps included implementation of the tools found in our study and additional study with nurses as a target sample, were recommended.

Key words: *pharmacovigilance, adverse drug reaction, health care professional, distributor*

Povzetek: *Cilj študije:* Cilj študije je bilo določiti farmakovigilančno prakso, znanje in odnos do farmakovigilance pri zdravstvenih delavcih in zaposlenih, ki delajo za distributerje podjetja Baxter v izbranih državah (Hrvaška, Srbija, Makedonija, Bosna in Hercegovina, Romunija) Jugovzhodne Evrope in ugotoviti nadaljne ukrepe, ki bi povečali kulturo poročanja z vidika podjetja. *Metode:* Pismo namere in 115 vprašalnikov je bilo preko elektronske pošte poslanih distributerjem v izbranih državah Jugovzhodne Evrope, ti pa so nato razdelili določeno število vprašalnikov še zdravstvenim delavcem. Izpolnjeni vprašalniki so bili analizirani na opisni način. *Rezultati:* 44% (24) distributerjev in 33% (20) zdravstvenih delavcev je vrnilo vprašalnike. Največ vrnjenih vprašalnikov je bilo s strani prodajnih zastopnikov in zdravnikov specialistov iz bolnišnic. Rezultati so pokazali nizko stopnjo poročanja ADR za obe vrsti anketirancev. Ugotovljene so bile glavne ovire pri poročanju in pomembni motivacijski dejavniki. *Zaključek*: Podjetje bi moralo dati večji poudarek na dostopnost formularjev za poročanje, intenzivno izobraževanje o pomenu ADR poročanja in zagotavljanje povratnih informacij o neželenih učinkih, da bi se izboljšala stopnja poročanja v JVE regiji. Priporočeni so nadaljnji koraki, ki bi vključevali implementacijo teh orodij v prakso in izdelava dodatne študije, ki bi vključevala medicinske sestre kot ciljni vzorec.

Ključne besede: *farmakovigilanca, neželeni učinki zdravil, zdravstveni delavci, distributerji*

1 Introduction

In the past decade the safety of medicinal products has become increasingly important to the manufacturers of pharmaceutical products and regulatory agencies. Since the early 1960s, after the Thalidomide tragedy, many voluntary schemes for reporting adverse drug reactions (ADR) have been introduced in different countries and reporting systems have been developed to enable health care professionals to report ADRs (1, 2). It was recognized that ADRs are one of the major cause of hospitalization and have therefore high impact on the healthcare system from economic point of view (3, 4).

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Some of the multinational pharmaceutical companies were faced with high profile safety concerns resulted in withdrawals of their major drug products or even lawsuits that cost them millions of dollars and their good reputation. The history of catastrophic consequences of some ADRs for public health and therefore for manufacturers, has been driven the regulatory agencies to set up more stringent regulatory requirements and manufacturers to use proactive approaches to monitor drug safety (5, 6, 7).

The importance of pharmacovigilance (PhV) today is not only to follow the regulations; it is also to have influence on improving the awareness of importance of drug safety and to reduce the problem of under-reporting as much as possible. The focus in PhV should be to improve and sustain a good relationship between all partners involved in the PhV arena and to establish effective and qualitative communication between them (2, 8).

1.1 Under-reporting of adverse drug reactions

Underreporting related to spontaneous ADR reporting is a common practice and a big challenge for PhV experts all over the world. Even if the PhV system is precisely described in the legislation, this does not mean that it is also accurately and fully performed. The PhV system

Table 1: *Reasons of underreporting confirmed in published studies.*
Preglednica 1: *Razlogi za neporočanje v objavljenih študijah.*

Publication	Reasons for underreporting
Hasford, J., et al. (2002). Pharmacoepidemiology report. Physician's knowledge and attitudes regarding the spontaneous reporting system for adverse drug reactions. Journal of Clinical Epidemiology, 55, 945-950.	- ADR well known - Doubt of causality - Not know the spontaneous reporting system - Not know how to report
Vallano, A., et al.(2005). Obstacles and solutions for spontaneous reporting of adverse drug reactions in the hospital. British journal of Clinical Pharmacology, 60(6), 653-658.	- Lack of time, forgetfulness to report, clinical workload - Not know the spontaneous reporting system - Uncertainty of the ADR diagnosis - Potential conflicts derived from reporting ADRs
Herderio, M.T., et al. (2005). Physicians' attitudes and adverse drug reaction reporting. A case-control study in Portugal. Drug Safety, 28(9), 825-833.	- Belief serious ADRs are well documented by the time a drug is marketed - Belief it is impossible to determine the causality - One case could not contribute to the safety - It is only necessary to report serious or unexpected ADRs
Figueras, A., et al. (1999). Influence of Physician' attitudes on reporting adverse drug events. A case-control study. Medical Care, 37 (8), 809-814.	- Belief serious ADRs are well documented by the time a drug is marketed - Belief it is impossible to determine the causality - ADR is reported only if one is sure that it is related to the use of a particular drug - One case could not contribute to the safety
Belton, K. J. and the EU Pharmacovigilance research group. (1997). Attitude survey of adverse drug-reaction reporting by health professionals across the European Union. Eur J Clin Pharmacol,52, 423-427.	- Uncertainty of the ADR diagnosis - Not know how to report - Lack of time - Types of ADR to be reported are misconcepted
Aziz, Z., et al. (2007). Reporting of adverse drug reactions: predictors of under-reporting in Malaysia. Pharmacoepidemiology and Drug safety, 16, 223-228.	- ADR too trivial and well known - Doubt that reaction is being certainly caused by a drug - Not knowing the PhV system - ADR not diagnosed - Lack of time
Toklu, H.Z., Uysal, M.K. (2008). The knowledge and attitude of the Turkish community pharmacists toward pharmacovigilance in the Kadikoy district of Istanbul. Pharm world sci, 30, 556-562	- Do not know how / where to report - Not essential - Not enough knowledge - Not enough time - Not mandatory - Doctors responsibility
Eland, I.A., et al. (1999). Attitudinal survey of voluntary reporting of adverse drug reactions. Journal of Clinical Pharmacology. 48, 623 – 627.	- Uncertain association - Too well known ADR - ADR too trivial - Lack of time - Not know how to report
McGettigan, P., et al. (1997). Reporting of adverse drug reactions by hospital doctors and the response to intervention. British Journal of Clinical Pharmacology, 44, 98 – 100.	- Unavailability of reporting form - Lack of time - Unsure how to report

involves different partners: health care professionals, marketing authorization holders and regulatory agencies, patients, lawyers and media. All parties should be closely involved in the system if they would like to benefit from it (7, 8).

It is expected that PhV stakeholders will do their best to follow the product once launched on the marked and to share information about its safety with each other. But, regardless the mandatory legal requirements and efforts of the pharmaceutical companies to collect spontaneous ADRs of their products from the market, the under-reporting rate is still very high (3,7, 9).

In non-EU countries, the underreporting issue is the same as in United Kingdom, France, Germany or even United States where underreporting rate is around 90% (3,10,11,12,13, 14,15,16). In the literature, the most recent published articles related to the improving of ADRs reporting describe Nepal, Malaysia and Turkey knowledge and attitude of the health care professionals regarding the post-marketing PhV and improvement of the reporting rate. (17,18,19). No studies conducted in former Republics of Yugoslavia or in Romania were found in published literature but it could be stated that the common major problem in PhV, regardless the region or country, is underreporting.

In his commentary Lexchin (2006) described some pluses and minuses of the current spontaneous reporting system and he emphasised the responsibility of the health care professionals, especially doctors, in the underreporting issue (20). The role of health care professionals in spontaneous reporting system is much bigger than one could expect.

In the mid 1970s Dr. Bill Inman conducted a study through which he identified the attitudes, so called "seven deadly sins", responsible that ADRs are not reported (10, 21, 22). After 30 years the reasons for not reporting ADR are slightly modified to those in 1970s and insecurity was added as an additional sin (22, 23). Inman's sins related to the attitude and knowledge were studied in studies presented in table 1 and showed high association with underreporting of ADRs regardless the geographical location of the country. Lack of time appears to be one of the leading reasons for underreporting in six of nine studies presented in table 1. This is a difficult obstacle to overcome and it is important to bear in mind when educating health care professionals and other partners in PhV arena. Another very important obstacle shown in these published studies is uncertainty about ADR diagnosing and causality. This could be overcome much easier than lack of time, by proper education and communication. Studies in table 1 show also that well known ADRs even if they are serious are not reported due to believe of reporters that only unexpected and serious reactions should be reported. Again, education could be an important tool to overcome these common believes.

Although the most important reasons for underreporting (table 1) are known from the mid 1970s, they are still causing this high degree of underreporting.

1.2 Development of pharmacovigilance system in South East European (SEE) countries

Baxter is as a multinational company and covers with its portfolio also all former Republics of Yugoslavia (SFRJ) (Slovenia, Croatia, Serbia, Macedonia, Bosnia and Herzegovina, Kosovo and Montenegro), Albania, Bulgaria and Romania. These countries form so called SEE region. Slovenia, Bulgaria and Romania among these SEE countries are a part of EU community and therefore their PhV regulation is completely harmonised with EU regulation (24). Other SEE countries have their own national regulation. Our study included only Romania, Croatia, Serbia, Macedonia, and Bosnia and Herzegovina.

Baxter local affiliate situated in Slovenia is responsible for marketing, regulatory activities and PhV activities in a cluster of countries that include Croatia, Serbia, Macedonia, BiH and Romania.

The specific of some SEE countries is also the fact that the marketing authorisation holder (MAH) should originate from the country and because Baxter is not legally present there it works through the distributors in the respective region. In Serbia, Croatia, Macedonia and Bosnia and Herzegovina, all Baxter products are authorized and sold by different distributors who act as a MAH for Baxter products in the region. In Romania distributors are not MAH and therefore Baxter itself is responsible for all PhV activities in Romania with the help of distributors due to a language barrier and allocation of the country.

SEE countries differ from the western EU countries or USA due to the fact that each country had started new era and independence from 1989. Each country had to face with the newly developed health care system, reforms and very hard political situation (25, 26, 27, 28).

After the collapse of Socialistic Federative Republic of Yugoslavia (SFRY), all newly organized republics were forced to establish among others also new drug agencies, new regulation on medicinal products and new regulation on PhV. This has started after 1995, when the political situation in these countries has stabilized (5, 29, 30, 31, 32, 33).

The structure of PhV system among SEE countries slightly differs. This is due to the fact that some countries are already in EU (as Romania), some are harmonizing their national legislation with EU legislation since they are accession countries and some has their own national legislation originated from EU regulation with some slight modifications (5, 24, 29, 30, 31, 32, 33).

2 The scope of the study: opportunities to improve pharmacovigilance activities in see countries

Although there is a local regulation, distribution agreement or other legal tool describing how to report ADRs, the underreporting of ADRs in SEE countries is still very high.

The study was conducted to evaluate the knowledge, practice and attitude of all parties involved in PhV arena regarding ADR reporting and PhV activities, and to find improvements to the reporting between health care professionals, distributors and Baxter.

Baxter distributors and their customers (mainly specialists from the hospitals where Baxter products are available) from Croatia, Serbia, Bosnia and Herzegovina, Macedonia and Romania were included in the study.

The scope of the study was to determine the awareness of PhV importance, the actual knowledge and implementation of PhV in the daily practice at the subjects who are responsible for reporting ADRs in the SEE region. The tools found through the results of the study will assist in the development of PhV in terms of reporting especially between employees at the distributor site and health care professionals, and thus contribute to increase reporting of ADRs.

3 Methodology

In this study the knowledge, attitude and practice (KAP) of PhV were studied using self-administered questionnaires (KAP questionnaires) in English language.

Due to the fact that the target population for the study comes from a wide geographic area, the mail survey was used to get the information. This option supposed to be cost effective, since e-mail was used to transfer the questionnaires, the cost was negligible, but greater probability of non-responders existed (34).

The pilot test was performed to examine the questionnaires in linguistic and interpretive way (35). Each of these two types of questionnaires was piloted between the Baxter employees from two different countries where English language is not a native language: Belgium and Slovenia. Time spent to complete the questionnaire and the understanding of the questions was also evaluated.

Two types of the KAP questionnaires were used: one for the distributors and the other for health care professionals. Minor differences existed between these two types, related to the questions referring to either only health care professionals or only to the employees working at the distributor. Each questionnaire contained a cover letter describing the purpose of the study briefly and concisely, including the time required to complete the questionnaire.

The questionnaires were mailed to the distributors in Croatia, Serbia, Bosnia and Herzegovina, Macedonia and Romania. Contact persons at the distributor site were asked to distribute the predefined number of the questionnaires to the employees at the distributor site and to the health care professionals at the hospitals, pharmacy, etc., and also to collect the questionnaires after completion and return them back in the defined timeframe by fax, post or mail in a scanned version.

The number of questionnaires differed from county to country. The number was determined taking in account the portfolio of the products in each country, number of employees at the distributor site and the number of distributor companies in the country.

Number of questionnaires sent was limited due to the limited number of the employees at the distributor site and the number of final customers of Baxter products, who mainly are specialists at the hospitals. To achieve the appropriate statistical power higher number of questionnaires should be used and completed (34).

Therefore, the simple descriptive data analyse was used to evaluate the data according different parameters such as country, job position, type of respondent, etc.

4 Results

4.1 Response Rate

4.1.1 Total response rate

In total 44 (38 %) questionnaires of 115 distributed were returned by fax or as a scanned document via e-mail in pre-defined time frame. The number of returned questionnaires varied according to the country, type of respondent and their job position. The response rate was higher among distributors (44 %) than at the health care professional site (33 %).

4.1.2 Response rate by a country

Among the respondent countries, Romania had the highest respondent rate among distributors (60 %) and health care professionals (87 %), followed by Serbia and Croatia. The minimum response rate was achieved by Bosnia and Herzegovina what could be attributable to a lower number of employees and end customers of Baxter products. Macedonia did not respond.

4.1.3 Response rate by a job position

In countries where Baxter works with one or more major distributors, the highest response rate was reached at the sales representatives. This was expected due to the fact that sales representatives communicate with health care professionals as the final Baxter customers on a daily basis and they are very important in obtaining the information about ADR from the market. At the health care professional level, the highest response rate was achieved among specialist. This result was expected due to the nature of Baxter products.

Graphically the response rate by the job position, country and responder type is presented in the Figure 1.

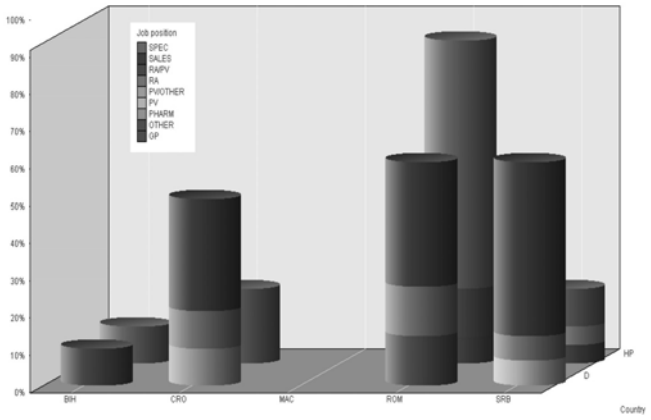

Figure 1: *Response rate by a job position, country and responder type.*
Graf 1: *Prikaz deleža odgovorov glede na delovno mest, državo in tip anketirancev.*

Legend: BiH = Bosnia and Herzegovina, CRO= Croatia, MAC = Macedonia, ROM = Romania, SRB = Serbia, D = distributors, HP = Health professionals, SPEC = specialists, SALES = sales representatives, RA = regulatory affairs, PhV = pharmacovigilance, PHARM = pharmacists, GP = general practitioners

4.2 Pharmacovigilance practice of responders

Among all 44 responders 24 (55 %) were aware of at least one patient experiencing an ADR. The results of reporting history in relation to the type of respondent are presented in a Figure 2.

Seventy five percent of the health care professionals who responded had been aware of at least one patient experiencing an ADR. But only 25 to 30% of them reported an ADR to the national drug agency or the manufacturer or licence holder of the product. The situation was reverse with respect to the distributor responders, where only 38% of them had been aware of a patient experiencing an ADR, but the reporting practice was between 20 and 30 %. Distributors usually do not have daily contact with patients, therefore the awareness of a patient experiencing ADR was lower than for health care professionals. Comparing the reporting practice between distributors and health care professionals it is clear that the underreporting practice of health care professionals is higher.

The most preferable method for reporting ADRs was to send the reporting form by fax, e-mail or post to the corresponding person or institution. The answers were similar for both types of responders.

Question related to the communication about ADRs between distributors and health care professionals showed that health care professionals who responded (mostly specialists) were not prone to communicate ADRs with MAH representatives (Figure 3).

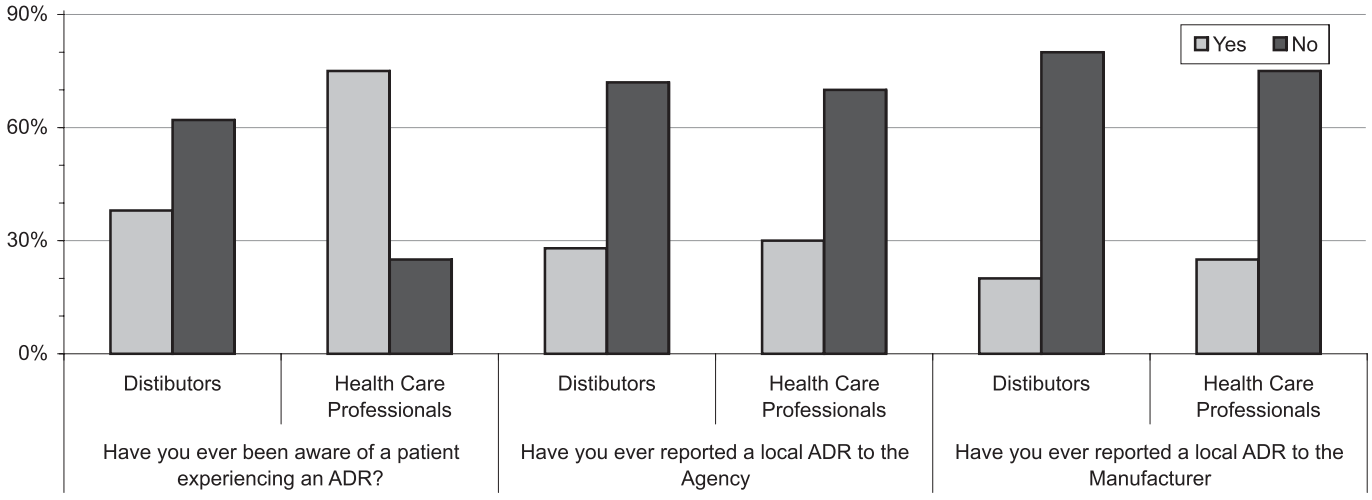

Figure 2: *Comparison of reporting practice between distributors and health care professionals.*
Graf 2: *Primerjava prakse poročanja med distributerji in zdravstvenimi delavci.*

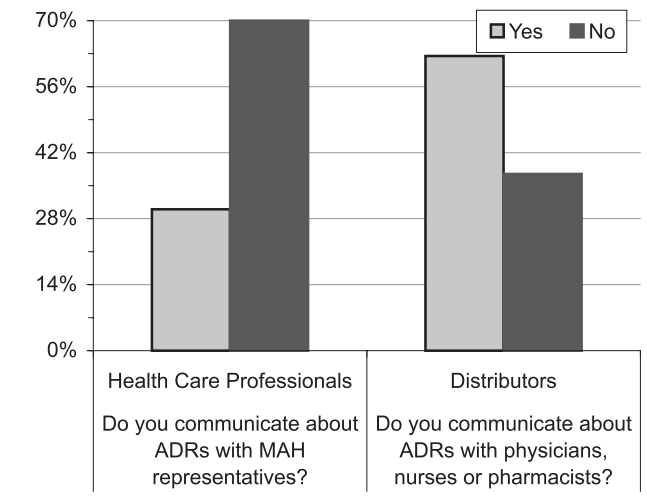

Figure 3: *Communication of ADRs.*
Graf 3: *Medsebojna komunikacija o neželenih učinkih.*

4.3 Pharmacovigilance knowledge of responders

Knowledge about PhV of health care professionals and distributors was evaluated with different questions referred to the PhV literature they received, their awareness of the local PhV system and their personal opinions regarding the importance of reporting ADR information.

The results showed that very high percentage of both type of respondents was not receiving pharmacovigilance literature. About 40% of responders received national PhV literature, mostly on yearly basis and this percent is almost equal for both types of responders.

Almost 100% of the responders regardless the type believed that the reporting of ADRs is important to improve drug safety and 95% of them agreed it is good for the company to report ADRs to the authorities. An additional question was added for distributors asking if it is sufficient if they receive ADRs only from the manufacturer of the product. Seventy five percent did not agree.

The results of the final two questions determined the PhV knowledge of both type of responders showed very good knowledge especially

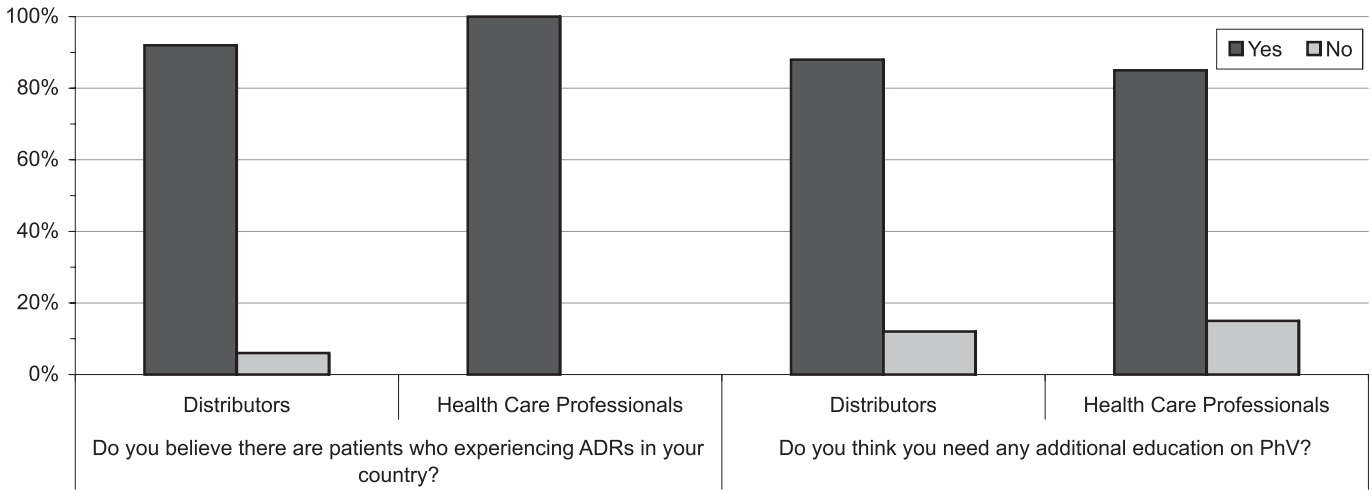

Figure 4: *PhV knowledge of responders.*
Graf 4: *Znanje o PhV glede na tip anketirancev.*

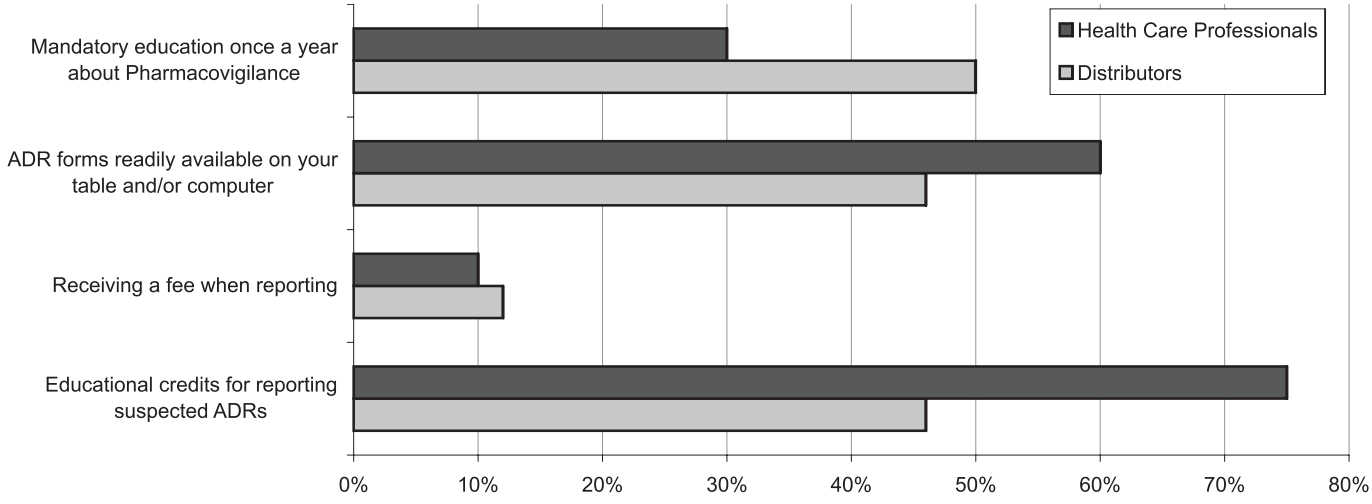

Figure 5: *Motivation for reporting ADRs.*
Graf 5: *Motivacija za poročanje neželenih učinkov.*

about the patients experiencing ADRs and about the PhV education. All health care professionals participated in the study and 92% of distributors believed there are patients experiencing ADRs in the country. The majority of distributors (88%) and health care professionals (85%) also thought they need additional education regarding Pharmacovigilance (Figure 4).

4.4 Attitude of responders towards adverse drug reactions reporting

Factors that would motivate the responders to report ADR are presented in Figure 5. The maximum deviation between both types of responders was obtained for educational credits what was expected since health care professionals are obliged to collect these credits in order to maintain the medical licence.

Regardless the type of responders the most important factors that would prompt the reporting of ADR was serious and not-expected ADR, unusual ADR and serious expected ADR. For more than 58% of distributors new drug on the market and increased frequency of non-serious ADR were the reasons that would prompt them to report ADR, while only 30 - 35% of health care professionals selected these options. Minority of responders would report an ADR if ADR was a drug interaction or ADR was 100% related to the drug. The distribution of

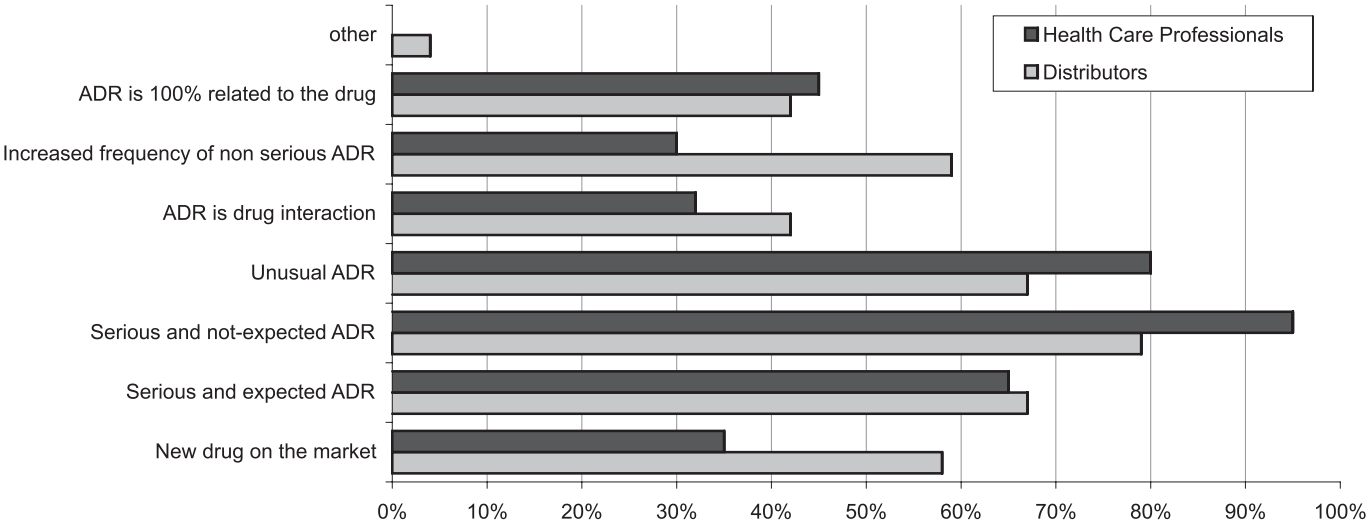

Figure 6: *Factors affecting the reporting of ADRs - comparison between D and HP.*
Graf 6: *Faktorji, ki vplivajo na poročanje o neželenih učinkih – primerjava med distributerji in zdravstvenimi delavci.*

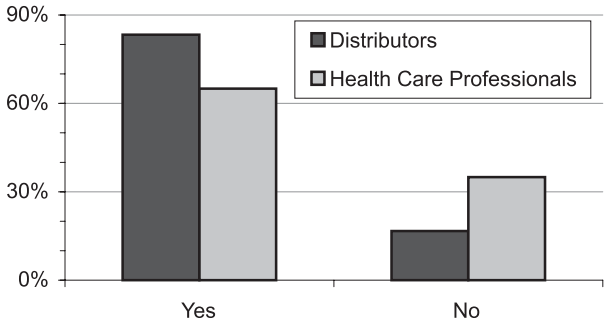

Figure 7: *The importance of information feedback.*
Graf 7: *Pomembnost povratnih informacij.*

results for distributors and health care professionals (Figure 6) showed the importance of factors affecting ADR reporting was similar for both types of responders although two factors are far more important for distributors (new drug on the market, increased frequency of non serious ADR).

Interestingly the distribution of the importance of factors that would adversely affect the reporting was very different for distributors and health care professionals.

The majority of distributors would not report an ADR because of the believe just one report would not make any difference if it is not reported (58%), because they did not have enough time due to other responsibilities (54%) and because they believed it is bad for the company if reporting ADR for their products (50).

On the other hand, the reporting addresses and not knowing how to report were the most important factors for health care professionals (60%, 65%) to deter reporting of ADRs.

The Figure 7 clearly presents the importance of information feedback for both types of responders. It is slightly more important for distributors where more than 80% responded with »yes«. Due to statistically not representative samples in terms of number of respondents, larger samples would probably show less difference between the types of responders and higher difference between the »yes« and »no« answers within the type of responders.

5 Discussion

According to our knowledge and reviewed published literature, this is the first study which evaluates and compares the knowledge, attitude and practice of health care professionals and personnel at the distributors in SEE countries, in order to facilitate the reporting of ADRs between the pharmaceutical company, its distributors and health care professionals as final customers.

The intention of the study was exploratory rather to provide precise estimates that would be applicable to whole population of distributors and health care professionals in SEE region. The major limitation of the study was low number of study population and low response rate. This was due to the fact that the study was conducted with Baxter distributors in the region and the fact that one person from each participating distributor's office was responsible to distribute the questionnaires to the health care professionals. It was not possible to compare the pharmacovigilance practice, knowledge and attitude between SEE countries and to evaluate the influence of job position, gender or age to the reporting rate and to get some statistically significant results, because of small number of participants. Nevertheless, the study reflects the way the Baxter distributors in the selected SEE countries and their final customers (as health care professionals) cope with ADRs and also showed comparable results with other published studies.

5.1 Current pharmacovigilance practice and knowledge of responders

The response rate among the participating SEE countries varied widely. The highest response rate (87%) for health care professionals was achieved in Romania. This could be attributable to the higher involvement of employees at the distributor site since they were responsible to deliver and collect the questionnaires to the health care professionals and the fact that Romania is already a member of European Union. Interestingly, response rate of health care professionals from other countries had not exceeded 20%. One speculated explanation for this observation could be that non-EU countries are less aware of the importance of PhV and without a proper knowledge they fear to involve with PhV. Macedonia did not respond what could be contributable to the fact that they still have no national legislation concerning PhV activities and their health care system is still in its early stage. This was also the reason why Albania, Kosovo and Montenegro were not included in our study.

The majority of health care professionals were medical specialists, working in hospitals. This is related to the fact that the questionnaires for health care professionals were distributed mainly to the hospitals. Response rate for distributors showed high involvement of sales representatives in our study. Sales representatives are very important from the company point of view since they are the primary contact with the health care professionals and are usually the first who receive information about ADR.

The percentage of responders who stated they had observed a patient with ADR before was the highest among health care professionals. This result was expected since the medical doctors, who generally completed our questionnaires work with patients on a daily basis and the result indicates that medical doctors have no problems diagnosing an ADR. But despite the awareness of ADRs among health care professionals, the reporting rate of ADRs to the national agencies or product manufacturers was very low for both types of responders. There are several published reports that commonly describe the problem of underreporting (23, 36, 37, 38, 39), therefore it could be concluded that the reporting culture is virtually the same regardless the geographical location of the country or its PhV historical background. This awareness of ADRs and reporting ADRs to the agencies or the company was also described in Belton study (1997). The study was multinational and the discrepancy between observing and reporting ADR was seen for most of the participated countries (40).

MAH representatives in the region are Baxter distributors and as such they are fully involved in PhV trainings conducted by Baxter and PhV trainings mostly conducted by their national agencies. It is interesting that the results showed distributors communicated with health care professionals regarding ADRs in much higher percent than opposite. From our experiences in Baxter we have received only one or two ADRs directly from the distributor in SEE region in the past two years. Although it is in the distribution agreement that distributor should report ADRs to Baxter and more than 60% of distributors communicate about ADRs with health care professionals, the underreporting to the company is still a big issue. Baxter experiences of very low reporting rate of ADRs are compatible with the results about PhV reporting practice in SEE region. Obviously there is a gap in communication between the company and distributor, not so much between the distributor as MAH representative in the region and health care professionals as final customers. There are no published studies where the communication between company representatives and health care professionals was studied which could confirm our results.

Our study showed that a large percent of both types of responders usually not receive international literature about PhV but mostly national literature mainly on a yearly basis. This situation is of concern given that these journals usually contribute to greater knowledge in the PhV field. Distribution of ADR bulletins is stimulation in terms of reporting rate of ADRs, but it is mostly an instrument to improve the knowledge about PhV.

Regardless the availability of PhV literature, our study showed very good knowledge about the importance of ADR reporting and national PhV system in SEE region. National agencies from non-EU countries perform seminars in order to improve PhV knowledge of any personnel participating in PhV system (33, 41).

By interpreting the results from our study, it could be concluded that the low reporting rate of ADRs to the company or to the national agencies may be secondary to the communication gap especially between MAH representative in the SEE region and the company. The PhV knowledge is not on a very low level, due to the education input of the national agencies but it still indicates the possibility of improvement.

5.2 Attitude of responders towards pharmacovigilance

Health care professionals believed that not know how to report an ADR would be the most important reason for not reporting it, followed by unavailability of reporting form and reporting address. These results were similar to other published studies. Lopez-Gonzales et al. (2009) systematically reviewed published literature on determinants of underreporting ADRs and confirmed that lack of knowledge and unavailability of reporting forms were the major excuses for not reporting (22). Belton (1997) study suggested that unavailability of reporting forms and addresses deterred reporting especially in countries where the form was a stand-alone document, not a part of prescription pads (40). This could be extrapolated to SEE countries where forms are mostly available as independent documents.

Interestingly, lack of time was only a minor obstacle in reporting ADRs according to health care professional's type of respondents. This is not in line with most of the published studies where the majority of responders agreed the lack of time was the major determinant for reporting (23, 40, 42) but Aziz et al. (2007) study had confirmed that lack of time was not a significant obstacle in reporting (32). Therefore it might be also speculated that the pressure on health care professionals to evaluate more patients per day and thus having less time for other so called "paper work" is not yet expressed in SEE region as it might be in more developed countries.

Distributors showed different results about the factors that deter reporting of ADRs. It is the fact that distributors has no direct daily communication with patients and therefore their view on these factors is different than of health care professionals. Since these responders are working as a MAH representative and their primary responsibility is not collecting ADRs, it is obvious why lack of time is important deterioration factor. Other two factors (one case would not make any

difference if it is not reported and it is bad for the company if ADR is reported) clearly showed lack of basic PhV knowledge and national regulatory requirements of distributors.

The most important reasons that would prompt health care professionals and distributors to report an ADR were serious not-expected ADRs, serious expected ADRs and unusual ADRs. Most of serious ADRs are seen in hospitals or patients are admitted to the hospital due to the serious ADRs (23, 40) and majority of health care professionals participated in our study work in hospitals. The study suggested the same attitude of health care professionals toward PhV as in other published studies (40), although new drug on the market was not among important reasons for reporting. Distributors also believed if a new drug is on the market and if there is an increase in frequency of non serious ADR, this would prompt them to report. This could be attributed to distributor's better knowledge in regulation compared to health care professionals, because regulation knowledge is important in their daily work.

Our experiences in Baxter showed great underreporting of serious ADRs from health care professionals in SEE region if comparing the reporting rate for the same products in other EU countries or US. One explanation for such discrepancy could be the number of patients treated in SEE countries. Statistics showed if we would like to detect one rare ADR with the incidence 1/10 000, 30 000 patients should be treated (35). Considering the above statistics and the health care professional's perception that serious ADRs prompt the reporting it is obvious why the reporting rate in SEE countries is so low.

The most motivating for health care professionals would be however to receive educational credits for reporting suspected ADR. Educational credits were not important for majority of distributors that is due to the fact that these credits are related only to physicians who need to update their medical licence. Regardless the low number of responders, our study also indicated that receiving a fee when reporting an ADR is not an important motivating factor for reporting.

Results about the importance of information feedback showed that responders would like to actively participate in PhV, to gain knowledge about the cases they had reported. It also showed that the communication within PhV arena is not ideal and should be improved.

5.3 Opportunities for improvement

Results from the study, showed the current practice, attitude and knowledge of MAH representatives (distributors) and health care professionals from SEE countries. These parameters are not corresponding to the current national legislation in terms of reporting ADRs. All three parameters showed some differences between both types of responders. Following results from the study the following opportunities reflect the improvements that could be implemented by the company:

Opportunities for improvements for health care professionals

This type of responders included in our study was mostly specialist from the hospitals. The results lead us to the following possible options for improvement the reporting of health care professionals working in hospitals :

Availability of reporting forms and reporting address

Looking from our company perspective, to improve the reporting rate of ADRs concerning our products, reporting forms could be distributed to the final customers via distributors in a paper version together with a computer version on a CD. This could be done as a part of a regular visit of a distributor representative or at a conference meeting. As another factor to deter reporting is unavailability of reporting address, this could be incorporated on the form. Considering that health care professionals has a preference to submit the report via e-mail, post or fax, the reporting form should also include address and fax number where to submit the reports. This kind of action would probably improve the reporting rate directly to the company not so much to the national agency, however this study aim was mostly to find some tools to improve reporting rate to the company not so much to the agencies.

Education about PhV reporting

Not knowing how to report was the major obstacle for health care professionals. Education is a key goal also for the national agencies in SEE countries, but what a company could do is to incorporate PhV training of health care professionals into different conferences or health care professional training's agendas.

Improve feedback about ADRs

Medical investigators and their teams should cooperate more in providing feedbacks about ADRs for the products in the way it would be appropriate for the company. When ADR is reported from the country, this should not be treated as a one-way street. The company should provide some transparent information about the cases and not keep it as a secret. It is a regulatory obligation for the company to report ADRs to the agencies but it should be also taken into account that reporters are usually excluded from the circle.

Educational credits for reporting ADRs are the domain of national institutions and Baxter has no influence or power to motivate the reporting of health care professionals in such way.

Opportunities for improvements for distributors

The key points for improvements the reporting rate of distributors result from the fact that the majority of responders in our study were sales representatives. The possible options for improvements are:

Education of consumer facing employees

Following the results from the study, education is also an important motivation for distributors to report ADR. But from other results concerning attitude and knowledge of responders towards reporting, some lack of basic PhV knowledge and some misconceptions regarding the spontaneous reporting of ADRs can be seen. Educational intervention is important especially for sales representatives who usually disagree with PhV specialists about the importance of the reporting ADRs. Since effects of intervention might diminish over time, some appropriate educational interval should be implemented. As only majority of responders receive some national PhV bulletins on a yearly basis, this is a good indicator that lack of PhV knowledge is a major problem in SEE region.

Improve feedback about ADRs

This is an important gap in current PhV system for distributors. Again as for health care professionals, the company should consider how to

provide appropriate feedback information for distributors. With regard that sales representatives are in contact with health care professionals, the company might consider to prepare information on reported ADRs in such way, it would benefit both types of responders at the same time.

6 Conclusion

The underreporting issue exists also in SEE countries. Only a good will of reporters, who are mostly health care professionals and their good knowledge about PhV, could run the system in a proper way. Pharmaceutical companies usually expect that reporting ADRs from local markets is an automated process. The companies should invest more in communication with local markets and local reporters especially in countries with a short history of PhV. If companies would really like to benefit from spontaneous reporting from different countries, they should first get the clear picture of the current reporting culture.

Our study was useful as a preliminary study in detecting the attitudes and practice of PhV among health care professionals and distributors in SEE region. Results showed important obstacles in current PhV system and tools were proposed to overcome these obstacles. The tools that could be employed to tackle the underreporting problem in SEE region are the following:

- ✓ Availability of reporting forms
- ✓ Improved education about ADR reporting
- ✓ Feedback about ADR information available to reporters

Since this was the first study that evaluated the attitudes, practice and knowledge of health care professionals and distributors in SEE region, it would be useful to define some future steps that would help to improve the reporting of ADRs in the region and the following is proposed:

- ✓ To set up a group of medical experts and other representatives from the PhV group and plan how and to what extent the feedback information could be given.
- ✓ To perform an additional study that would include only nurses would greatly contribute to the overall picture of ADR reporting situation in the region and consequently to improve the situation.

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