

POLYPHARMACY TREATMENT ISSUES

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Alongside the positive effects, the use of medicines may also be associated with side effects. Multi-drug administration, while often necessary, is not always efficient or safe [1]. The use of several drugs simultaneously relates to the concept of polypharmacy (≥ 5 drugs) taking into consideration some other elements such as: duration of use (≥ 60 days) or exclusion of certain groups of drugs (topical drugs, herbal, vitamins, and microelements) in this concept. The higher the number of drugs used, the higher the likelihood of adverse effects occurring [2, 3, 4].

Problems encountered due to polypharmacy with regard to causes or mechanisms are considered multi-factorial. Factors related to the patients vary: from old age (also related to the trend of increased life expectancy), level of communication, chronic comorbidities, tendency to self-medication or use of medication without a physician's recommendation, and incorrect data referenced by patients themselves. The incorrect behavior of patients toward the physician recommendations on the drug therapy is named as lack of adherence to the drug therapy. The factors related to the physician are: level of staff knowledge, as well as protocols or trends in drug administration. Other contributing factors relate to the institutional systems, such as: simultaneous prescription of medicines from several sources, storage and access to data, as well as the way patients communicate in different sectors. The latter relates to the transmission of accurate data from the staff during the transfer of the outpatient patient to the hospital or vice versa, as well as to different sectors / institutions. Other factors contributing may be related to the issues of reimbursement schemes and economic burden of disease and medication. Adverse events can be considered as: drug reactions, interactions between drugs or drugs and diseases, failure to achieve the desired effect of medication, as well as cognitive disorders, patient falls, or the need for hospitalization and prolonged stay in hospital, increased financial costs, and even death [5, 6, 7, 8].

The incidence of polypharmacy increases with age. The data report that in patients >65 years of age, up to 40% of the cases use 5 drugs, while up to 12% are users of 5-10 drugs. These values have the tendency to be higher in patients of the fourth age (>85 years), with values up to 81.5% reported [9, 10].

The use of medicines, besides the positive effects, may also be associated with side effects. The use of several drugs simultaneously relates to the concept of polypharmacy, the higher the number of drugs used, the higher the likelihood of adverse effects occurring during the treatment. Problems encountered due to polypharmacy with regard to causes or mechanisms are considered multi-factorial. The incorrect behavior of patients toward the physician recommendations on the drug therapy is named as lack of adherence to the drug therapy.

The incidence of polypharmacy increases with age. Polypharmacy may be more common in some patient groups such as the elderly, nephropaths, patients with hepatic pathology or patients with mental disorders, etc. In hospital settings, polypharmacy has been considered a predisposing factor in the manifestation of problems related to the drug use. The effect of polypharmacy on surgical interventions, more specifically anesthesia, relates to the elderly population undergoing surgery, which has the tendency to increase in the coming years. Polypharmacy seems to have a negative role in the drug-to-drug interaction effects and on the reactions that may occur in the perioperative period in the high risk peroperatively evaluated patients; therefore, a great deal of attention should be paid to the careful evaluation of the associated pathologies and the tailor-fit adaptation of the therapy to the elderly patient undergoing surgery.

Physicians need to treat polypharmacy patients, especially the elderly, very carefully, requiring patient collaboration, beginning with information sharing, selection, application and follow-up of therapy. Proper implementation of such measures can have a positive impact on avoiding or minimizing side effects and complications of drugs used in the context of polypharmacy.

Keywords: polypharmacy, comorbidity, treatment.

Polypharmacy may be more common in some patient groups such as the elderly, nephropaths, patients with hepatic pathology or patients with mental disorders, etc., who have some specific features. Changes in the structure and function of organs in the elderly, who make up the largest group of drug users, decrease metabolizing and excretory abilities, leading to problems such as: hypoglycemia, drowsiness, falls, nutrition disorders, prolonged bed rest, or/and hospitalization and its associated problems [11, 12]. As a consequence of chronic kidney pathologies, pharmacokinetic and pharmacodynamic disorders can cause adverse effects from interactions between drugs. Also age-related changes in excretory function require careful dose adjustment according to the nephropathic patient conditions [13]. Polypharmacy in patients with hepatic pathology increases the possibility of hepatotoxic phenomena with all its relevant consequences. When to mentally ill patients treated with psychotropic or non-psychotropic drugs are added other medications, adverse effects may occur as a result of drug interactions that paradoxically worsen their condition [14]. Problems may also be influenced by other factors, such as overdose or inappropriate duration of drug use [15].

In hospital settings, polypharmacy has been considered a predisposing factor in the manifestation of problems related to the drug use. Emergency hospitalization is associated with a higher risk for drug-related complications, which may also result in poor post-operative outcomes [16, 17]. Seniors over 85 years of age are referred to make up about 12-21% of hospital emergency admissions [18].

In addition to the negative impact of increasing hospital stays and various complications, polypharmacy

has a negative economic impact. Factors such as drug overload, use of expensive drugs, and introduction of new drugs also play an important role [19, 20].

The effect of polypharmacy on surgical interventions, more specifically anesthesia, relates to the elderly population undergoing surgery, which has the tendency to increase in the coming decades. Patients >65 years are predicted to increase up to 50% [21]. The problem regarding the risk of perioperative complications in these patients relates mainly to the drugs not directly related to the surgery which they use. Specifically, data in noncardiac surgery in elderly patients treated with polypharmacy show a 3-4 fold increase in complications associated with decreased survival in the postoperative period [19, 22, 23].

Patients considered high risk in preoperative evaluation who are indicated for scheduled interventions need to be treated more intensively, in order to keep their condition under control and acceptable to perform the planned intervention. This maneuver is generally accomplished by adding and / or adapting the necessary medications. Withdrawal of medication during surgery may cause the patient to return to their previous condition, which exposes them to greater perioperative risks. On the other hand, unexpected or prolonged withdrawal of the maintenance therapy at the time of surgery has shown to increase non-surgical complications in those patients, also influenced by the stress of the perioperative period. The longer the withdrawal on non-surgery-related drugs, the more the complications may increase for the patient [12, 22].

Polypharmacy seems to have a negative role in the drug-to-drug interaction effects and on the reactions that may occur in the perioperative period in this category of patients, who, for the reasons mentioned above, are affected by the pharmacokinetic state and during this phase will be in contact with anesthetic and analgesic drugs. The basic disease status of polypharmacy patients should also be considered as an important element. In elderly surgical patients with multimorbidity problems it is considered that their condition may be affected by multi-drug therapy, unlike patients without multimorbidity problems, whose condition is mostly affected by perioperative period stress. Therefore, a great deal of attention should be paid to the careful evaluation of the associated pathologies and the Taylor-fit adaptation of the therapy to the elderly patient undergoing surgery [24].

Physicians need to treat polypharmacy patients, especially the elderly, very carefully, requiring patient collaboration, beginning with information sharing, selection, application and follow-up of therapy, while keeping a keen eye on rapid detection and treatment of potential complications. To this end, it is also recommended to apply the Comorbidity-Polypharmacy Score (CPS) for more efficient management of treatment impact on the condition of concomitant diseases [25, 26]. There have been different attempts to establish methodologies to avoid inappropriate prescribing and to predict the most common medication errors in old patients. Starting from Beers criteria in 1991, and evolving more recently in STOPP (Screening Tool of Older Persons' Prescriptions) / START (Screening Tool to Alert to Right Treatment) criteria; physicians have

actually a set of tools that can help avoid medication errors, reduce drug adverse events and improve drug therapy in different clinical settings. [27]

One of the aspects that was noted during the COVID-19, was the increased complexity in medication regimens of polypharmacy patients. Moreover, the health care system had to face an unexpected increase in morbidity, causing extreme strain to it. The most vulnerable population to suffer its consequences is the older adults group.

During the COVID-19 pandemic, there were observed issues related to: exposure (receptivity) of polypharmacy patients to Covid, the role of dosing different drugs in this situation, interaction of polypharmacy drugs with anti-covid treatment drugs or possible complications due to abrupt medication discontinuation. [28, 29]

In the treatment strategy for this category of patients, the medical staff decision to administer a specific drug plays an important role, while balancing the benefits and risks of the prescribed medicine. The aim is to reduce the drug intake and also their rational use, which requires patient compliance and collaboration, especially communication between the medical teams that will continue the follow-up and treat the patient in a long term.

The strategy should focus especially on some elements such as: useful patient information, description of effective drugs (considering generic drugs where possible, also for cost reasons) [30], as well as good communication between staff and clear and accessible evidence of the patient's data during their transfers in different institutions, thus avoiding misunderstandings or misinterpretations. In this regard, information technology, related to data on patient, medications, etc. should be implemented and used effectively. Careful evaluation in the preoperative period should also focus on concomitant patient therapy, which is not a specific part of the surgical problem. This may require, in addition to co-operate with specialists (various specialties, pharmacists, etc.), the correct application of specific protocols regarding perioperative strategies (withdrawal of prescription drugs, replacement / substitution, etc.). Clear guidelines should also be followed rigorously in the postoperative phase, in order to return early to the basic maintenance therapy [31, 32].

Proper implementation of such measures can have a positive impact on avoiding or minimizing side effects and complications of drugs used in the context of polypharmacy, having a direct effect on other indicators as well, such as length of hospital stay, cost, and mortality.

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