

## Polypharmacy in elderly: A cautious trail to tread

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### Abstract

Polypharmacy has now increasingly come into focus as the recipient of healthcare in old age worldwide. In elderly it is associated with frequent adverse drug reactions (ADRs) and drug-drug interactions resulting in significant morbidity. Geriatrics is still an emerging specialty in South Asia, especially in Pakistan, where multiple reasons for polypharmacy exist. An extensive literature review of articles using key words like 'polypharmacy,' 'elderly' was conducted. The recently updated Beers Criteria of classification of inappropriate drugs in the elderly was reviewed in detail. Articles of relevance to polypharmacy and evaluation of guidelines for appropriate interventions to minimise inappropriate drug prescribing were also reviewed. Commonly prescribed drugs like psychotropic, cardiovascular, non-steroidal anti-inflammatory drugs (NSAIDs) and oral hypoglycaemics can cause significant adverse events when prescribed to the elderly.

Primary care physicians may use evidence based non-pharmacological interventions which may be appropriate to use in selected cases. Drugs can affect quality of life and morbidity in the elderly. A basic understanding of ageing physiology and pharmacology along with a step-wise approach to prescribing in the elderly maybe helpful in minimising iatrogenic complications of commonly used drugs in this age group.

**Keywords:** Polypharmacy, Elderly, Adverse drug reactions, Inappropriate prescribing.

### Introduction

Polypharmacy, defined as the use of five drugs or more, has now increasingly come into focus as the recipient of healthcare age worldwide. The elderly, with greater number of co-morbidities, tend to consume more medications. In the US, about one-fifth of all prescriptions are written for patients 65 years and older.<sup>1</sup> Drugs tend to behave differently in the elderly compared to the non-elderly patients. Ageing brings about several changes in the functioning of organ systems which in turn affect drug behaviour and metabolism. Prolonged drug half-

lives, adverse drug reactions (ADRs) and drug-drug interactions thus become more frequent and often result in significant morbidity in the elderly. A meta-analysis reported that elderly patients were two times more likely to get hospitalised due to an ADR than non-elderly patients.<sup>2</sup> An Australian study reported a rising number of ADRs with approximately 30% in 2003.<sup>3</sup> Inappropriate medications were prescribed to one-third of the elderly.<sup>4</sup> National health surveillance data identified inadvertent high drug dosing as a cause of hospitalisation in almost 66% of the elderly.<sup>5</sup> A study from India cited 7% of hospital admissions in the elderly were related to an ADR.<sup>6</sup>

Although Western medical literature has extensive literature on polypharmacy in the elderly, studies in the eastern hemisphere are scarce. Geriatrics is still an emerging specialty in this region where the care of an aged individual is still not clearly understood. Most of the elderly are cared for by non-geriatric physicians and comprehensive geriatric assessment and care is limited.

There are multiple reasons for polypharmacy in Pakistan. Elderly patients are often treated by multiple healthcare providers, all prescribing medications individually. Physicians also tend to over-prescribe at times.<sup>7</sup> Patients often indulge in self-medication in an environment where drugs can be easily purchased over the counter. Physician practice may further perpetuate inappropriate drug use, e.g. benzodiazepine usage initiated via physician prescription was reported in almost half of subjects in a study.<sup>8</sup> This situation appears to be alarmingly similar to elderly patients in Pakistan where a recent study on delirium cited a 39% usage of psychoactive drugs in patients 65 and older.<sup>9</sup>

As the medical community in this part of the world begins to manage an increasing population of aged patients, the need to understand the role of polypharmacy, the dissimilarity of drug behaviour in the elderly, and risk-benefit ratio of each drug prescribed to an older individual becomes important for the provision of quality healthcare to this growing section of our population.

The aim of this article is to enhance awareness of appropriate prescribing in the elderly based on recent evidence, especially for primary care physicians and non-geriatric specialists.

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## Methods

A thorough literature search was conducted using PubMed and Google Scholar to select articles from 2000 till 2012 using key words like polypharmacy, geriatric patients, elderly care, Beer's criteria, inappropriate prescribing and adverse drug events. Key phrases like "oral hypoglycaemic drugs and elderly" were also used to search articles for specific drugs.

A literature search from Asia was also done through the Index Medicus for South East Asia region (IMSEAR) and PakMediNet, a Pakistani medical journal database, to identify regional articles.

Thousands of citations were found during the initial literature search from which 70 most relevant articles were reviewed in detail. From the regional search, only a handful of articles were available<sup>10-12</sup> of which none was found in PakMediNet.

Some older articles which were historically relevant to polypharmacy and inappropriate prescribing were included in this review.

Evidence-based non-drug interventions, and other interventions to minimise inappropriate prescribing were reviewed and included as well.

## Discussion

In 1991, inappropriate prescribing in the elderly was first investigated in detail by Mark Beer who established the Beer's criteria of drugs that were likely to cause more harm than benefit when prescribed to the elderly.<sup>13</sup> His list included psychoactive drugs of various classes like anti-depressants, sedatives, anti-psychotics, NSAIDs; all included after employing a panel of experts working through the Delphi method. In 2012 the American Geriatric Society revised and updated the Beer's list, dividing drugs into three separate categories.<sup>14</sup> The first category included drugs known to cause potential adverse events when prescribed to the elderly and hence avoidance is strongly advised. The second category included drugs that may cause potential drug-drug interaction or harm when given to patients with certain co-morbidities. The third category included drugs that should be prescribed with caution as they have the potential of causing adverse reactions as well; maybe used, however, if no other alternatives existed.

## Psychoactive Medications

Psychoactive drugs have been associated with a 2.5 times decline in ability to perform daily activities in the elderly.<sup>15</sup>

Of note in our setting are benzodiazepines which are very commonly prescribed and often self-prescribed<sup>8</sup> for sleep induction. Other studies have also cited frequent use of

benzodiazepines in the elderly.<sup>16,17</sup> One study identified up to 14% adverse drug events related to benzodiazepine use.<sup>18</sup> Altered pharmacokinetics and pharmacodynamics in ageing make both short-acting and long-acting benzodiazepines risk factors for falls and memory loss in the elderly.<sup>19-21</sup>

A systematic review showed anti-depressants, especially tricyclic antidepressants and antipsychotics, to be a factor in falls.<sup>22</sup> It reported a five-time increased risk of falls with tricyclic antidepressant use.

Drugs with anti-cholinergic properties are common culprits causing confusion, urinary retention, constipation etc. These include tricyclic anti-depressants, certain selective serotonin reuptake inhibitors (SSRIs), and commonly self-prescribed anti-histamines. Anti-spasmodic and anti-motility agents also fall into this category on account of their strong anti-cholinergic properties.

Tricyclic anti-depressants have multiple therapeutic uses e.g. in depression, insomnia, chronic pain, neuropathic pain and, therefore, deserve special mention as their anti-cholinergic properties are often not taken into consideration while prescribing to the elderly.

Physicians, therefore, need to weigh the risks and benefits of using psychoactive drugs for each patient on an individual basis and familiarise themselves with evidence-based non-pharmacological methods for insomnia and behavioural symptoms before prescribing these medications whenever possible.<sup>23-25</sup>

## Cardiovascular Drugs

The South Asian population has a greater burden of hypertension.<sup>26</sup> With age-related arteriosclerosis, rates of isolated systolic hypertension are high in the elderly,<sup>27</sup> making anti-hypertensives a frequent addition to their drug list. Commonly prescribed anti-hypertensive drugs, especially angiotensin converting enzyme (ACE) inhibitors and alpha blockers are linked to syncope and orthostatic hypotension in the elderly.<sup>14</sup> Diuretics have been implicated in falls<sup>16</sup> and are more likely to cause hyponatraemia in older vs. younger patients due to altered renal function. An Italian study identified diuretics to be causing 10% of hospitalisations because of an adverse event.<sup>28</sup>

The changing pharmacokinetics in the elderly, combined with altered physiology of the cardiovascular and renal system, make the elderly more vulnerable to the side effects of common anti-hypertensive agents, including calcium channel blockers especially those suffering from co-morbidities like heart failure or prior syncope.<sup>14</sup> Calcium channel blockers were cited as causing 9% of hospitalisations due to an adverse event in one study.<sup>28</sup>

Using reduced drug dosages<sup>29</sup> and slow drug titration

based on therapeutic response of the patient may help mitigate serious adverse events.

Primary care physicians also need to know that drug-drug interactions are more likely with use of anti-arrhythmic drugs.<sup>30</sup> Risk-benefit ratio of such drugs needs to be weighed carefully before prescribing.

### NSAIDs

Age-related wear and tear of the joints often leads to chronic pain for which NSAIDs are commonly prescribed by primary care physicians. As with other drugs, tolerability of these drugs diminishes with age, often leading to gastric and duodenal ulcers which are on the rise in the elderly.<sup>31</sup> NSAID use also quadruples the risk of gastrointestinal bleeding in the elderly.<sup>32</sup> Aspirin and NSAIDs were also accounted for about 30% of ADRs causing hospitalisations in one study.<sup>28</sup>

Lower dosages and judicious selection of the type of NSAID and screening of risk factors prior to the start of treatment is advised.<sup>22</sup> In addition, the use of topical NSAIDs is now also recommended for reduction of pain and inflammation of osteoarthritis.<sup>33</sup>

### Other drugs

Statins are added to reduce cardiovascular risk in the elderly who often have co-morbidities like diabetes and hypertension. While the risk reduction is important, polypharmacy is a key factor implicated in increasing risk of myopathy, especially in the elderly who lose muscle mass with ageing and have declined hepatic function. In addition, risk of myopathy is dose-dependent. Another caveat is prescribing statins to patients 80 years and older, in whom benefits of medicating are still unclear and may vary from patient to patient.<sup>34-36</sup>

With the rapidly rising burden of diabetes in developing countries<sup>37</sup> oral hypoglycaemic drugs deserve a special mention as well. Long-acting sulphonylureas have been implicated in prolonged hypoglycaemia due to their reduced metabolism in the elderly.<sup>38</sup> Short-acting sulphonylureas are a safer option.

In addition to awareness of adverse effects of commonly prescribed drugs, it is also important that other therapeutic considerations while caring for the elderly is the need to apply strategies of appropriate prescribing to reduce the burden of iatrogenic complications due to non-judicious drug dispensing. Several options have been proposed:

The Cochrane review suggests that involving pharmacists in monitoring drugs dispensed to the elderly may have a role in identifying drugs of concern and mitigate inappropriate prescribing.<sup>39</sup> Another review suggested a

role of educational strategies in improving prescribing practices in nursing homes.<sup>40</sup> A concrete framework is provided by a recent article which describes a step-wise approach to addressing the problem of inappropriate prescribing in the elderly, starting from a complete listing of medications used to a detailed benefit analysis of the drug to be dispensed and continued monitoring of medications that are prescribed by a single care provider.<sup>41</sup> Literature does cite that the higher the number of providers, the more likely the incidence of polypharmacy and subsequently an adverse drug event. This study also cited that the presence of four to five chronic health conditions increased the risk of an adverse drug event two-fold.<sup>42</sup>

A few key points, therefore, to remember are that complexity of care of an elderly patient not only lies in dealing with their co-morbidities but also an awareness of how drugs can affect quality of life and morbidity in this age group. A simple but detailed review of medications (both prescribed and over-the-counter), reduced drug dosing, weighing the risk-benefit ratio of each drug, awareness of drug interactions and ongoing surveillance of medications may help the primary care providers to provide better quality of care to their elderly patients. One would do well to be familiar with basic ageing physiology and pharmacology; consider possible drug interactions before prescribing; consider risk-benefit ratio before prescribing; start with reduced 1/2 to 1/3 of regular adult dosage and gradually increase if needed; monitor patient carefully for adverse reactions due to drug or drug interactions; and perform a detailed drug review at every patient visit.

### Conclusion

Polypharmacy is a common occurrence in elderly patients and may at times cause considerable morbidity in the life of an aged patient. The importance of judicious prescribing aligned with a basic understanding of ageing physiology and pharmacology is necessary for primary care physicians to adopt in their practice while caring for the aged.

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