DISPENSING PROCESS AS A CORNERSTONE OF IMPROVING PHARMACOVIGILANCE

by Aldo Alvarez-Risco[1], Shyla Del-Aguila-Arcentales[2], Santiago Diaz-Risco[3]

The dispensing process is the clinical process that the patient receives to ensure that the use of medications is optimal from the point of effectiveness and safety. At the same time, it serves as a filter for the detection of adverse drug reactions. Therefore, plans to improve the detection of adverse drug reactions should be based on the effective implementation of the dispensing process in community pharmacies. Pharmaceutical companies have a role in this process in educating the pharmacist on their products and receiving feedback on any adverse reactions.

Dr. Aldo Alvarez-Risco is a pharmacist in Lima, Peru, with the following degrees, Master in Pharmaceutical Care, Master in Pharmacology and Doctor of Pharmacy and Biochemistry. He is a full-time researcher in the School of Administrative Sciences and Human Resources at the Universidad de San Martin de Porres. He has participated in various pharmacy practice and pharmacy policy research units; and currently, he is carrying out research in sustainability issues. He has presented various sessions at the annual FIP Congresses. He is co-editor of the book "Pharmaceutical Care Implementations - The Clinical Pharmacist's Guide" and co-editor of the book "Building Sustainable Cities – Social, Economic and Environmental Factors". He has been speaker at Pharma events in 20 countries.

1. Prescription process

To ensure the correct dispensing process, a previous activity must be improved: namely the prescription process. The following are some specific issues related to this aspect:

A. Study of the rules

The purpose of the study of prescribing norms is to determine the magnitude of the difference between prescribing norms and prescribing behavior in practice. This is a good starting point to discuss how to correct the identified differences. Authors vary in the definition of "rational prescription" norms; most authors give only a vague definition: "a drug treatment must be appropriate, effective, safe and economical". To analyze how much prescription in practice deviates from the opinion of a group of experts or from a number of clinical studies, the standards must be specified in detail; to do this it is necessary to analyze different medical conditions separately. For each of these conditions an "acceptance" rule must be specified, which means that sales data or prescription data are not the best way to study this problem, because these methods include information about the medical condition for which the prescription was made. One way to obtain this information is to analyze medical records or give prescribers "patient papers" or "patient videos" for those who receive the prescription; these results can be compared with norms derived from the data from clinical studies or from experts[1].

B. Patient safety

According to the Institute of Medicine (www.iom.edu) of the National Academy of Sciences of the United States of America (www.nationalacademies.org), more than 7,000 deaths occur each year as a result of medication errors, and more than 700,000 patients are damaged; between 2% and 7% of hospital admissions are attributable to medication errors, and the annual cost related to these errors can be as high as 5.6 billion dollars[2]. Although there is not a large amount of published data related to Adverse Drug Reactions (ADR) in the outpatient setting, a study done by the Academy of Managed Care Pharmacy reported that 394 of 2248 patients (18%), who had received a prescription, reported complications, but the documentation of an ADR was only present in 64 of the cases (3%); half of the 394 patients reported complications in medical care, while 3 of the 64 patients who presented ADR required hospitalization; 8 of the 64 patients had a documented previous reaction to the causative drug[3].

Likewise, other studies identified that several patients with cardiovascular diseases use vitamins that are not supported by a medical prescription[4-5]. In spite of everything, over- prescription is also found in developed countries; Thus, for example, in a study, 18% of patients receiving aspirin are more likely to be harmed than to benefit from the administration of said medication[6].

The reasons for irrational prescription have generated an intense discussion over many years. In a memorable publication, the Swedish doctor Linnie[7], mentioned 21 reasons for irrational prescription; among these: incorrect diagnosis, outdated medical knowledge, inappropriate combination of medications. In addition, the authors

currently agree that irrational prescription is the result of a number of factors such as knowledge and education that influence the quality of the prescription, the absence of independent sources of information together with aggressive marketing by of the pharmaceutical industry among others[8-9]. Forms committees have been another strategy to handle the problem of irrational prescription; however, their influence has been largely restricted to prescription in hospitals.

C. Sociological Studies – Structural

The studies here refer to those investigations aimed at analyzing the relationships between prescribers and their environment; the most famous being those of Coleman, Katz and Menzel in the 1950s. They analyzed a specific situation when a widely used antibiotic was introduced in a number of small cities in the US. They looked at the point when the doctor started prescribing the medication, and they called it "adoption time". The antibiotic studied was more effective than the drugs they were replacing, which meant that a doctor who started prescribing the medication continued to do so. This is not the general pattern of drug dissemination, since normally a doctor who treats a drug once can prescribe it later in several, but not in all, similar clinical situations. In addition, the doctor can stop prescribing a medication after use if the beneficial effects do not occur. Coleman *et al* studied the prescription pattern by analyzing the prescriptions collected in local pharmacies. From these prescriptions they recorded the adoption time and the medical prescription. The analysis was based on a sociological structure and the doctors were asked to name those colleagues in the city who were their friends, those with whom they discussed pharmacotherapies and those from whom they normally took advice about medications. Based on this information, 3 networks were built: a network of friends, a discussion network and a network of counselors; it was found that those doctors who were in the center of the networks began prescribing the new medication earlier[10].

D. Change of selection standards

As mentioned before, physicians generally have a limited number of options available when they treat the majority of their patients. The standard options for prescribers can vary between 50 and 500 different medications; Over time these options change. Changes occur due to external influences or the doctor's experience after a patient has used a medication of his/her choice. Normally, a doctor will begin to use a new medication when an old one has not produced the expected effects in a patient or if the patient has experienced adverse effects. The doctor will then try a new medication chosen through a selection process. The most influential sources in this process vary from country to country and from condition to condition[11]. A course aimed at health professionals aimed at reducing the prescription of benzodiazepines for sleep and socio - psychological problems, was evaluated by the presentation of a video showing patients experiencing these types of problems. The 3 videos used before and after the course were the same; each video was shown to the participants and then they had to answer a questionnaire evaluating the cognitive aspects of a numerical scale and suggest a treatment for the condition of each patient.

The results of the study were summarized in the following points:

- Prescription habits changed considerably due to the course, which was measured as changes in the prescription with respect to the videos, before and after the course. Benzodiazepines were prescribed less frequently after the course compared to before.
- Participants were not aware of the fact that they had changed their prescription behavior; they were asked before and after the course about their attitudes toj prescribing benzodiazepines for sleep disturbances assessed on a 5-point scale and no significant difference were found when comparing attitudes before and after the course. This could be interpreted as an indication that people do not want to accept that in a short time they could change their prescription habits. People seem to want to see themselves as having a stable identity and habits.
- There was a tendency to see medical conditions as less serious after the course compared to their assessments before the course; this is one of the explanations for evidence of changes in prescribing behavior. Discussions in the group probably make participants more comfortable if a prescription is not required for all of the patients' socio-psychological problems.

E. Placebo prescription

A placebo is a biologically inert substance which is provided by a health professional to satisfy a patient. Discarding that they are ineffective substances, placebos can produce physical effects[12] which vary according to the individuals, situations and medical conditions. Placebos can have different effects, both psychological and physical, in a beneficial (placebo) or adverse (nocebo) way[13]. There are now multiple definitions of placebo and placebo effects[14-15].

F. Electronic prescription (e-prescribing)

Although there is little evidence of the effect of electronic prescribing to the costs of medications, there is evidence that shows improvements in the compliance of forms and increase in the use of of generics[16-17]. At the same time, service providers have been working collaboratively with groups of physicians to manage these costs, and it is possible to share both risks and incentives; likewise, the efficiency of the system is improved. Thus, according to the Institute of Safe Medication Practices, pharmacists make 150 million calls a year to physicians related to out-of-form medications, potential drug interactions, incorrect dosage regimens and illegible manuscripts[18]. Having to correct and clarify the prescriptions generates delay for the patient and extra work for the doctor and the pharmacist. The good news is that electronic prescription is improving the efficiency of the prescription. To ensure this outcome, standards should be created that allow for the application of both hospitalization and ambulatory drug therapy[19].

Barriers that must be overcome[20]:

a Previous negative experience with the use of technology.
b Initial and long-term cost.
c Loss of productivity.
d Training in technology for the use of systems.
e Absence of standards.

G. Minimum standards of a recipe

a Provide the exact weight and age (or date of birth) in all prescriptions of pediatric patients.
b Clearly display critical patient information such as allergies (including description of the reaction), weight and height in each patient record.
c Do not use abbreviations of medications.
d Avoid abbreviations that could cause confusion (eg gr for g, U for units, etc.). Include the date, name of the medication, dosage form, dosage, route of administration, frequency, duration and mode of contact with the prescriber (telephone, email, etc.).
f Specify the type of salt in the electrolyte prescriptions.
g Note the specific administration rate for medications IV.
h Write all prescriptions using the metric system (avoid the use of the Apothecary system).
i Specify the exact dose (as mg) instead of only the pharmaceutical form (as bottle, tablet, ampoule).
j Write the complete instructions. Do not write ambiguous orders that require additional interpretation or clarification. Example of ambiguous orders include: "Continue with the previous indications" "Take as indicated", etc.
k Ensure dose adjustment in children, the elderly and those patients with impaired renal or hepatic function.
l Resolve the questions related to the prescription directly between pharmacist and doctor in order to solve the patient's needs.
m Read verbal or telephone orders twice to ensure the accuracy of the prescription.
n Mention the indication of medication when verbal commands are given to avoid misunderstandings.
o Prescribers should speak directly with the pharmacy staff instead of trying to solve or clarify some aspect over the phone. If this is not possible, fax the prescription to the pharmacy or send it after the phone call.

H. Recommended practice

a Provide prescriptions for allergies, weight and date of birth of the patient.
b Always use the international common denominator (DCI) and also the brand name.
c Include indication and goal of therapy in all prescriptions.
d Have pharmacists who actively participate in the prescription process of medicines:
(1) Collaborating with prescribers
(2) Working in areas of patient care in direct collaboration with the prescribers and those professionals responsible for the administration of the medication
e Assign them to areas of patient care to participate in medical rounds, medication monitoring and provision of information.
f Have medication dosing information in special populations (as children, the elderly and patients with renal or hepatic insufficiency.
g Have relevant and specific information for each patient (as laboratory reports, medical history) and therapeutic goals available for health professionals in charge of patient care (prescribers, nurses, pharmacists, nutritionists, physical therapists, etc.)
h Incorporate pharmacists in the transition planning processes of levels of care (eg hospital admissions and admissions, admission to nursing homes, etc.).
i Maximize the use of pre-printed formats and evidence-based protocols for the prescription of potentially toxic medications or those with a narrow therapeutic range (computerized prescription orders can facilitate this with alerts,

restrictions or suggestions for safer substitutes). Involve pharmacists in the process of initial and annual review of the processes and, whenever possible, include references in the orders and protocols based on evidence.

j Include the expected time of treatment for all orders of antimicrobials.

k Avoid all abbreviations.

l Record all therapies for all new patients in order to ensure the transition of this information between the hospital and outpatient departments.

m For pediatric patients, include the calculated dose and the mg / kg dose in the prescription.

n Coordinate so that prescribers have the responsibility of entering the information system. Ideally, the systems will provide the following criteria:

(1) Interfaces with access to data from other clinical departments (as laboratory).

(2) Clinical support decision when prescriptions are issued from other services.

(3) Pediatric automated dosage based on weight.

(4) Precautions based on age for certain medications.

(5) Automatic checks for interactions and incompatibilities.

(6) Maximum dose alerts.

(7) Orders requesting the verification and approval of the pharmacist before the medications are delivered.

(8) A system that forces prescribers to review laboratory values before proceeding to prescribe.

(9 Use electronic prescriptions to pharmacies.

(10) Accurate and current product information.

o. Ensure policies and procedures that maximize the use of written / printed orders and limit verbal / telephone orders to specific and strictly necessary situations.

p. Include in the data forms information that is mandatory for the prescription (Name of the active ingredient, dose, route, schedule, indication, weight and age of the patient and signature).

2. Dispensing process

The process of dispensing medicines in community pharmacies and hospitals is the cornerstone of the activities of pharmacists and yet, is one that does not occur in many countries in a generalized manner. While it is true that not all patients need to be explained in detail how to use their medications, there are many that do.

Patients who would need more guidance from pharmacists can be grouped by different criteria such as:

a High risk medications
- – Patients using warfarin
- – Patients using digoxin

b Medications that require adherence to ensure patient's life
- – Patients with HIV
- – Patients with Tuberculosis

c Medications whose administration involves the use of a device that may be difficult for the patient to use
- – Patients with asthma who use inhalation
- – Patients with glaucoma using ophthalmic drops

The pharmaceutical industry must have an interest in this process to be sure that the dispensation can be achieved as safely as possible. The dispensing of the pharmacists will serve as a filter to record the Adverse reactions to industry medications and thus be able to contribute to the safety of treatments in patients on the one hand and also contribute to the interests of pharmaceutical laboratories. Thus, there is a symbiosis between the clinical professional activity of pharmacists and the organizational interests of pharmaceutical companies.

However, in order for this activity to be carried out, it is necessary to have pharmacists who have the skills to develop the dispensation in an efficient way.

So where will the pharmacists learn the dispensing activities?

Although currently the process of drug dispensation is taught in a theoretical and practical way in many faculties of pharmacy, in some countries this does not occur. Thus, some pharmacists only receive basic theoretical training of an activity that is eminently practical and that is carried out daily in community pharmacies. Therefore, there is a need for continuous pharmaceutical training in order to cover the knowledge gaps and ensure the competencies of drug dispensing.

Pharmaceutical companies can also give this training to pharmacists in a more specific way for the dispensation of their own medicines. The companies can also provide specific information on the use of the medicines and may even report adverse reactions to medications that have occurred in patients. For this to work in practice it is important that these pharmacists provide feedback, every three months, of any adverse reactions to medications to ensure improved future dispensing and detection of these adverse reactions.

References

[1] Lilja J. How physicians choose their drugs. *Soc. Sci. Med.,* 1976; **10:** 363-365.

[2] Kohn, Linda T., Janet M. Corrigan, and Molla S. Donaldson. *To Err is Human: Building a Safer Health System.* Washington, D.C.: National Academy Press, 1999.

[3] Elson B. Electronic prescribing in ambulatory care: a market primer and implications for managed care pharmacy. *J Manag Care Pharm* 2001; **7**(2):115-20.

[4] Artz MB, Harnack L, Duval SJ, Armstrong C, Arnett DK, Luepker RV. Use of nonprescription medications for perceived cardiovascular health. *Am J Prev Med.* 2006 Jan; **30**(1):78-81.

[5] Greenhalgh T: Drug prescribing and self-medication in India: An exploratory survey. *Soc. Sci. Med.* 1987; **25:** 307-318.

[6] Manes C, Giacci L, Sciartilli A, D'Alleva A, De Caterina R. Aspirin overprescription in primary cardiovascular prevention *Thromb Res.* 2005 Nov 28.

[7] Linné C: Hinder for liikekonsten. Originally published 1752, translation published in Ekenias 1948.

[8] Passarelli MC, Jacob-Filho W, Figueras A. Adverse drug reactions in an elderly hospitalised population: inappropriate prescription is a leading cause. *Drugs Aging.* 2005; **22**(9): 767-77.

[9] Giachetto G, Banchero P, Telechea H, Speranza N, Wolaj Mijal, Toledo Mauricio, Olmos I, Gabriela Camacho, Silvia Kegel, Luciana Nanni6, Carolina Seade. Uso racional de medicamentos: ¿Qué conocen los médicos residentes sobre los fármacos de uso corriente? *Rev. Méd. Urug.* vol.19 no.3 Montevideo Dec. 2003.

[10] Coleman JS *et al:* Medical Innovation: A diffusion study, Bobbs-Merril, 1966.

[11] Lilja J, Larsson S. Social pharmacology: unresolved critical issues. *Int J Addict.* 1994 Nov; **29** (13): 1647-737.

[12] Byerly H. Explaining and exploiting placebo effects. *Perspect Biol Med* 1976; **19:** 423–36.

[13] Rosenzweig P, Brohier S, Zipfel A. Pharmacoepidemiology and drug utilization. *Clin Pharmacol Ther* 1993; **54:** 578–83

[14] Shapiro AK. Attitudes toward the use of placebos in treatment. J Nerv Ment Dis 1960;130:200–11) (Shapiro AK. Factors contributing to the placebo effect. *Am J Psychother* 1961; **18:** 73–88.

[15] Shapiro AK. Iatroplacebogenics. *Int Pharmacopsychiatry* 1969; **2:** 215–48.

[16] Pestotnik, Stanley, David Classen, Scott Evans, John Burke. Implementing Antibiotic Practice Guidelines Through Computer-assisted Decision Support: Clinical and Financial Outcomes. *Ann Intern Med,* May 1996; **124:** 884-890.

[17] Ross SM, Papshev D, Murphy EL, Sternberg DJ, Taylor J, Barg R. Effects of electronic prescribing on formulary compliance and generic drug utilization in the ambulatory care setting: a retrospective analysis of administrative claims data. *J Manag Care Pharm.* 2005 Jun; **11**(5):410-5.

[18] ISMP. A Call to Action: Eliminate Handwritten Prescriptions Within 3 Years! [En línea]. Accesado el 27/09/2017 de www.ismp.org/Newsletters/acutecare/articles/Whitepaper.asp

[19] Spiro RF, Saxton C. Electronic-prescribing: will long-term care be ready? *Consult Pharm.* 2005 Aug; **20**(8):651-61.

[20] Halamka J, Aranow M, Ascenzo C, Bates DW, Berry K, Debor G, Fefferman J, Glaser J, Heinold J, Stanley J, Stone DL, Sullivan TE, Tripathi M, Wilkinson B. E-Prescribing Collaboration in Massachusetts: Early Experiences from Regional Prescribing Projects. *J Am Med Inform Assoc.* 2006 Feb 24.

Affiliation and Contacts details

[1] Universidad de San Martín de Porres, Perú

[2] Universidad Nacional de la Amazonia Peruana, Perú

[3] Centro de Fertilidad Cajamarca, Perú

* Corresponding Author:
Aldo Alvarez-Risco
Email: aalvarezr@usmp.pe