DRUG-RELATED PROBLEMS: THEIR STRUCTURE AND FUNCTION

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ABSTRACT: In order to better focus the role of the pharmacist on patient need and patient outcome, a means of categorizing drug-related problems (DRPs) is presented. A DRP essay when a patient experiences or is likely to experience either a disease or symptom having an actual or suspected relationship with drug therapy. Eight different categories of DRPs are described and examples of each category are offered. This categorization serves a number of functions, such as: (1) to illustrate how adverse drug reactions form that one category of extent DRPs, (2) to make tangible the pharmacists role for the future, (3) to serve as a focus for developing a systematic process whereby the pharmacist contributes significantly to the overall positive outcome of patients, (4) to bring to pharmacy practice a vocabulary consistent with that of other healthcare professionals, and (5) to aid in the development of standards of practice for pharmacists.


PATIENT-ORIENTED CLINICAL PHARMACY is coming of age at a time when the healthcare system it characterized by change, particularly in the form of powerful economic forces. During this time when the healthcare system is caught up in economic determinism and its impact on shaping policy, there are increasing demands for pharmacists to define their function, purpose, and value in terms of the pharmacotherapeutic impact pharmacy has on actual patient outcome. If the profession is serious about developing a rigorous, comprehensive, and patient-specific clinical pharmacy service, then the concept of patient outcome must be addressed. Pharmacists must define their professional function from the perspective of the whole patient, in the biopsychosocial sense, and not primarily (from that of the pharmaceutical agent in question (e.g., gentamicin, theophylline) or the technical instrument employed (e.g., pharmacokinetic dosing, cholesterol measurement, blood pressure monitoring, nutritional protocol development). The purpose of this paper is to provide the practicing pharmacist with a means of categorizing drug-related problems (DRPs), in order to focus on the patient and move away from the pharmacists preoccupation with the pharmaceutical agent or the technical process employed to understand the agent. All eight categories presented here are "patient" problems that need the attention of the pharmacist. The identification, resolution, and prevention of these problems is a focus of the professional role that is truly proactive and patient-focused, and contributes to positive patient outcome.

Patient Outcomes

It is the primary objective of all healthcare providers to improve the quality of each patients life to the extent that they are able. Physicians, nurses, pharmacists, and other healthcare providers work continually to produce four general patient outcomes: (1) to cure a disease, (2) to eliminate or reduce a patients symptomatology, (3) to arrest or slow a disease process, and (4) to prevent a disease or symptom. These can be clearly delineated as essential patient outcomes to which knowledge, techniques, and judgment are directed in a systematic, comprehensive manner.

The achievement of the general patient outcomes described above depends on each healthcare practitioner to contribute expertise to solve those patient problems rea-
vis to the practitioner's specific practice. Pharmacists contribute to these general patient outcomes by ensuring successful drug therapy. The pharmacist employs unique knowledge, skills, and tools to determine if a patient is experiencing potential or actual DRPs. When the pharmacists' processes resolve any actual DRPs, very specific, desired pharmacotherapeutic outcomes are identified for each patient's problems. When these specific outcomes are successfully achieved, the pharmacist has contributed to the general patient outcomes described above.

A systematic process, the Pharmacist's Workup of Drug Therapy, helps the pharmacist to determine if a patient has the potential to experience or is actually experiencing a DRP, and has been described elsewhere. However, to intervene in a patient's drug therapy prospectively and consistently, and to document how that intervention can lead to positive patient outcomes, it is important to understand the different types of patient-specific DRPs that a patient might develop.

Structure of Drug-Related Problems

A DRP is an undesirable patient experience that involves drug therapy and that actually or potentially interferes with a desired patient outcome. It should be noted here that the use of the term "problem" in the phrase "drug-related problem" is used to denote a drug-related event amenable to detection, treatment, or more appropriately, prevention, and should not be interpreted in the common usage wherein it vaguely communicates the idea that "something (puzzle, paradox, perplexity) is wrong here."

In order for an event to qualify as a DRP, at least two conditions must exist: (1) a patient must be experiencing, or must be likely to experience, disease or symptomatology; and (2) these conditions must have an identifiable or suspected relationship with drug therapy. For example, a patient may present with cellullitis that requires antibiotic treatment or a patient may experience hypotension due to an inappropriate dose of clonidine.

Practitioners frequently perceive that there are an infinite number of DRPs. However, we have concluded that such perceptions are largely the result of unstructured observations and experience. When approached for the purpose of creating major categories within the above conceptual framework, the possibilities appear to be limited. We submit that there are eight major categories of DRPs.

Categories of Drug-Related Problems

DRPs may be identified or characterized by the following distinctions:

1. The patient has a medical condition that requires drug therapy (a drug indication) but the patient is not receiving a drug for that indication.
2. The patient has a medical condition for which the wrong drug is being taken.
3. The patient has a medical condition for which too little of the correct drug is being taken.
4. The patient has a medical condition for which too much of the correct drug is being taken.
5. The patient has a medical condition resulting from an adverse drug reaction.
6. The patient has a medical condition resulting from a drug-drug, drug-food, drug-laboratory interaction.
7. The patient has a medical condition that is the result of not receiving the prescribed drug.
8. The patient has a medical condition that is the result of taking a drug for which there is no valid medical indication.

It should be emphasized that although at times there may be actual problems experienced by the patient or potential problems to be prevented. It may also be helpful to reiterate that classification of DRPs mandates the inclusion of the patient's undesirable experience: (a) a symptom or disease; and a statement of that event's actual or potential relationship to drug therapy. With this in mind, it should be clear that many of the undesirable experiences of drug therapy problems focus on the drug and not the patient, and, therefore, do not meet the criteria established here that help to ensure the pharmacist is able to have a tangible impact on actual patient outcomes. Some of the categories that fall short of this definition of a DRP include the correct drug, dose, frequency, duration, route, and monitoring. These descriptions fall short because they do not include the patient or the relationship of the problem to the patient, and the category does not indicate specific action that needs to be taken by the pharmacist. Although inappropriate decisions or behavior falling into these four categories can easily cause patient-specific DRPs, as they are defined here, they do not represent the actual DRP itself. Other traditional ways of conceptualizing problems with drug therapy include drug prescribing, dispensing, administering, and monitoring.

Placing these DRPs in a practice context facilitates an understanding of the circumstances in which each might develop. Also, specific examples are provided for clarification.

Examples of Drug-Related Problems

MEDICAL INDICATION FOR DRUG THERAPY

A number of common circumstances develop where the patient is not in need of drug therapy but is not receiving it. For example, a patient is being appropriately treated for peripheral vascular disease but is not receiving treatment for a developing anemia. Here, the primary focus is on the patient's past medical history.

In a more holistic view, we could find a patient who has been transferred from one hospital to another, from one physician to another, or who has changed pharmacies. Thus, the continuity of drug therapy has been interrupted. These conditions in which the patient is in need of prophylaxis or premedication are additional examples of such a particular type of DRP. Moreover, in some cases, patients need a synergistic or potentiating effect from a drug, which defines the need for additional drug therapy. For example, cancer chemotherapy often uses combination therapy to effect a greater cell kill than could be achieved with monotherapy. Similarly, at least two antibiotics are always necessary to eradicate active tuberculosis because of the rapid emergence of resistance associated with single-drug therapy.

THE WRONG DRUG IS BEING USED

Sometimes the drug therapy used to treat a patient's medical condition is determined to be ineffective, or a drug
therapy likely to be more effective exists but is not being used. Additionally, some patients receive a particular drug therapy in the presence of an allergy to that drug, or receive drug therapy when contraindications exist. Other obvious situations present themselves in the clinic. For example, if an effective drug is being used to treat a patient's medical condition but there is an equally effective but less expensive drug available, then it could be argued that the wrong drug is being used. Here the consensus theme of patient involvement is central to the decision-making process. The burden-to-benefit calculation would be considered if, for example, there exists an equally effective, safer drug than that presently being used. If a patient is receiving combination therapy when a single drug would be expected to be equally effective, then the patient has a DRP requiring attention.

TOO LITTLE OF THE CORRECT DRUG

Although it may be a fundamental, positive tenet of homoeopathic medicine, too little (suboptimal) drug may be classified as a DRP when the desired outcome for a patient is not being realized (i.e., infection is not responding to suboptimal antibiotic treatment). In essence, if a drug dose is not individualized for a specific patient, taking into consideration all of the appropriate drug, disease, and patient-specific information, then the dose may be deemed less than optimal. Also, if a desired serum drug concentration was calculated appropriately and not achieved (taking with all the appropriate clinical signs/symptoms) then it might be argued that this type of DRP is present.

There are other parameters, which, if not attended to, would lead to suboptimal therapeutics. A patient who is receiving an inappropriate dosing interval or a regimen not continued long enough could result in too little drug being available to the patient. For example, only the Kapral's form of Dillantin is labeled as "extended" and provides the support for once-daily dosing. Use of more rapidly absorbed preparations at a steadily daily basis may lead to widely fluctuating serum concentrations and potential loss of seizure control in a patient.

It is also important to note that calculations based on varying bioavailability and conversions to different formulations of a drug therapy may also lead to suboptimal treatment. For example, when switching from phenytoin suspension to capsules, one must take into account that the capsules are formulated with phenytoin sodium, which contains only 92 percent phenytoin acid. Therefore a slightly larger dose will be required when using the capsule. The importance of applying pharmacokinetic principles as a means to help resolve the problem of suboptimal concentrations must be emphasized here.

TOO MUCH OF THE CORRECT DRUG

All of the situations described in the previous section may also result in the opposite effect—too much of the correct drug. Clearly tuning the balance is the major enterprise. In situations where a patient's dose is increased rapidly and the rate of increase itself may cause complications, we have another instance of this type of DRP. For example, rapid equilibration of nicotine acid doses are very often associated with severe cutaneous reactions.

It is also possible for drugs to accumulate over a long period of time and produce toxic complications. For example, patients with compromised renal function will accumulate N-acetylcysteine (NAPA), the active metabolite of procainamide. Therefore, if a patient has the potential to, or actually experiences adverse effects, then the dose and dosing interval must be adjusted according to the level of accumulation. Preparations of the same drug (e.g., digoxin, levotheroxine) are not absorbed uniformly and the change from one brand to another can produce unpredictable differences in absorption rate, thereby causing a drug-induced illness. This problem frequently occurs in an nursing home or psychiatric hospital where the excessive use of antipsychotics, sedatives, and hypnotics is prevalent.

In sum, patients who experience or have the potential to experience toxicity brought about by too much drug are a common problem encountered in practice. The value of pharmacokinetic monitoring and dosage adjustments cannot be overemphasized in correcting or preventing this type of DRP.

ADVERSE DRUG REACTIONS

For reasons that are not inherently obvious, pharmacists have defined, described, and quantified adverse drug reactions (ADRs) more extensively than all other categories. In fact, numerous papers and books have addressed this topic. Rawlins has categorized adverse events as type A or type B. 4 Type A reactions are consistent with the pharmacological actions of the drug, occur commonly, are usually dose-dependent, and are fairly predictable. Type B reactions represent allergic and idiosyncratic reactions that are independent of drug pharmacology. These are rare, not dose-related, and cannot be predicted. Only those that are idiosyncratic should cause the patient and pharmacist significant problems because one of the assumptions underlying this discussion is that the pharmacist is playing a proactive role in the patient's drug therapy. Through the introduction of a unique knowledge base able within into the context of a rational treatment plan, the pharmacist can, at the very least, minimize the consequences of ADRs, and at best, eliminate them through effective therapeutic monitoring. It should be emphasized that when a particular ADR is unavoidable, as in the case of many antihypertensive drugs where at least a minor adverse reaction or inconvenience is to be expected, or with oral contraceptives where fluid retention is frequently experienced, patient preferences and the burdens-to-benefit calculation should be considered an essential part of clinical decision making. This is particularly important when there is some degree of trade-off, and a patient may have to select discomfort or inconvenience from a range of possibilities.

DRUG—DRUG, DRUG—FOOD, DRUG—LABORATORY INTERACTIONS

There are many circumstances in which this type of DRP is found. Isolated, the possibility of a patient experiencing an adverse event resulting from physical/chemical interaction between a particular drug and food consumed is always present. For example, milk will inhibit the absorption of oral lead preparations. Laboratory tests administered for further diagnosis and monitoring are also possible causes of in-
interactions with drugs. Ascorbic acid, beta-lactam antibiotics, levodopa, and salicylates have all been well documented to interfere with urine glucose testing, thereby interfering with the collection of valid patient data. In addition, enzymatic inhibition or induction often changes the characteristics of a drug’s absorption, distribution, metabolism, and/or elimination. Enzyme inducers such as carbamazepine and rifampicin potentiate the hepatic metabolism of warfarin. In most patients the drug interaction results in the inhibition of the hypo- prothrombinemic response and a lowering of the prothrom- bin time. Displacement of a drug from protein binding sites may result in an interactive problem requiring attention. For example, high doses of salicylates may displace first-genera- tion oral hypoglycemic agents from protein binding sites and may potentiate hypoglycemia in a patient.

PATIENT NOT RECEIVING THE PRESCRIBED DRUG

Patients do not receive the intended drug for a number of reasons, those within the patient’s control and those outside of it. Noncompliance with a drug regimen occurs for reasons that fall into both of these categories depending upon the nature of the cause. Poverty, beyond the individual’s control, often precipitates compliance. Not taking the drug for reasons such as intolerance or apathy are within the pa- tient’s control. In all cases, the pharmacist must work to un- derstand the cause so that behavior may be changed to achieve the desired pharmacotherapeutic outcome.

A drug distribution or administration system that fails the patient will precipitate this category of DRP. For exam- ple, if the wrong drug is dispensed, a health practitioner (or other caregiver) fails to administer the drug, or if a tech- nical device such as an insulin pump is not functioning, then the patient will not receive the correct drug.

In addition, there may be formulation problems with the drug produce itself that do not allow the active ingredient to be absorbed or metabolized by the patient. For instance, chloralhydrate must be hydrolyzed in an acidic medium to yield the active diazepam derivative, N-desmethyldiazepam. Pa- tients with conditions resulting in elevated gastric pH may experience therapeutic failure due to an inability to convert chloralhydrate to its active form.

No VALID MEDICAL INDICATION

This category tends to be far too frequently overlooked as a DRP. It is this possible because self-treatment, sub- stance abuse, and the like are major factors in defining the situation. Tobacco, alcohol, and coffee consumption, for example, can do lead to this type of problem. Narcotic abuse is, of course, the extreme form of drug misadventur- ing with no legitimate medical indication, although the patient may very well insist that the drug abuse is a valid solution to a pain problem.

A significant cause of this type of DRP is unnecessary drug therapy. One common example is the concurrent use of antidepressant drugs with antipsychotics without docu- mented extrapyramidal symptoms experienced by the patient.

In all cases these the pharmacist is capable of functioning as a problem solver. It is ironic that this category receives less attention than the others when in fact it represents the entire range of self-treatment possibilities and probabilities.

Functions of Drug-Related Problems

Categorizing DRPs into the eight categories of patient problems described above is useful in a number of ways. First, it illustrates how ADRs form one category of ex- tant DRPs. This point emphasizes the need to develop mechanisms by which pharmacists are able to prospectively identify, solve, prevent, quantify, predict, and intervene in DRPs. Second, the categories make tangible the pharmacist’s role for the future. Few administrators need to be convinced that these problems are real and therefore require the resolution of those individuals responsible. Finally, their identification in and their resolution in need of an expert. If pharma- cists and pharmacy managers are able to develop systems that put into operation this proactive role, then justification for pharmacy personnel should become a pleasure and not a distasteful, impossible task.

Third, this latter goal of DRPs can serve as the focus for de- veloping a systematic process whereby the pharmacist con-tributes significantly to the overall positive outcomes of patients. Two systematic processes that facilitate the pharma- cist’s efforts are Thomasma’s rational therapeutic plan and the Pharmacist’s Workgroup of Drug Therapy developed by Strand et al. A systematic process will not only aid the pharmacist in achieving successful outcomes on an individ- ual patient basis, but will aid in the pharmacoeconomics- ologist’s development of a national database concerning DRPs.

The fourth function of this categorization is to bring to pharmacy practice a vocabulary consistent with that of other healthcare professions. By defining the pharmacist’s role in terms of DRPs, the function of the pharmacist is placed in a patient-care context consistent with the respon- sibilities of other healthcare providers. The patient, and not the drug product, is the major focus of the pharmacist’s decisions and actions.

It will be a reasonably straightforward task to create stan- dards for pharmacies that reflect the pharmacist’s ability to identify, solve, and prevent these drug categories of patient-specific DRPs. This focus for the pharmacist’s function will provide the essence missing to date around which to structure standards of practice. The patient and the pharmacist’s desire pharmacotherapeutic out- comes, and the pharmacist’s ability to achieve these out- comes, will now serve as that focus.

Finally, pharmacy educators should benefit from having a tangible, clearly defined purpose for students. Course content, curricular design, and faculty priorities should focus on general patient outcomes that are accomplished through specific pharmacotherapeutic outcomes resulting from appropriate drug therapy. This “model-of-reality” should begin to focus discussion and decisions about phar- macy’s practice for future graduates.

Summary

Although many of the common circumstances under which DRPs develop have been delineated, the list is by no means exhaustive. The major purpose in producing eight conceptual categories is to provide order in a pharmaceuti- cal universe considered by many to be chaotic. Heuristics do have limitations, but when properly used they provide considerable clarity to areas seemingly replete with ambigu- ous, complex phenomena. Thus, if we accept the eight
Categories as a model of reality, i.e., a representation of clinical realities, thence perhaps the order provided will effectively素质教育 clinical perceptions in a manner consistent with a patient-specific pharmacy practice.

The progression of pharmacy must continue its development of practice, its collective identity as therapeutic problem solver, and its commitment to patient outcomes, and make a significant move from passive to proactive participation in clinical work.

References

EXTRACTO
Los aspectos categorizan los problemas relacionados al uso de medicamentos que puedan ser experimentados por los pacientes. Existe un problema de medicamento cuando el paciente tiene o puede tener una interrelación de farmacología con la frecuencia de medicamentos. Se presentan otros aspectos de problemas relacionados a medicamentos. Estos son: (1) el paciente tiene una condición médica que requiere un medicamento; (2) el paciente está recibiendo el medicamento para esa indicación; (3) la CA está usando el medicamento correcto; (4) el paciente está tomando el medicamento de manera correcta; (5) el paciente tiene una condición médica que es resultado de una mala acción; (6) el paciente tiene una condición médica que es resultado de una mala acción. Esto es un resultado de una interacción con otros medicamentos, con comida, con ocho de pacientes. (7) el paciente tiene una condición médica que es resultado de un medicamento. (8) el paciente tiene condiciones importantes que no son resultado de un medicamento. Estos problemas pueden ser adquiridos o potenciales y los pacientes manifiestan que esta categoría se parece de la forma más lógica del enfoque farmacéutico, para ser un tema frecuente de la imagen. (9) el paciente tiene una condición importante que no es resultado de un medicamento. Este es un resultado de una interacción con otros medicamentos, con comida, con ocho de pacientes. (10) el paciente tiene una condición médica que es resultado de un medicamento. (11) el paciente tiene una condición médica que es resultado de una mala acción; (12) el paciente tiene una condición médica que es resultado de una mala acción. Estos problemas pueden ser adquiridos o potenciales y los pacientes manifiestan que esta categoría se parece de la forma más lógica del enfoque farmacéutico, para ser un tema frecuente de la imagen. (13) el paciente tiene una condición médica que es resultado de un medicamento. 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