

# Polypharmacy and the elderly

The accumulation of prescribed medicines is a recognised effect of ageing. Polypharmacy is an important issue when treating the elderly patient, as it is one of the main reasons why this age group have a higher frequency of adverse drug reactions compared with younger groups.

**Dr Richard Fitzgerald** and **Professor Munir Pirmohamed** discuss how polypharmacy can occur and how to reduce the pill burden for the elderly patient.

In the Western world, the proportion of the population who are 65 years and older is continuing to grow. In the UK, at present, nearly 20 per cent of the population are elderly. This is forecast to become around 21 per cent by 2026 and to continue rising at a similar rate for the future<sup>1</sup>. The demands of the elderly for healthcare and, more importantly, for medicines are significant when compared with the wider population.

In the UK, 80 per cent of people aged 75 years or over are prescribed at least one medicine and greater than two thirds are prescribed four or more medicines<sup>2</sup>. This is one of the main reasons for the higher frequency of adverse drug reactions in the elderly, estimated to be up to 17 per cent in one study<sup>3</sup>. The importance of polypharmacy has been recognised by the Royal College of Physicians in their report on medications for older people<sup>4</sup>, and the Department of Health also published extensive guidelines on medicines on older people in the National Service Framework (NSF) for Older People<sup>5</sup>.

## Polypharmacy and the elderly

Polypharmacy has no strict definition. It is accepted, however, that polypharmacy constitutes a situation in which a patient is taking a large number of drugs of which some may be necessary and some may not be<sup>6</sup>. The study of polypharmacy is thus not

straightforward. One issue to consider is the representativeness of the population being studied. For example, the patients involved in a study may be healthier than their average cohort<sup>7</sup> and thus appear to have a lower number of prescribed medicines. This partly explains the discrepancies in the literature on this issue; for example, between the figures from a Dutch study (3–4 per cent; which incorporated a relatively small healthy sample from North Holland) and those quoted by the Royal College of Physicians<sup>4</sup> (16–17 per cent).

The accumulation of prescribed medicines is a recognised effect of ageing<sup>8</sup>, and intuitively, it would be expected that, over time, patients tend to have more medicines prescribed. This may be attributed to deterioration in health status<sup>9</sup> through either a worsening of a known disease or development of another disease process. The degree of polypharmacy in the elderly, however, varies from country to country — being greater in the UK and US than in other countries. In other countries, the development of polypharmacy can be quite slow. In the Netherlands, it was found that in a four year period the average long-term drug use increased from 1.3 to 1.7 drugs per person — a 31 per cent increase<sup>7</sup>.

The degree of polypharmacy is influenced by various factors apart from ageing, including: the natural progression of disease, moving to residential or nursing care and hospitalisation<sup>9</sup>.

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Specific medical conditions that have a higher prevalence in the elderly, such as atrial fibrillation, hypertension, ischaemic heart disease and dementia, have also been identified as contributing significantly to polypharmacy<sup>7</sup>. Furthermore, polypharmacy begets polypharmacy; a higher baseline number of medicines leads to increasing polypharmacy in the future<sup>10</sup>. The Dutch study also highlighted that drugs without clear indications (such as sedatives) are most associated with polypharmacy<sup>7</sup>. Residence in a nursing home is also a frequent predictor of polypharmacy<sup>11</sup>, with an average of 7.2 drugs prescribed per person in a large cohort of US nursing home residents. More worryingly, much of this prescribing in nursing homes may be inappropriate when compared with the population as a whole<sup>11</sup>.

### Pharmacokinetic changes in older people

Polypharmacy is becoming more common in younger patients; in itself, this creates problems. However, in the elderly, the problems are compounded by the physiological changes that occur with ageing, which in turn leads to changes in drug pharmacokinetics (the process of drug absorption, distribution, metabolism and excretion of drugs) and pharmacodynamics (the action of drug on its target). In some cases, this is enough to lead to an adverse drug reaction or interaction<sup>12</sup>.

As patients age, there is a decline in the function of most organ systems. Pharmacologically, of most importance is the decrease in renal function which, in turn, alters the clearance of many drugs, especially the water-soluble compounds. It has been estimated that approximately two thirds of the population have a reduction in the glomerular filtration rate (GFR) as they age. This often remains unrecognised. Many elderly patients are assumed to have normal renal function on the basis of a normal serum creatinine; however, this is misleading because the elderly often have a decrease in muscle mass, and thus a normal serum creatinine in a thin elderly patient may hide quite significant renal impairment. GFR in the elderly must therefore be measured or estimated according to the recent recommendations of the NSF for renal disease<sup>13</sup>. The NSF mentions the use of the Cockcroft-Gault (CG) equation or the newer eGFR (electronic GFR)<sup>13</sup> (see Table 1).

The CG equation has been shown to be useful in estimating GFR<sup>14</sup>. However, it does have flaws as

**Table 1.** Equations for measuring GFR

**CG equation:**

$$\text{CrCL} = (140 - \text{age}) \times \text{weight} \times 0.85 \text{ (if female)} \\ 72 \times \text{Creatinine}$$

**eGFR equation:**

$$\text{GFR} = 186.3 \times (\text{creatinine})^{-1.154} \times (\text{age})^{-0.203} \\ \times 0.742 \text{ (if female)} \times 1.21 \text{ (if black)}$$

it may have significant and variable bias<sup>15</sup>. The eGFR measure was developed from the Modification of Diet in Renal Disease (MDRD) study<sup>15</sup> and produces less biased estimates, which can also be easily calculated by a hospital laboratory and appended to standard electrolyte reports. Because of its more accurate estimation and potential for widespread use, eGFR has been recommended as the standard estimation for GFR by the NSF<sup>1</sup>. Caution with eGFR measures, however, must be exercised when the serum creatinine is changing rapidly or when the GFR is close to normal. The measure has also not been validated in certain ethnic groups (for example, in Afro-Caribbean patients)<sup>15</sup>.

Liver function remains largely intact during the ageing process, particularly when the metabolic capacity of each hepatocyte is compared with that in a younger individual. However, ageing is associated with an overall decrease in liver mass, and this can lead to some reduction in metabolism, particularly of the phase I pathways responsible for metabolism of narrow therapeutic index drugs. For instance, it is well known that ageing is associated with a lower daily warfarin dose requirement. Disease may further affect metabolism in the elderly; for example, heart failure, which is common in the elderly, is associated with reduced liver blood flow, which can decrease the first pass metabolism of high extraction compounds such as morphine, isosorbide dinitrate and some antidepressants<sup>16</sup>.

Drug distribution also changes in the elderly because of a reduction in total body water and an increase in body fat as a percentage of the body mass. The net effect of this is a reduction in the volume of distribution for some drugs, which requires a change in loading dose. For example, the loading dose of digoxin should be reduced because of a smaller volume of distribution in the elderly<sup>16</sup>.

Elderly patients also have an increased sensitivity to the side effects of some drugs, particularly antihistamines (sedation, antimuscarinic actions leading to urinary retention in men), benzodiazepines (sedation, falls) and diuretics (falls, incontinence)<sup>16</sup>.

### Adverse drug reactions and the elderly

Changes in the pharmacokinetics of many drugs and polypharmacy inevitably increases the number of adverse drug reactions (ADRs) suffered by the elderly. The incidence of ADRs in the elderly is often underestimated. Approximately 19 per cent of hospital admissions of older people in the US are attributable to ADRs<sup>2</sup>. In the UK, the corresponding figure is 17 per cent<sup>3</sup>. There is also a direct correlation between the number of drugs prescribed and the number of hospital admissions due to an ADR<sup>17</sup>.

The causes of ADRs are multifactorial and often relate to altered pharmacokinetics, iatrogenic errors, drug interactions, self medication, poor patient education and non-compliance. An important factor in causing ADRs, however, remains the number of drugs taken by the patient<sup>3, 18, 19</sup>. This finding is supported by studies that show between 24 and 36 per cent of elderly patients are exposed to drugs that may potentially interact with one another. The drugs most commonly implicated are potassium-sparing diuretics prescribed with ACE inhibitors and non steroidal anti-inflammatory drugs (NSAIDs) prescribed concurrently with anticoagulants<sup>20</sup>.

The consequences of ADRs in the elderly can be precipitous. For instance, acute renal failure (ARF) is a serious consequence of an ADR and can lead to multi-organ failure and death. Even following recovery from ARF, a patient may have residual damage from the acute event and be left with reduced renal clearance<sup>16</sup>. Gastrointestinal (GI) haemorrhage may be a result of ingestion of NSAIDs for arthritis or other pathologies. GI bleeding and renal failure often appear high up in the list of ADRs causing admission in elderly patients — this reflects their wide usage and narrow therapeutic index.

Another important ADR to consider in the elderly is falls. These may be due to many drugs such as diuretics, which can result in postural hypotension causing a fall<sup>5</sup>. Falls may also be the

result of benzodiazepines prescribed for night-time insomnia or sedating antihistamines<sup>12, 21</sup>.

### Guidelines for prescribing in the elderly

Polypharmacy exerts a considerable effect on the elderly health as a whole through (a) predisposing to ADRs, and (b) leading to non-compliance of important life-saving medicines. Prescribing in the elderly is therefore an important public health issue, one which needs more attention by all healthcare professionals at all stages from education and training right through to the actual prescribing, administration and monitoring of medicines.

Clearly, elderly patients benefit from correct and astute prescribing for their particular conditions. The NSF for Older People states that older people should 'gain the maximum benefit from their medication to maintain and increase their quality of life' but should not 'suffer from illness caused by excessive, inappropriate or inadequate consumption of medicines'<sup>5</sup>. Prescribing of too many medicines, however, will inevitably lead to problems with adherence. In the UK, up to 50 per cent of the elderly population may not be taking their medication as intended and some medicines are under-prescribed (eg, anti-depressants, anti-thrombotics)<sup>22, 23</sup>. In order to deal effectively with the problems that prescribing in the elderly can present, consideration must be given to why a drug is being prescribed and, following its prescription, the drug must be reviewed at regular intervals. In particular, one should consider whether the drug is still needed and if so, if the dose is still correct. A typical example here is with diuretics — while high doses may be very useful during the initial treatment of heart failure, failure to reduce dose (a common occurrence) when the patient is stable often leads to dehydration, renal impairment and in the worse case-scenario, acute renal failure and death<sup>24</sup>.

The NSF has highlighted the patients that may be at risk of medicines-related problems. First, polypharmacy is a primary risk factor as identified above. Secondly, following discharge from hospital, there may be significant changes in a patient's medication. Unintentional duplication of prescribing is frequent<sup>25</sup>, through the use of both brand names and generic names. Thirdly, patients who have any symptom that may identify a drug-related problem such as dizziness, falls or a GI haemorrhage may need in-depth evaluation of their prescription<sup>5</sup>.

One further area highlighted in the NSF is that of repeat prescribing. Repeat prescriptions in the elderly are frequently necessary but unfortunately may be under-monitored<sup>5,26,27</sup>. This can lead to redundant drugs still being prescribed, which not only predisposes to ADRs but affects adherence to the medicines that are actually needed. Prescribers may be scared of stopping drugs because of their belief that it may be doing some good or because it has been started by a different clinician.

It is important to evaluate the patient and if the assessment suggests that the drug is not having an effect, the drug should be stopped<sup>6,24</sup>. But, the patient should be monitored afterwards to confirm that there was no need for the drug. A particular problem to be aware of in the elderly is that of sequential prescribing — where an ADR related to the first drug is treated with another drug (for example treating incontinence caused by diuretics), which then leads to another adverse effect, and so on<sup>7</sup>. The correct intervention in such a situation may be to stop the drug, consider an alternative or reduce the dose.

What can we do about the problem of polypharmacy? Several trials have shown that there are interventions that can influence polypharmacy and prevent ADRs<sup>5,7</sup>. First, it is important to have a specific indication for any medication being prescribed. Secondly, medications should be discontinued when they are no longer relevant for the patient's condition — for example diuretics may worsen renal impairment, cause incontinence, postural hypotension and electrolyte imbalances<sup>24</sup>. Thirdly, drugs should be titrated slowly on commencement of therapy with adequate monitoring in order to prevent overshooting the therapeutic level and causing an ADR.

Most medicines are prescribed and administered in the community. Thus, it is there that strategies for reducing polypharmacy will be most effective. A regular medication review in which each medication is scrutinised either by the GP or by a community pharmacist has been shown to reduce the level of polypharmacy and the number of ADRs experienced by elderly patients<sup>28,29</sup>. The components of this comprise a review of all aspects of the patient's drug history, review of currently administered medications (both prescribed and over-the-counter), drug education (frequency of administration, side effects) and finally ensuring that the patient is adequately monitored (for example, renal function when

prescribed ACE inhibitors). The NSF for older people also recognises this as an important method of improving elderly health. One note of caution, however: although monitoring is important and most guidelines recommend it, there are no specific data on how often monitoring should take place (even with the most commonly prescribed drugs such as diuretics) nor is there any information on what should be done when an abnormality is found. There is an urgent need for further research in this area.

There are conditions in which the NSF makes specific recommendations. Falls, for example, are frequently a result of polypharmacy<sup>5</sup> and hypotension and sedation are key causes of this. The NSF recommends that following a fall, the patient should have all their medication reviewed in order to prevent recurrence. This strategy has been shown to reduce further falls in two studies<sup>30</sup>. The NSF also makes extensive recommendations for the treatment of mental health disorders. For instance, tricyclic antidepressants and neuroleptics are frequently inappropriately prescribed<sup>31</sup> causing ADRs. Whilst it is recognised that mental health problems in the elderly have to be treated effectively, it is clear that the drug used must be carefully selected. To that end it is recommended that a selective serotonin reuptake inhibitor (SSRI) be prescribed in preference to tricyclic antidepressants. This is not to say that SSRIs do not have any adverse effects, but they are better tolerated than TCAs.

Finally, education of prescribers is important. This not only relates to the teaching of pharmacology and therapeutics to undergraduates, (about which there has been heated debate recently<sup>32,33,34,35</sup>), but also continuing professional education for GPs and hospital doctors. The latter has not received much attention, but it is probably

### Key Points

- > Polypharmacy is a major health issue that is predisposed to adverse drug reactions.
- > The elderly are particularly prone to the adverse consequences of polypharmacy because of changes in the way they handle drugs and because of concomitant disease.
- > Proactive strategies that aim to rationalise prescribing in the elderly, and thereby reduce the frequency of polypharmacy need to become a routine part of clinical practice.

as important to educate these groups as well as the undergraduates. Another aspect that everybody has to be aware of is the increasing number of prescribers with the Government strategy to increase access to medicines for the public by extending prescribing powers to nurses and pharmacists. The effect of this change needs to be carefully monitored.

## Conclusion

In conclusion, polypharmacy has a huge impact on the health of the elderly in the UK. Whilst it is relatively easy to accumulate medicines, it is more difficult to stop them, which often only happens when an ADR occurs. The importance of

polypharmacy has long been recognised, and the fact that it still remains a problem highlights the difficulties facing us in reducing the problem. We need a multifactorial approach to reduce polypharmacy, as highlighted in this article. The NSF guidelines go some way in providing guidance on reducing polypharmacy, but ultimately, it will require very different working practices than are current now. An opportunity in the UK in the near future is the implementation of the single electronic patient record which will allow us to monitor polypharmacy, assess and detect potential problems early on, and develop intervention strategies.

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