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Research Article

Benefits of a National Program for Adverse Drugs Reactions (ADRS) Surveillance in Diabetic Patients

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Abstract

Voluntary notification of suspected adverse drug reactions (ADR) is the most worldwide method to detect these events. Unfortunately, health professionals in Latin American countries have no "culture" to notify ADR. For this reason, the National Diabetes Program (NDP) in Paraguay decided to regularly contact their patients, in order to increase ADR detection. To evaluate the results of this experience, this study was performed.

Methods: a descriptive, observational, cross-sectional study with an intervention phase was performed. A non-probabilistic sample of patients belonging to NDP was selected and compared with historical results of the program. The intervention activities consisted in a monthly contact of the patients by a member of the program.

Results: 2,390 patients with type II diabetes were enrolled in the study and compared with the same number of patients belonging to the program but with classical follow-up. Concerning the adverse drug reactions, 146 reports were registered during the study period, which mean 6.1% of all patients enrolled, while in the same period, historically the ADR reports were 0.94%. 66.9% of these reports were performed by the patients while 42.1% were notified by health professional. Main ADRs reported were vomiting 28.8%, dizziness 28.4%, diarrhea 10.8%, hypoglycemia 10.2% or abdominal pain 6.5%. The antidiabetic drugs that presented the greatest suspicion of ADRs were metformin 45.31%, glimepiride 21.8%, glibenclamide 6.25% and insulin 3.13%.

Conclusion: Periodical contact of patients covered by a National Diabetes program was able to increase 6 times the historically annual of report of pharmacovigilance adverse drug reactions.

Keywords: pharmacovigilance, adverse drug reactions, reports, voluntary, active notification, program.

INTRODUCTION

A drug approval for its commercialization at a national level implies that its efficacy has been demonstrated and that the undesirable effects detected in pre-marketing studies were acceptable. However, until the time of marketing, the efficacy and safety of the drug have only been proven in the short term and in a small number of carefully selected people. Hence, it could be said that the information obtained in the clinical studies of the different phases until drug approval by the health authority are not sufficient to predict what will happen in routine clinical practice in terms of the appearance of infrequent or slow-onset adverse reactions, which are more feasible to detect in the post-marketing stages.¹

To prevent or reduce these harmful effects, it is essential to have pharmacovigilance mechanisms. Pharmacovigilance, according to the WHO, is defined as the science and activities related to the detection, evaluation, understanding and prevention of adverse effects of medicines or any other problem related to them².

Systematic notification of adverse reactions and their permanent statistical analysis would make it possible to generate an alert or "signal" about the behavior of medicines in the population of the region. The success or failure of any pharmacovigilance activity depends on the reporting of suspected adverse reactions.

Pharmacovigilance is particularly important in drugs destined to treat prevalent chronic diseases since a large amount of the population will receive the medicines.

In Paraguay, diabetes became one of the most prevalent disease since exceeds 6.5% of the adult population. For this reason, the National Diabetes Program considered it a priority, and because of that several efforts have been done in order to improve the quality of health care, including pharmacovigilance policy for drugs used in the treatment of this disease (4).

The most widespread pharmacovigilance method is the spontaneous notification system, also known as the "yellow card system". Unfortunately, the number of reports is mince,

especially in Latin American countries where the culture of spontaneous report is weak.

This work intends to determine the most frequent adverse drug reactions (ADR) in diabetic patients using a special tool as the ADR Suspected Notification Form designed by the National Directorate of Sanitary Surveillance under the Ministry of Public Health and Social Welfare.

METHODOLOGY

Type of study: a descriptive, observational, cross-sectional study with an intervention phase.

Patient selection: a non-probabilistic sample was recorded for the convenience of the patients.

Groups of study: the reports obtained from patients enrolled in the study were compared with the notification ratio obtained from a same number of patients randomly selected from the historically data base of the National Diabetes program.

Intervention: active notification sheets of suspected adverse reactions to drugs validated by the National Directorate of Sanitary Surveillance of the Ministry of Public Health and Social Welfare, and report directly by the patients belonging to the National Diabetes Program. The program included not only the spontaneous report but also a monthly contact of patients by the Program in order to educate in

Pharmacovigilance importance, methods and way of notifications.

Period of Study: one year period from 01-01-2021 to 31-12-2021

Data Collection Tool: a) active notification sheets of suspected adverse reactions to drugs validated by the National Directorate of Sanitary Surveillance of the Ministry of Public Health and Social Welfare. b) a review of documents and medical records in order to obtain data from each patient in the program.

Study variables: patient coding correlated with the initials of the name and surname, weight, height, age, sex, clinical features, HbA1c, cholesterol and triglycerides blood level, BMI, blood pressure, complications associated with diabetes, type of adverse reaction, drug used for treatment.

Ethical Considerations: Patients were coded to hide their identifications throughout the study. The study protocol was approved by the Institutional Ethics Committee (FCQNA).

RESULTS

2,390 patients were enrolled in the study all of them with type II diabetes.

The initial features of these patients were similar with those reported by the patients belonging to the historical data from National Diabetes Program (table 1).

Table 1: General features of patients at the initial medical examination

Feature	Patients enrolled in this study	Patients selected from NDP database	P value
Number of patients	2390	2390	NS
Age	62.4±5.2	63.0±4.9	NS
Sex	F: 52.8%, M:47.2%	F: 53.2%, M:46.8%	NS
Body Mass Index	N:28.6%, OW: 38.8%, O: 32.6%	N:28.9%, OW: 38.3%, O: 32.8%	NS
Additional illness	73.5%	75.2%	NS
Initial HbA1c	N:43.8%	N:44.2%	NS

Only 26.53% of the patients enrolled in the study had no other added pathologies apart from type II-Diabetes, while 64.29% of them had associated arterial hypertension, 41.84% had dyslipidemia, 38.78% had the three joint pathologies (hypertension and dyslipidemia), while 3.06% reported having other pathologies (osteoarthritis, thyroid disease, rheumatoid arthritis, etc.).

43.8% of the patients surveyed had normal values of HbA1c at initial examination, 26.5% of them had values in the limit of the normal range and 29.6% had abnormal high level of this protein.

Concerning the adverse drug reactions, 146 reports were registered during the study period, which mean 6.1% of all patients enrolled, while in the same period, historically the ADR reports were 0.94%.

66.9% of these reports were performed by the patients (n=98, 4.1% of all ADR) while 42.1% notification were developed by health professional (n=48, 2.0% of all ADR).

Among all patients enrolled in the study that reported the 98 ADRs, 62.5% were female and 37.5% were male. The main range of age of those patients that reported ADRs was 50-59 years (average 55.2 yrs.).

Health professionals that reported ADR were in 66.3% general practitioners, and their average age was 41.2 yrs.

The type of ADRs reported were: vomiting 28.8%, dizziness 28.4%, diarrhea 10.8%, hypoglycemia 10.2%, abdominal pain 6.5%, bruising 6.2%, spasms 4.4%, pain at the site of insulin application (if they were in treatment for her) 4.3%, constipation 4.1%, gastritis 2.3%, heartburn 2.2%, and itching 2.0%.

The antidiabetic drugs that presented the greatest suspicion of ADRs were metformin 45.31%, glimepiride 2mg 9.38%, glimepiride 4mg 12.5%, glibenclamide 5mg 6.25%.

Among the patients who used insulin, 3.13% reported adverse reaction associated to NPH or intermediate-acting insulin such as hypoglycemia or pain/hematoma at the injection site; 7.81% of those individuals that used regular or crystalline insulin, presented suspected ADRs; while users of insulin lispro, 3.13% presented bruising or pain at the injection site.

DISCUSSION

Pharmacovigilance has four major stages: detection, deduction, decision, communication/dissemination. However, "detection" is a key point, since without detection it is not possible to develop the other phases. Most commonly

detection stage employs observational / pharmacoepidemiological methods like spontaneous reports, case series, cohort studies or case-control studies; which mean that either patient's self-report or health professional reports are needed. The classic spontaneous or voluntary notification methods are techniques in which the researcher (generally members of the health care team) does not control the variables, but simply is attentive on the use of drugs and the consequences of their use. The weaknesses of this method are that it's depend on the willingness of the person to report, it has little sensitivity, its monitoring is difficult, and it is generally associated with low quality of information and false alarms.

On the other hand, epidemiological methods are usually designed to determine the adverse reactions of drugs before or after their commercialization, and are generally carried out in a limited group of individuals.

Finally, intensive methods are used in health institutions where data collection in a systematic way is available and where adverse effects of drugs can be collected without major problems. Unfortunately, because a great number of staff members are needed to develop a follow up of drug utilization at population levels, these active methods are usually unviable for the majority of the health systems.

Based on these arguments, is that the National Diabetes Program in Paraguay decided to adopt the voluntary reports to alert for ADR of the medicines provided for patients included in this Program. However, as previously mentioned, these spontaneous reporting depends on country's culture. Unfortunately, in all Latin-American countries has not in the habit of self-reporting. This low ratio of reports is due for many reasons, some of them are associated with people's lack of time, lack of will and commitment, fear of being identified or due to the population discredit in their own health authorities and in how they can use the information properly (6). On the other hand, health professional reporting is low mainly due to the belief that it exists a potential risk in being personally involved in ADR (7).

Data about adverse drug reactions that are provided by patients in local levels have a great relevance and a main educational value, since might help to make future regulatory decision-making at the national level.

Information obtained from abroad may not be relevant for other countries of the world, since culture, health perception, and circumstances are different. When information for a country/region/town does not exist, it can take longer for drug regulatory authorities, pharmacists, patients and pharmaceutical companies to detect a potential health problem.

In Paraguay, the notification of suspected adverse reactions is voluntary and it is essential that health professionals become aware of the importance of strengthening the implementation of a Pharmacovigilance Program at the National level that include a monthly contact of patients.

It is interesting that the majority of the reports came from the patients. It is clear, that health professionals still need to be train in ARDs reporting.

Through the information obtained from the clinical records of the patients, it was possible to identify that, patients in range of 50-59 years old were the most motivated range of age to perform an ADR report.

Regarding the frequency of suspected adverse reactions to antidiabetic drugs, it was determined that metformin 850 mg was the most frequent drug that gives ARDs.

The implementation of the ADR Suspected Notification Sheet with periodically patient's contact has great importance in pharmacovigilance strategy, since an alert signal regarding possible ADRs is given by the combination of experiences reported in several countries and provides scientific contributions for the rational use of medicines.

Medical doctors should be also be contact periodically in order to maintain their alert status to detect ADR.

CONCLUSION

Periodical contact of patients covered by a National Diabetes program was able to increase 6 times the historically annual of report of pharmacovigilance adverse drug reactions. Patients that more notified ADR are women between 50 to 59 yrs.

CONFLICT OF INTEREST

All authors confirm that it does not exist conflict of interest in this research.

REFERENCES

1. PAHO. Drug Safety Surveillance. Guide for the installation and start-up of a Pharmacovigilance Center. . Uppsala, Sweden. Published by the Uppsala Monitoring Center (the UMC). 2001. 22-26.
2. WHO. WHO policy perspectives on medicines. Pharmacovigilance: guarantee of safety in the use of medicines. Geneva. WHO/EDM/2004.8, 2004. P. 3-9. Available in: <https://apps.who.int/iris/handle/10665/68782>
3. Murillo MD, Fernández-Llimós F, Tuneu i Valls L. Pharmacotherapeutic follow-up guide for diabetes. Ed.: Espai Gràfic Anagrac, S.L. Barcelona, Spain. 2019. P. 45-62. Available in: https://www.ugr.es/~cts131/esp/guias/GUIA_DIABETES.pdf
4. Paraguay-PAHO. National Diabetes Program. Ministry of Public Health. Paraguay Government. 2021. P. 24-35. available at: www.paho.org/spanish/ad/dpc/nc/diabetes-atlas-par.pdf.
5. Sweetman SC., Martindale. Pharmacotherapeutic Follow-up Guide. 3rd Edition. Barcelona. Spain. 2007. P 3515-31.
6. Aspinall MB, Whittle J, Aspinall SL, Maher RL, Jr, Good CB. Improving adverse-drug-reaction reporting in ambulatory care clinics at a Veterans Affairs hospital. Amer J Health Syst Pharm. 2002; 59:841-845.
7. Leghari Q., Chand S., Bushra R. et al. Exploration of Perception, Need and Barriers against Pharmacovigilance and Adverse Drug Reactions Reporting: Healthcare Professionals' Insight. Journal of Pharmaceutical Research International 2021; 33(7):78-86.