

The complex issue of medication management in older persons: a challenge for nurses

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Abstract: With increasing life expectancy, the share of older persons with coexisting multiple chronic degenerative diseases (comorbidity / multimorbidity) is expanding. These conditions require the use of multiple drugs, leading to polypharmacy, which plays a central role in making the therapeutic approach to the elderly particularly complex, together with age-related changes in pharmacokinetics and pharmacodynamics.

Physicians and nurses both are challenged by polypharmacy and by the other drug-related issues involving older patients, in all care settings. In particular, nurses should be aware of the main issues of pharmacotherapy in older persons, because they are often the frontline for older patients care, especially in nursing homes.

This review addresses the main issues related to pharmacotherapy in late life, such as pharmacokinetics and pharmacodynamics changes, limitations of evidence-based medicine, polypharmacy, drug interactions, adverse drug reactions, and lack of adherence. Focus will be on how these problems may impact on nursing, and on what nurses should know and do to improve drug treatment of older patients.

In the last decade, the role and responsibilities of nurses in the management of drug therapy have significantly changed in most countries. There is consensus in educational programs and legislation that the preparation and administration of medications are essential aspects of nursing practice. These are considered as collaborative tasks with physicians and not purely mechanistic tasks. The nurse must intervene in the event of a perceived error, and he/she must report doubts about congruity or relevance of the therapy.

Although nursing students gain knowledge and develop skills on drug therapy during their education, these are often perceived as insufficient. The need for post-graduation continuing

education should be also emphasized. Thus, graduate and post-graduate educational programs should be developed, in order to offer adequate answers to the increasing and challenging share of older patients seen in clinical practice.

Keywords: Elderly, Polypharmacy, Nurse skills, Nurse competences, Therapeutic adherence, Adverse Drug Reaction

Introduction

Across the entire world, individuals aged ≥ 60 years increased from 9.2% to 11.7% between 1990 and 2013 and will reach 21.1% (over 2 billion) by 2050¹. In Italy and in other industrialized countries life expectancy at birth is nowadays more than 80 years in men and close to 85 years in women. Although a good share of this overall survival gain is represented by healthy life expectancy, i.e. the average number of years lived in good health and independently, a sizable portion of late life is characterized by comorbidity / multimorbidity and disability². Both comorbidity and disability indicate the coexistence of multiple, usually chronic degenerative diseases³: the term comorbidity is preferred when it is possible or convenient to consider one index disease as the focus of interest, whereas the term multimorbidity is used when all clinical conditions affecting an older person have the same relevance.

Comorbidity / multimorbidity have several important consequences on the clinical management of older persons, but probably the most relevant involve drug therapy. Indeed, the presence of coexisting multiple chronic diseases requires the use of multiple drugs, leading to polypharmacy. In turn, polypharmacy plays a central role in making the therapeutic approach to the elderly particularly complex⁴.

With the obvious differences in their roles and responsibilities in this regard, physicians and nurses (and, in other countries, also pharmacists) are greatly challenged by polypharmacy and by the other drug-related issues involving older patients, in all care settings. In this paper, we will first briefly review the most important issues on the therapeutic approach to the elderly that may critically involve nurses, then we will focus on nurses' role and competences.

I - What nurses should know on pharmacotherapy in older persons

Age-dependent changes in pharmacodynamics and pharmacokinetics

Even in healthy aging, changes in body composition and in the physiology of many organs affect the way drugs are absorbed, distributed, metabolized, and eliminated (pharmacokinetics), as well as their effects on target organs at the same plasma concentration (pharmacodynamics). Among a number of age-related pharmacokinetics and pharmacodynamics modifications, decrease in Glomerular Filtration Rate (GFR) is probably the most important, as it reduces the clearance of renally excreted drugs: if not adequately accounted for, this may increase the risk of overdose of such medications^{5,6}. Unfortunately, formulas to estimate GFR from serum creatinine are poorly accurate in older age⁷, whereas measurement of drug plasma levels is commonly unavailable. Therefore, cautious administration and close monitoring of drugs' expected and adverse effects are recommended to all healthcare providers caring for older persons, including nurses.

Limitations of Evidence Based Medicine

In all advanced healthcare systems, approval of drugs for clinical use requires the availability of sufficient evidence of efficacy and safety, which mostly stems from phase-3 randomized clinical trials (RCT). Yet, participants enrolled in RCT on many drugs commonly prescribed to older persons are usually younger and healthier than the unselected geriatric population, with lower burden of multimorbidity, disability, and cognitive impairment. Some authors believe that this may even bias our knowledges on geriatric pharmacotherapy: to highlight this paradox, the expression Evidence Biased Practice, instead of Evidence Based Practice, has been provocatively introduced⁸.

Polypharmacy

As anticipated above, polypharmacy is a major issue in the therapeutic approach to older persons, being responsible for most of

the drug-related problems in the elderly⁹. Yet, agreement on the definition of polypharmacy is limited in the literature: a review on this topic, where associated terms were also considered, reported as many as 138 definitions of the condition¹⁰. In more than 80 percent of the studies surveyed, polypharmacy was identified on a purely quantitative basis, that is, when the number of drugs taken at a given time is above a certain threshold, which is usually set at 5 or more. In 15 studies, a numerical definition was always proposed, but referred to a specific length of observation or a specific care setting (i.e., hospital stay). Depending on the time window, polypharmacy can then be qualified as concurrent, cumulative, or continuous, and eventually it may take the characteristic of true chronic polypharmacy. In the review, 12 definitions were not strictly quantitative, but only descriptive, such as “co-prescription of multiple drugs” and “simultaneous, long-term use of different drugs by the same individual.” Moreover, in 7 studies, the definition of polypharmacy was articulated in a more complex way, with a distinction between appropriate (or rational) and inappropriate forms.

The review also showed that the problem of polypharmacy is global, affecting different countries and healthcare systems across the world: however, such a great heterogeneity in the definition makes it difficult to compare different studies that, depending on the definition applied, reported prevalence figures ranging from 4 to 57 percent. Similar data were reported in a multicenter study from Europe enrolling approximately 34,000 65+ year-olds, in whom the prevalence of polypharmacy ranged from 26.3 to 39.9 percent¹¹. Drugs most frequently involved in polypharmacy are those for the cardiovascular and digestive systems, and metabolic drugs¹⁰.

Prevalence increases with aging, as expected, but also over time within the same age range. A review from the United Kingdom reported that the number of Scottish adults prescribed 5-9, 10-14, or 15 or more medications in a 3-month period in 2010 was 16.3%, 4.7%, and 1.1%, respectively, a considerable increase from 1995, when prevalence figures as low as 9.7%, 1.5%, and 0.2% were observed. Similar findings were reported also in a population-study conducted in Dicomano, a rural town nearby Florence, Italy, exploring different forms of suboptimal drug prescription in community-dwellers aged 65+¹²: the prevalence of participants taking 5 or

more medications increased from 8.8% in 1995 to 21.6% in 1999, independent of the number of associated diseases. Both these studies suggest that physicians' therapeutic approach to older persons is becoming more aggressive with time¹³.

It is therefore imperative to grab a comprehensive understanding of the reasons for polypharmacy and for this trend. Several factors may play a role:

1. First, as mentioned above, comorbidity and multimorbidity: as coexisting diseases increase with aging, this is followed by an almost inevitable increase in the number of drugs used to treat these conditions.
2. Uncritical application of disease-specific guidelines. The majority of treatment guidelines have been developed on the basis of RCT conducted in subjects not representative of the unselected older population, and they are usually directed to the treatment of single diseases. Thus, the complexity of older patients with multipathology is beyond their scope and perspective. Thus, strict and uncritical adherence to these guidelines may end up multiplying the opportunities for polypharmacy⁶.
3. Fragmentation of care. Older patients often see several different specialists, one for each specific disease they have. A moment of synthesis and concern for priorities usually lacks.
4. Patient's expectations. Not rarely, patients themselves are unsatisfied when their complaints do not elicit drug prescription from their physician.
5. On the other hand, it is often a physician's attitude to over-prescribe, as it may be easier and quicker to prescribe medicines than to pause and search, together with patient and family, possible nonpharmacological alternatives.
6. Self-medication. A variety of drugs, including some with a serious potential for severe side effects such as non-steroidal anti-inflammatory drugs (NSAIDs) can be purchased “over-the-counter” without a prescription. Often older patients self-medicate themselves simply based on the advice of a relative or friend. Self-medication may involve irregular and inappropriate use of drugs and is therefore potentially problematic, especially when it remains unknown to the physician: serious risks may stem, particularly of unrecognized

adverse side effects and drug interactions¹⁰.

7. Therapeutic cascade. Sometimes drug side effects are misinterpreted as manifestations of previous or emerging clinical conditions. Therefore, rather than reviewing existing prescriptions to identify a potential cause of these symptoms, a new drug may be added.

Bearing in mind all these causes of polypharmacy may help healthcare providers find opportunities to reduce it and, eventually, to prevent its ominous consequences, that will be described below.

Interactions and Adverse Drug Reactions

Together with age-dependent changes in pharmacokinetics and pharmacodynamics, polypharmacy is a major determinant of drug-drug interactions and adverse drug reactions, which may sometimes even result in death.

Drug-drug interactions can be pharmacokinetic (i.e., one drug increases or decreases the plasma levels of the other) or pharmacodynamic (when, for the same plasma levels, the effects of the first drug are modulated by the second)¹⁵. Although interactions are not always potentially harmful, the number of drug-drug interactions and, therefore, the risk of serious consequences, increase with polypharmacy: taking 10 drugs or more per day leads to a 50 percent chance of at least one clinically relevant interaction and 10 percent chance of a potentially serious interaction¹⁵.

The term Adverse Drug Reaction (ADR) refers to any “harmful and unintended effect resulting from the use of a drug”; this definition was recently updated by the European Community in 2010 with European Directive 2010/84/EU and EU Regulation 1235/2010. Polypharmacy is considered responsible for the development of ADRs in the elderly population: in fact, the risk increases exponentially with the number of drugs taken¹⁶.

The manifestations of ADR are protean, in particular in patients with several coexisting diseases. ADR are often thought of as events, if not strictly atypical and distinct from spontaneous pathology, at least entirely new to the patient, such as a skin rash. Yet, this is often not the case, especially in the elderly: sometimes they are indistinguishable from the manifestations proper to the patient's already known diseases, and for this reason their recognition may be difficult. Thus, the principle applies that, when

a new clinical manifestation appears after the introduction of a new therapy, to consider it a potential ADR, until proven otherwise: such a high degree of suspicion may suggest treating the emerging condition by suspending the newly introduced drug, rather than adding another drug, in order not to fuel the “prescribing cascade”.

Inappropriate medications

Some medications have such an unfavorable risk/benefit ratio in older persons that they can frankly be considered as inappropriate¹⁷. Some authors and scientific societies have compiled lists of drugs to be explicitly considered as Potentially Inappropriate Medications (PIM). The first PIM list was initially proposed by Dr. Mark Beers and it was later endorsed by the American Geriatrics Society (AGS). Its most recent version is directed towards physicians, nurses, and pharmacists, but also towards older patients themselves and their families. The Beers-AGS criteria include three categories of medications: those that are potentially inappropriate in the majority of older patients, those that should be avoided in subjects with certain conditions, and finally those that should be used with caution, considering possible drug-drug interactions and carefully adjusting drug doses according to renal function¹⁸. The Beers-AGS criteria have been approved by the US Federal Government and are considered so important that they are used to evaluate quality of care in nursing homes across the USA.

For several reasons, Beers-AGS criteria remained almost unapplied in Europe, where instead the STOPP/START criteria have been developed and are largely recognized as a screening tool of prescriptions for the aged to alert physicians to the right treatment¹⁹. Some medications in the list are reported not to be prescribed, or even to be discontinued, in older persons because of an unfavorable risk/benefit ratio, or simply because they are unsuitable in terms of dosage or duration of therapy (STOPP: Screening Tool of Older Person's Prescriptions). Other drugs are recommended because of an evidence-based potential benefit for disease treatment or prevention (START: Screening Tool to Alert doctors to Right Treatment): prescribing inappropriateness, in fact, may also include undertreatment.

Therapeutic adherence

Undoubtedly, complex drug regimens dramatically reduce treatment adherence at any age, but in particular in older persons, especially those with sensory or cognitive issues.

According to the World Health Organization (WHO), therapeutic adherence is defined as the degree to which the patient follows the doctor's recommendations regarding doses, timing and frequency of medication intake throughout the duration of therapy. The greater the number of medications prescribed, the greater the risk of poor adherence to the prescribed therapeutic regimen; errors may occur regarding doses and timing of intake or even involve complete omission or duplication. Missing assumption is perhaps the most common form of nonadherence, which can result in the risk of disease progression.

Adherence is affected by several factors belonging to five categories: patient's characteristics, the medication, healthcare personnel's behavior, the "system," and other elements. Among factors related to the patient, cognitive and mental disorders assume a very important role in older persons, along with certain forms of physical disabilities (e.g., visual impairment or poor manipulation ability) that may reduce autonomy in the management of medicines. Moreover, cognitive impairment, which is very common in old age²⁰, can impair an older person's ability to understand prescriptions and to take medications as prescribed, while depression may demotivate patients to adequate treatment²¹. Finally, behavioral and socio-cultural conditions, such as lack of awareness of one's own illness, poor education and health literacy, and loneliness should also be considered, as they may contribute reducing the ability of older patients to follow prescriptions²². Among drug-related factors, polypharmacy certainly plays a prominent role, referring to both the number of therapeutic preparations and the number of administrations. Factors related to the prescribing physician may be represented by a poor personal relationship, ineffective communication, lack of involvement of patients, family members and caregivers. Finally, the main systemic and other factors may be represented by fragmentation of care, lack of medication review, cost of treatment, and caregiver stress²³.

II - How nurses are faced by pharmacotherapy in older persons and what they should do

In recent years, the role and responsibilities of nurses in the management of drug therapy have significantly changed in most countries, including Italy. This is especially true when dealing with older persons and, among them, with those living in long-term care facilities and nursing homes (corresponding to the Italian Residenze Sanitarie Assistenziali, RSA), where nurses have direct and prolonged patient contact and represent the first healthcare professionals patients consult.

There is consensus in educational programs and legislation that the preparation and administration of medication are essential aspects of nursing practice²⁴: in this field, nurses have no longer a subordinate relationship with physicians, but a collaborative one. In the forensic field, it has been now established that nurses' role in drug therapy is not purely mechanistic, but rather a task of full professional engagement and responsibility, in collaboration with physicians. The nurse must intervene in the event of a perceived error, and he/she must report doubts about congruity or relevance of the therapy, otherwise potentially incurring in criminal responsibilities (Sentence no. 20270 - 13.05.2019 of the Italian Court of Cassation, Criminal Section).

Students in the School of Nursing gain knowledge and develop skills on drug therapy during their education, although this is often perceived as insufficient²⁵. After graduation, skills are supposed to increase through the "real world" experience²⁶, when nurses become an essential figure for the management of therapy, both in hospital and out-of-hospital. However, evidence that these skills truly increase is lacking, whereas needs for a specific training on this topic have been frequently reported^{27,28}.

Involvement and responsibilities of nurses are definitively greater in the drug management of older patients, especially in an out-of-hospital setting and in the RSA, the Italian nursing homes or long-term care facilities. In most RSA there is no resident medical staff and general practitioners (GP) are responsible for patient care. However, GP have sporadic contacts with their patients and, therefore, nurses are the frontline healthcare professionals of immediate reference for the resident. Consequently,

monitoring of the therapeutic effects of a drug, as well as of potential ADR, largely relies of nurses, who are an important component of the pharmacovigilance network²⁹. ADR are among the most serious concerns about medication use in nursing homes³⁰: a cohort study of 28,839 long-term care residents in 18 nursing homes in Massachusetts reported as many as 546 adverse drug events (1.89 per 100 resident-month) and 188 potential adverse drug events (0.65 per 100 resident-months) over a 12-month observation period. Therefore, improving nursing knowledge, competence, and skills in pharmacology would allow maximizing the effectiveness and minimizing the risks of drug therapy in this setting³¹.

The role of nurses regarding ADR reporting is also important in the hospital. In a Swedish hospital, nurses that have received a short period of education were proven to be a useful resource for improving the detection and reporting rate of ADRs: out of a total of 56 reports with 86 ADRs sent to the regional centers from the participating departments during the 12-month study period, 23 reports and 39 ADRs had been filled in by participating nurses³².

Another area of drug therapy in older patients where the competences of nurses can be crucial is therapeutic adherence. Several strategies to improve adherence have the nurse as a key player. These strategies include therapeutic review of all medications actually taken (including “over-the-counter” medications), both in the hospital and at home; education about medications and their possible benefits and side effects; use of simple and easily understandable treatment forms; finally, use of verbal and written reminders or, in selected cases, of electronic devices³³.

With the aim of identifying the areas where an educational intervention can be more effective, surveys have been conducted to assess knowledges, competences, and skills of the nurses on drug therapy in the elderly. In a Canadian study conducted in long-term care facilities, nurses were asked to complete a questionnaire before and after the delivery

of an educational program, in order to assess their level of knowledge on the main issues of medication administration in older persons, as

Figure 1. Nurses and pharmacotherapy in older patients

What nurses should know on pharmacotherapy in older persons

- Age-dependent changes in pharmacodynamics and pharmacokinetics
- Limitations of Evidence Based Medicine
- Polypharmacy
- Interactions and Adverse Drug Reactions
- Inappropriate medications
- Therapeutic adherence

How nurses are faced by pharmacotherapy in older persons

- Preparation and administration of medication
- Reporting doubts about congruity or relevance of the therapy
- Monitoring of therapeutic effects therapy, including ADR
- Improving therapeutic adherence

discussed in this review. The program proved effective, as post- responses showed improved knowledges in all aspects³⁴.

Conclusions

In this brief overview, many critical aspects of pharmacotherapy in older persons were addressed, as summarized in Figure 1. We believe that nurses have a major role in the therapeutic management of the elderly, especially in the long-term care setting: therefore, their level of expertise and competence on this topic should be enhanced. Therefore, graduate and post-graduate educational programs should be developed, to offer adequate answers to the increasing and challenging share of older patients seen in everyday clinical practice.

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