Polypharmacy and ageing

More than 450 participants gathered in Prague for the 50th European Society for Clinical Pharmacy Symposium. Topics included the challenges of managing multimorbidity and frailty, medication errors and appropriate medicines' use

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Polypharmacy and multimorbidity are closely interlinked, according to Graziano Onder (Director of the Department of Cardiovascular, Endocrine-metabolic Diseases and Ageing, Italian National Institute of Health). Polypharmacy is defined as taking five or more prescription drugs and multimorbidity as the co-occurrence of two or more chronic conditions. Multimorbidity is estimated to affect more than 60% of older adults. It represents a challenge for health care systems because they tend to be focused on single conditions, he said.

The I-CARE4OLD network (www.icare4old.eu) has analysed data from more than 170,000 older adults (60 years or older) and found that five common patterns or classes of disease predominate. They are: cardiopulmonary diseases, psychiatric conditions, stroke/hemiplegia, Alzheimer's disease and 'other dementia'.

Multimorbidity leads to polypharmacy and a report from Italy study showed that one third of over-65s were taking 10 or more medications.[1] Anti-hypertensive agents, PPIs and antibiotics were especially widely used. The risk of drug–drug interactions is high – for example, nearly one million Italians are estimated to be at risk of bleeding as a result of drug-drug interactions, explained Professor Onder.

Guidelines for management of multimorbidity and polypharmacy have been published by the National Institute for Health and Care Excellence (NICE) in the UK, the American Geriatric Society and an Italian group. All cover broadly similar ground and stress the importance of the patient's own wishes and preferences. One important idea is the concept of 'inflammaging'. This suggests that disease processes start years or decades before overt evidence of disease is apparent. It follows that early treatment is called for to 'switch off inflammation'. This marks a paradigm shift from treating individual conditions to targeting ageing, as is being done in the TAME (Targeting Aging with Metformin) trial,[2] explained Professor Onder.

Frailty

Frailty is a condition that affects about 30% of the over-70s and it is important to realise that it is not the same as being chronologically old, Professor Eva Topinkova (Department of Geriatrics, Charles University, Prague) emphasised. It is defined as "age-related alteration in physiology and pathology that leads to vulnerability with loss of organ system reserve, limited capacity to respond to internal and environmental stresses, unstable homeostasis and poor medical and functional outcomes". Thus, episodes of acute illness cause sharp declines in health and people do not recover to the same level as before.

The frailty phenotype is characterised by weight loss, weakness, fatigue and low level of physical activity (e.g., slow walking). There can also be signs of osteopenia and sarcopenia (loss of muscle mass and function). "Frailty and sarcopenia are two sides of the same coin", said Professor Topinkova. Adverse drug events and physical frailty are both associated with sarcopenia, she added.

A 2015 French study of frailty and polypharmacy concluded that frailty and excessive polypharmacy were independent predictors of mortality.[3] Moreover, frail people with excessive polypharmacy were six-times more likely to die during the follow-up period.

Some frailty indices are difficult to use in day-to-day clinical practice because they are time-consuming or require special instruments. A study comparing two frailty indices concluded that a simple, three-item instrument reliably predicts the risk of falls, disability, fracture, and death.[4] The Study of Osteoporotic Fractures (SOF) index uses only weight loss, inability to rise from a chair five times without using arms, and reduced energy level and is easy to use in routine daily practice, she said.

Pharmacists need key competencies to tackle frailty and polypharmacy. A recent article set out the measures required and recommended a structured review of prescribed medicines to enable rapid identification and management of potentially problematic medications.[5] Such medicines could include those which increased anticholinergic burden, benzodiazepines, and those likely to cause falls.

Drug-related problems and deprescribing

In order to reduce the number of drug-related problems, much effort has been directed at identification of potentially inappropriate medicines (PIMs) and measures to reduce prescribing of high-risk drugs, said Professor Tobias Dreischulte (Institute of Family Practice and General Medicine, LMU Hospital, Munich, Germany). The most obvious route was to educate doctors but in practice this has not always resulted in reduced prescribing of high-risk drugs. The EMPOWER study,[6] in Canada, targeted deprescribing of benzodiazepines by educating patients via community pharmacies, rather than doctors. The results of this randomised study showed that 62% of patients in the intervention group initiated a conversation with the physician or pharmacist and 27% (intervention) vs 5% (control) discontinued benzodiazepines.

Managing polypharmacy is complex and time-consuming, he said. Given that annual reviews are recommended and

nearly 10 million Germans will be eligible by 2030, each GP will need to take on about 216 medication reviews each year. Pharmacists could help with this, as medication review by pharmacists is now reimbursed in Germany. However, some practical issues, such as access to clinical information, will need to be resolved first, he concluded.

Potentially inappropriate prescribing (PIP) is associated with increased risks of adverse drug events, Professor Stephen Byrne (University College Cork, Ireland) told the audience. Furthermore, approximately 50% of patients in secondary care are estimated to be recipients of PIP, he continued. This has led to calls for 'deprescribing' to protect patients from adverse effects. However, in practice this may not be easy. A number of tools for deprescribing have been developed and several large multicentre trials have evaluated the process. Many of the tools can be found at the website www.deprescribing.org, he noted. Medicines optimisation in older people is multifactorial and requires a range of measures, including discussion with the patients about what they want out of it, he concluded.

Appropriate polypharmacy

Although often seen as a negative factor, appropriate polypharmacy can be a good thing, according to Carmel Hughes (Professor of Primary Care Pharmacy, Queen's University, Belfast). However, getting the balance between 'many' and 'too many' is critical, she acknowledged.

A Cochrane review of interventions to increase the appropriate use of polypharmacy had shown that many studies lacked detailed descriptions and the effectiveness of interventions turned out to be weak. Evaluation of the evidence suggested that the challenge of improving prescribing of appropriate polypharmacy was complex and required a correspondingly complex intervention – and this would call for changes in prescribing behaviour.

Professor Hughes and her team systematically identified the barriers to and facilitators of behaviour change and then considered the behaviour change techniques (BCTs) that would be needed. For example, if prompts and cues were needed to bring about a behaviour change, this might be achieved by simply placing a sticky note on a door as a reminder. In practice, moving from BCT to intervention package "requires a balance between science and creativity" said Professor Hughes. In this case the BCTs were embedded in the interventions. For example, when older patients who meet the inclusion criteria attend for scheduled appointments, the receptionist prompts the GP to perform a medication review.

> **Potentially inappropriate prescribing (PIP) is associated with increased risks of adverse drug events**

The Medical Research Council (MRC) framework for developing complex interventions calls for pilot and pre-testing before embarking on full scale study. With this in mind, the PolyPrime study was designed.

The Polyprime study is a pilot, cluster-randomised controlled trial (cRCT) trial of a theory-based intervention targeting prescribing of appropriate polypharmacy in primary care (PolyPrime) to assess the feasibility of a definitive cRCT of the PolyPrime intervention. This is a cross-border study involving six counties in Northern Ireland and in the Republic of Ireland. The study was started in August 2019 but had to be suspended during the coronavirus pandemic. Patients over →

70 years of age, taking four or more medications were included from 12 GP practices (10 patients per practice). STOPP/START criteria were used to assess medication appropriateness and quality of life (QoL) was assessed using the EQ5D and the MRB (medication related burden) QoL instruments. The study was not about the effectiveness of the intervention but about the feasibility of doing such a study, she emphasised.

The results showed that the intervention was delivered as intended and was acceptable to GPs, practice staff and patients. However, some uncertainties remain concerning patient recruitment and retention and these will need to be resolved before the full-scale trial can be launched.

Palliative care update

The objective of palliative care is to increase the QoL for the patient and family in the context of life-limiting disease. In his presentation, Professor Martin Henman (Trinity College, Dublin) focused on four key topics – pain, breathlessness, nausea and vomiting, and fatigue. Although the palliative care movement started in hospices, it is now realised that it should start as soon as therapeutic measures have been exhausted and it can be delivered by primary care teams.

Some 30% of patients with cancer-related pain have inadequate pain relief. Patients can have a combination of nociceptive, somatic and visceral pain and require multiple analgesics to tackle the different types of pain. The WHO pain ladder should be used to individualise treatment, he said. Ideally, analgesics should be administered orally and "by the clock". It is important not to wait until pain returns before giving the next dose because then the pain is harder to control, he emphasised. Paracetamol and NSAIDs are usually insufficient to control the pain. The next step is the weak opioids, codeine and tramadol. Alternatively, low doses of strong opioids could be used, although this is not currently in the WHO guideline, he noted. Morphine is always the first-choice opioid and has the advantage of being familiar to many prescribers, available and low-cost. In fact, 19 out of 20 patients who receive opioids will have their pain reduced within 14 days, said Professor Henman. Fentanyl patches are similarly effective but are less readily available and more costly. The most frequent opioid adverse effects are constipation, nausea and vomiting. Guidelines recommend the use of a laxative with opioids and this has to be a stimulant laxative and not a bulking agent, he emphasised.

Some 30% of patients with cancer-related pain have inadequate pain relief

Fentanyl and buprenorphine are the agents of choice for patients with advanced chronic kidney disease. The role of medical cannabis in cancer pain is unclear.

About 20% of patients will experience neuropathic pain and gabapentin, pregabalin or tricyclic antidepressants may be used. For localised bone pain radiotherapy is often effective.

Breathlessness can be frightening for both patients and families. Oxygen is good for hypoxia and a handheld fan can be valuable. The America Society for Clinical Oncology (ASCO) has clear guidelines for evidence-based management of dyspnoea, he said.

Chemotherapy-induced nausea and vomiting (CINV) can be acute, delayed or anticipatory. The emetogenic potential of chemotherapy needs to be taken into account when selecting treatment. A number of anti-emetic agents is available and olanzapine has now been added to the list. ASCO recommends a combination of three or four agents including treatment for the most emetogenic agent that the patient is receiving.

Fatigue can range from tiredness to exhaustion. "Exercise is one of the best things", said Professor Henman, while methylphenidate and modafinil have limited effectiveness. Dexamethasone may be effective for a short time but long-term safety and efficacy are not known.

A review of prescribing in palliative care found a variety of study types. Of note, the prevalence of potentially inappropriate prescribing ranged from 6% to 92% and only one study reported on under-prescribing.[7] In conclusion, Professor Henman said that palliative care is (or should be) holistic care. Patients and families want to be cared for at home as much as possible and for this to happen coordination is critical, especially in primary care.

The 50th ESCP Symposium took place on 18–21 October 2022 in Prague, Czech Republic

References

1 OsMed. The use of drugs in the elderly population in Italy, National Report – 2019. www.aifa.gov.it/-/l-uso-dei-farmaci-nella-popolazione-anziana-in-italia-2019 (accessed Novenber 2022).
2 Barzilai N et al. Metformin as a Tool to Target Aging. Cell Metab 2016;23(6):1060–5.
3 Herr M et al. Polypharmacy and frailty: prevalence, relationship, and impact on mortality in a French sample of 2350 old people. Pharmacoepidemiol Drug Saf 2015;24(6):637–46.
4 Ensrud KE et al. Comparison of 2 frailty indexes for prediction of falls, disability, fractures, and death in older women. Arch Intern Med 2008 Feb 25;168(4):382–9.
5 Cudby S, Syan G. Frailty and polypharmacy: the role of the practice pharmacist. www.guidelinesinpractice.co.uk/multimorbidity-/frailty-and-polypharmacy-the-role-of-the-practice-pharmacist/455001.article(accessed November 2022).
6 Tannenbaum C et al. Reduction of inappropriate benzodiazepine prescriptions among older adults through direct patient education: the EMPOWER cluster randomized trial. JAMA Intern Med 2014;174(6):890–8.
7 Cadogan CA et al. Prescribing practices, patterns, and potential harms in patients receiving palliative care: A systematic scoping review. Explor Res Clin Soc Pharm. 2021 Jul 23;3:100050.