

## The treatment of the elderly is a tricky and hard job

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Everybody knows that to treat the elderly is a tricky and hard job. There are many reasons, but the main variables are: the different pharmacokinetics (PK) and pharmacodynamics in comparison to the adults, polypharmacy, drug interactions, the commonness of adverse reactions, the presence of multimorbidities and comorbidities, and patient compliance<sup>1</sup>.

A drug's PK changes with aging, primarily as a consequence of changes in body composition and in renal physiology, but also as a result of acute or/and chronic diseases, being male or female, and of treatment with other drugs; moreover, the gut is also able to affect drug destiny due to changes in the microbiota, in the diet, and to exposure to drugs that affect the microbiota itself. The changes in body composition (fat/muscle ratio) that are typically observed in the elderly have major effects on the water amount in the body and on the distribution volume of a drug. Similarly, changes in the function of the liver, which, together with the kidneys, plays a central role in a drug's metabolism, conjugation and excretion/demolition are also typical of the aging process and affect PK. In addition, the effect of the genetic background, the expression of enzymes (such as cytochromes), the competition or inhibition/stimulation induced by different drugs, and the density of receptors also account for the observed pharmacodynamics of a drug in the older patient.

Finally, factors that may make the response to a drug even more hard to predict include the extremely diverse effects of a molecule, resulting from the activation of intertwined and complex post-receptor pathways.

Despite extensive knowledge of drugs of common use, drug interactions frequently trigger unexpected adverse

events, which are sometimes negligible, but sometimes very dangerous, devastating, with harmful consequences, leading to a patient's hospitalization or even to his death<sup>2</sup>. The presence in a patient of a "hyper-polypharmacy" (more than 10 drugs) brings the probability of an adverse event very high. In Ireland, old people taking more than 10 drugs have increased from 1.5% in 1997 to 21.9% in 2012<sup>3</sup> with most of these medications likely being prescribed on the basis of recent guidelines for chronic diseases.

Finally, I mentioned the issue of compliance because this is another puzzling factor (how could you imagine the adherence to the therapy of your old patient?) that further complicate this problematic area. In this context, many studies show a very discouraging scenario: after six-to-twelve months from the beginning of a defined treatment, elderly patients will typically forget or voluntarily avoid to take the prescribed drug, and that become an even bigger problem if the patient is supposed to take several drugs<sup>4</sup>. The inappropriateness of many medications is another common problem, which I shall not address here<sup>5</sup>.

Finally, these issues become further compounded, when a caregiver is involved. The problems and complaints of the latter add complexity to the patient management and may make our treatment choices more difficult.

Overall, it is clear that it is almost impossible to foresee with reasonable certainty the effect of a prescription and the adverse events it will cause.

Besides these critical, but realistic, considerations, I'd like to recommend a brief, but stimulating, paper on this topic, that addresses the problem of the therapy prescription in elderly patients with dementia.

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In a recent paper <sup>6</sup>, Carole Parsons, an Irish clinical pharmacist, underlines that the appropriateness of drug prescriptions is frequently neglected in this group of patients and that very little information can be found in the literature to inform therapeutic decisions. Therefore, she hopes (and solicits) that more data will become available in the near future.

The patients diagnosed with dementia have a reduced life expectancy compared to patients who do not have a dementia <sup>7</sup>. In addition, a diagnosis of dementia is typically associated with an advanced age, and a high multi- and co-morbidity. In such complicated patients, no validated criteria or indications, no studies evaluating the burden of the therapy or describing the best choices have been published, and only some warning or potential threats were reported <sup>8</sup>.

The literature analysis performed by the Author showed that “considerable scope exists to improve the quality of prescribing for people with dementia” in term of mis-, over- and under-prescribing.

The Author reported that, surprisingly, 40-60% of the elderly affected by dementia are on anticholinergic medications, which are clearly contraindicated since they frequently cause a worsening in a patient’s cognitive functions.

The Author also showed that antipsychotic agents that are commonly prescribed to elderly are largely useless and that frequently physicians simply prescribe antipsychotics by habit or drift.

Similarly, the use of antibiotics in the late stage of dementia is also controversial, either because of the negligible or not significant symptoms that are associated with common infections in the elderly, such as urinary tract infections, or because antibiotics do not modify the clinical trajectory of the infection itself and because the latter commonly relapses anyways.

On the other hand, pain killers are frequently under-prescribed in the elderly, an aspect that has been extensively studied in literature <sup>9</sup>, in particular in cognitively impaired patients the treatment is even more neglected <sup>10</sup>. Such habit usually reflects the fact that pain is under-detected in the elderly, which, in turn is due to the inability of many patients to communicate properly. Notably studies also show that, although efficient and validated scales for detecting pain in not-communicating patients do exist, they are normally not used in routine clinical practice <sup>11 12</sup>. Thus the study stressed that more attention should be paid to fighting pain in the elderly.

Treating elderly is really complicated and it requires the geriatrician to pay considerable attention to his patients. The study by Parsons warrants further investigations to answer the many open questions in this area. I said that treating elderly is tough, but treating and

prescribing appropriately in patients with dementia is even tougher. Thus, it is mandatory to begin developing evidence-based guidelines to approach the problem, where the ultimate goal of this effort should obviously be improving patient care and quality of life, but also providing the caregiver with better information, and saving health systems’ budgets, which would otherwise be wasted in many useless or poorly prescribed medications.

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