Periodic Safety Update Report and National Report Assessment in Turkey: Scientific Letter

Türkiye'de Periyodik Güvenlilik Güncelleme Raporu ve Ulusal Rapor Değerlendirmesi

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Geliş Tarihi/*Received:* 07.01.2011
Kabul Tarihi/*Accepted:* 11.05.2011

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ABSTRACT Objective: To identify how many reports have been received either authorization/permission renewal reports or routine reports in 2009 and classify top 5 most evaluated active substance/pharmacological group based on these reports. **Material and Methods:** We performed a study in the Periodic Safety Update Report (PSUR) and National Report Assessment Department from March 2009 to December 2009. Complete data obtained about the drugs were entered into a database. The database was in MS Excel format. **Results:** Parenteral nutrition and electrolyte solutions reports (35%) were identified as the most received reports in 2009. Cough and cold medicines (24%), diclofenac (17%), estradiol (15%) and amoxicillin (9%) reports were the other substances/pharmacological groups that were ranked from 2nd to 5th respectively. The number of authorization/permission renewal reports were counted 553 (48.7%) while the number of routine reports were 582 (51.3%). **Conclusion:** It was determined that, the number of reports pertaining to parenteral nutrition and electrolyte solutions were higher than that of other substances/pharmacological group. It was assessed that this group's diversity on authorized/permitted pharmaceutical forms and dosage types was what caused the difference. This study can be supposed to provide a foresight to PSUR and National Report Assessment Department in the future. These data may be used for the development of report assessment plans.

Key Words: Diclofenac; amoxicillin; parenteral nutrition; estradiol

ÖZET Amaç: 2009 yılı içerisinde Sağlık Bakanlığına, ruhsat/izin yenileme amacıyla ve rutin olarak sunulan güvenlilik raporlarının sayısının belirlenmesi ve söz konusu raporlarda en fazla sunulmuş olan beş etkin madde/farmakolojik grubun tespit edilmesi amaçlanmıştır. **Gereç ve Yöntemler:** Sağlık Bakanlığı İlaç ve Eczacılık Genel Müdürlüğü Periyodik Güvenlilik Güncelleme Raporu (PGGR) ve Ulusal Rapor İnceleme Şube Müdürlüğü bünyesinde, Mart 2009 ve Aralık 2009 tarihleri arasını kapsayan dönem içerisinde toplanan veriler bu çalışmada kullanılmıştır. Tüm veriler MS Excel programına yüklenmiş ve bu program yardımıyla değerlendirilmiştir. **Bulgular:** Hastalarda kullanılan çeşitli parenteral beslenme ve elektrolit çözeltilerine ait raporların %35'lik bir oranla ilk sırayı aldığı tespit edilmiştir. Diğer dört etkin madde/farmakolojik grup ise sırayla; soğuk algınlığı ilaçları %24, diklofenak %17, östradiol %15 ve amoksisilin %9 olarak belirlenmiştir. Ayrıca ruhsat/izin yenileme kapsamındaki başvuruların sayısı 553 (%48,7) iken, rutin sunulan raporların sayısı ise 582 (%51,3) olarak tespit edilmiştir. **Sonuç:** Parenteral beslenme ve elektrolit çözeltilerine ait rapor sayısının diğer etkin madde/farmakolojik gruba oranla daha fazla olduğu belirlenmiştir. Söz konusu ürün grubunun ruhsatlandırılmış/izin verilmiş olan farmasötik form ve dozaj şekillerinin daha çeşitli olmasının buna neden olduğu düşünülmektedir. Bu çalışma ile PGGR ve ulusal raporların değerlendirilmesi hususunda yeni yaklaşımlar geliştirilebileceği ve daha sonra yapılacak çalışmalar için bir alt yapı oluşturulabileceği sonucuna varılmıştır.

Anahtar Kelimeler: Diklofenak; amoksisilin; parenteral beslenme; östradiol

Turkiye Klinikleri J Pharm Sci 2012;1(1):59-62

Pharmacovigilance is defined as the science and activities concerned with the detection, assessment, understanding and prevention of adverse reactions to medicines (i.e. adverse drug reactions or ADRs). The ultimate goal of this activity is to improve the safe and rational use of medicines, thereby improving patient care and public health.[1]

The safety reports [Periodic Safety Update Report (PSUR)s /National Reports] are one of the main components of the pharmacovigilance system.

A report contains all relevant clinical and non-clinical safety data only the period of the report (interval data) with the exception of authorization status information for initial and renewal applications, and data on serious, unlisted adverse reactions.[2]

The main focus of the report should be adverse reactions. The reports should include a scientific evaluation of the risk-benefit balance of the product(s).[2]

Reports must be submitted for all registered products regardless of marketing status. A single report may cover all products containing the same active substance(s) licensed by one marketing authorization holder (MAH).[2]

The report will usually include all dosage forms and formulations, as well as all indications, associated with such an active substance. Within the report, separate presentations of data for different dosage forms, indications or populations (for example, children vs. adults) may be appropriate, however an overview of the combined data should also be provided.[2]

For combinations of substances which are also registered individually, safety information for the fixed combination may be reported either in a separate report or be included as a separate presentation in the report for one of the separate components, depending on the circumstances. Cross-referencing all relevant reports is essential.[2]

A report is intended to provide an update of the worldwide safety experience of a medicinal product to competent authorities at defined time points post-authorisation.[2]

National Reports are the safety reports about the drugs which are authorized/permitted only in Turkey.

At these defined time points, MAHs are expected to provide succinct summary information together with a critical evaluation of the risk-benefit balance of the product in the light of new of changing information.[2]

As a result of this evaluation, it is decided if there is a necessity for further investigation or any changes about the product information.

Once a medicinal product is authorized in Turkey, even if it isn't marketed, the MAH is required to submit PSURs/National Reports at 6 monthly intervals for first 2 years, annual reports for the following 2 years on routine reports and the total 5 years period reports (preferably with summary bridging report) on authorization/permission renewal reports and thereafter at 5 yearly intervals. PSURs/National Reports should also be submitted upon requests of a competent authority at any time after granting of the marketing authorization/permission.[3]

The main focus of these reports should be presentation, analysis and evaluation of new or changing safety data received during the period covered by the report.

"PSUR and National Report Assessment Department" was established in March 2009. Before this date, the report assessment was being made by Turkish Pharmacovigilance Center (TUFAM). After March 2009, specially this department has taken over this function.

MATERIAL AND METHODS

"PSUR and National Report Assessment Department" performed a study with data obtained from March 2009 to December 2009. Complete data obtained about the drugs report were entered into a database. The database was in MS Excel format and contents of the database are product tradename, active substance, MAH information and correspondence personnel name for assessing the report in competent authority (Table 1).

TABLE 1: An example for the reports in MS Excel format database.

Submission number	Subject	MAH	Drug name	Active substance	Correspondence personel
215386	Renewal	A	B®	Sildenafil	Pharm.M.Sc. .Ebru ŞEN
227062	Routine	X	Y®	Zoledronic acid	Pharm.M.Sc. Ecem TOPÇU

MAH: marketing authorization holder.

All drugs were classified according to their active substances. They were listed in order of number of received reports in 2009 and the top five substances were identified. Additionally we counted all routine reports (6 monthly and annual reports) for brand new licensed products, authorization/permission renewals and thereafter 5 yearly reports which were received in 2009.

RESULTS

The results showed that; parenteral nutrition and electrolyte solutions reports (35%) were identified as the most received reports in 2009. Cough and cold medicines (24%), diclofenac (17%), estradiol (15%) and amoxycilline (9%) were the other substances that were ranked from 2nd to 5th respectively (Figure 1).

The number of reports received were 50 for the parenteral nutrition and electrolyte solutions; 35 for cough and cold medicines; 25 for diclofenac; 21 for estradiol and 13 for amoxicillin (Figure 2).

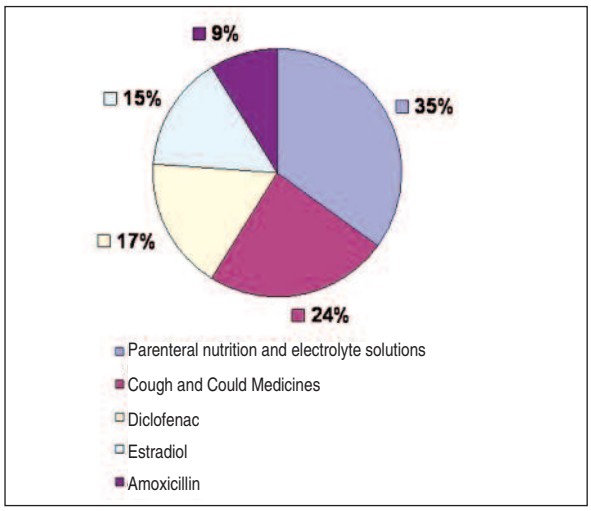

FIGURE 1: . Most frequently received reports in 2009 (%).
(See for colored form http://eczacilikbilimleri.turkiyeklinikleri.com/)

Of these reports 553 (%48,7) were authorization/permission renewal reports; while, 582 (%51,3) were routine reports (Figure 3).

DISCUSSION

The results showed that, the number of reports pertaining to parenteral nutrition and electrolyte solutions were higher than that of other substances/pharmacological group. It is assessed that this group's diversity on authorized/permitted pharmaceutical forms and dosage types was what caused the difference.

It has been identified that the number of routine reports were higher than the number of reports presented with regard to authorization/permisson renewal. The reason was that the routine reports periods are more frequent as in 6-month and 1-year intervals. Within this context, while totally six routine reports are submitted, for an authorized/permitted product, only one report is submitted for renewals. Therefore, this situation constitutes for the difference in the number of reports.

Based on literature review with regard to this research, because there were no related study in this context, no comparison has been made. This study is considered relatively important, because of its uniquness and provides a general insight to the subject mentioned.

CONCLUSION

Pharmacovigilance is subject to a number of developments including electronic reporting, mandatory reporting by companies with registrated products (also called MAH), inspections of pharmacovigilance activities of MAHs, risk management planning, development safety update reports, data

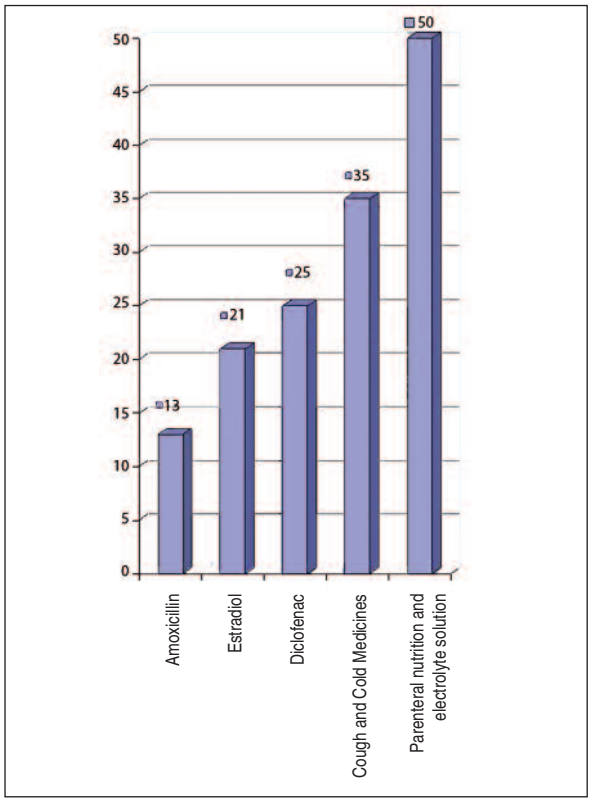

FIGURE 2: Most received reports in 2009 (number).
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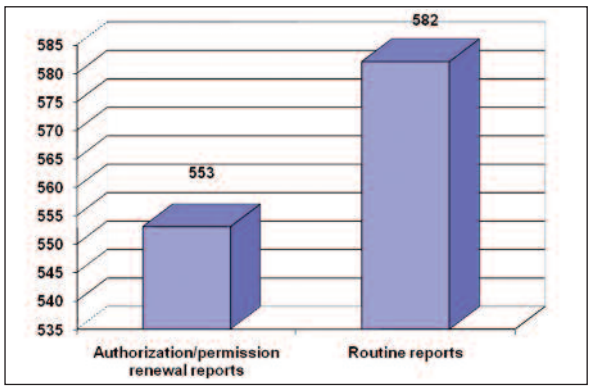

FIGURE 3: Reports content in 2009 (number).
(See for colored form http://eczacilikbilimleri.turkiyeklinikleri.com/)

mining and specialised staff training in pharmacovigilance.

Pharmacovigilance systems are necessary for all countries in order to decide the risk/benefit ratio of the drugs.[4]

Nowadays, pharmacovigilance is an overdeveloping system and every nation should establish and realise their own drug safety system to protect the public health and to be aware of their own population and it is performed since March 2005 in Turkey with published related regulation and guideline according to European Union (EU) regulations 2001/83/EC.[4] In EU an amendment was applicated to this directive. Because of our harmonization process with EU, our studies have still been continued for adapting revised regulations in pharmacovigilance. In this context, the PSUR/national report application dates and their scope will be revised as soon as possible in our country.

This study comprises of the data which has been obtained since March 2009. For this reason, results were not comprehensive enough. Nevertheless, future projects planned would constitute more detailed data. As a result, more comprehensive studies could be planned to be performed, in the future based on a variety of subjects and interpretations.

This study can be supposed to provide a foresight to PSUR and National Report Assessment Department in the future. These data may be used for the development of report assessment plans.

In conclusion, pharmacovigilance is the science and the activities relating to the detection assessment understanding and prevention of adverse effects or any other medicine-related problem.

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