Medicines and older people: Polypharmacy, adherence and safety

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Managing medicines is particularly complex for older people with diabetes as well as for family and health professional (HP) carers. Polypharmacy is common and often necessary because of pathophysiological changes associated with diabetes and older age. These changes affect prescribing decisions as well as methods used to administer medicines and to monitor medicine use. Beliefs and attitudes of people with diabetes and HPs about medicines influence their medicine preferences, behaviours and safety. Medicine errors and adverse events (AEs) are common reasons for admission to hospital and also occur in hospital. Insulin is the second most common medicine responsible for most errors and AEs after warfarin. Many older people with diabetes are on both these medicines. The purpose of this paper is to provide an overview of medicines error and AEs, discuss compliance/adherence and suggest some strategies to improve medicine safety in older people with diabetes.

Keywords: Diabetes, Older people, Medicines, Polypharmacy, Adherence/Compliance, Adverse events, Self-care

Introduction

Most older people with diabetes use medicines to treat the disease, prevent or slow the progression of complications and to manage symptoms. Thus, medicine management is an important self-care behaviour. The effectiveness of medicines depends on a number of factors, including whether the individual actually uses the medicines and adheres to medicine recommendations.[1] Health professional (HP)'s medicine knowledge and their beliefs, attitudes and preferences have a significant effect on older people with diabetes' medicine knowledge, self-management behaviours and can be positive and affirming or negative and disempowering. Positive, appropriate language and teaching skills are more likely to lead to medicine adherence and optimal outcomes.[2] HPs' medicine beliefs and behaviours reflect their personal and professional experiences including managing medicines, just as people with diabetes' experiences shape their beliefs and behaviours.

Several studies highlighted the importance of striving for safe euglycaemia[3,4] and resulted in guidelines that recommend HbA$_{1c}$ be maintained <7% (53 mmol/mol) and more recently <6.5% (48 mmol/mol).[5] It is now common for people with T2DM to take three to four anti-hypertensive agents, one or more glucose-lowering medicines (GLM) and/or insulin, lipid-lowering agents and medicines for other comorbidities. People with diabetes take an average of 7.4 medicines per day, range one to 25 and ≥ 25 doses at various times during the day,[6,7] which constitutes polypharmacy.

Polypharmacy

Mosby's Medical Dictionary[8] defined polypharmacy as follows:

> The use of a number of different drugs [medicines] possibly prescribed by different doctors and often filled in different pharmacies, by a patient who may have one or several health problems.

The missing element in Mosby's definition is differentiating between 'thoughtful' and 'unthoughtful 'polypharmacy'.[9,10] The former refers to carefully considered medicine combinations and the latter to the common *ad hoc* process of adding medicines to the existing medicine regimen, which often occurs when multiple prescribers are involved.

Diabetes-related polypharmacy can be thoughtful and consistent with recommendations in medicine algorithms and guidelines if medicines are prescribed to treat the multifactorial metabolic and other abnormalities associated with diabetes and the risks and benefits of using the medicine/s are considered for the individual. However, medicine decisions are more likely to be thoughtful if they are made *with* the individual and consider their functional status, self-care capacity, life expectancy and the medicine burden. Polypharmacy is a significant factor in medicine non-adherence.[11]

Polypharmacy must be monitored, regardless of whether it is thoughtful or not. Medicines, especially polypharmacy, are associated with many preventable errors, adverse events (AEs) and hospital admissions.[12,13]. People using 4.5 medicines are at an increased risk of falls and death; those using

Table 1 Some factors associated with medicine-related errors and AEs.

- Older people >age 65; for example, 30% of unplanned hospital admissions of older people are associated with medicine errors or AEs
- People with complications, frailty, renal and liver disease and geriatric syndromes using >5 medicines per day and more than 12 doses per day
- People using medicines with a narrow therapeutic index, which are usually HRMs such as insulin, heparin, cancer medicines and opioids. Significantly, some medicines commonly used to manage diabetes such as insulin are regarded as HRMs, because they have a high risk of causing harm, even when they are used as prescribed[19]
- Recent transitions between care facilities, for example, between hospital, rehabilitation or age care facilities and home
- Discharge form hospital within the preceding 4 weeks
- Not documenting changes to the medication regimen on discharge summaries to be communicated among relevant health care providers
- People consulting several HPs including CAM practitioners
- Changes to the treatment regimen within the preceding 3 months
- People using CAM and other CAM therapies, especially if they do not disclose the use and when CAM use is not documented
- People with low literacy and numeracy skills
- Administering medicines via the wrong route
- When HPs transcribe medicine prescriptions e.g. telephone medicine orders
- Distractions during medicine administration rounds[20]

Sources: The Australian Institute of Health and Welfare (AIHW),[21] Stowasser *et al*.[22]; The Australian Commission on Safety and Quality in Health Care[23].

5.5 and 6.5 medicines are at risk of disability and frailty.[14] The risk of falls, disability and frailty increases for every medicine added.[14] Medicine error and AE rates vary internationally: 0.2–15.7%, mean 5.3%. People older than 90 years have higher rates: 10.7.[15] Such errors and AEs also occur *in* hospitals and aged care homes and cause significant morbidity and death.[16]

The process of admission to hospital and the process of return to the community are high-risk times for AEs.[17] Twenty-five per cent of AEs occur within 4 weeks of a medicine being prescribed in primary care: 11% are preventable.[18] Some of the factors associated with medicine-related errors and AEs are depicted in Table 1 and some strategies used to reduce such errors and AEs are shown in Table 2.

Medicines commonly associated with AEs

Older people suffer a disproportionate number of medicine-related AEs even when adjustments were made for age and increased medicine use.[27] Some classes of medicines are frequently associated with AEs: over 50% of all potentially preventable AEs are associated with non-steroidal anti-inflammatory agents, cardiovascular medicines, including antihypertensive agents, diuretics and vasodilators, especially digoxin[15] and anticholinergic and sedatives reduce physical and cognitive function.[27] Older people with diabetes are highly likely to be using at least two classes of these medicines as well as other high-risk medicines (HRMs) such as insulin and sulphonylureas both of which are associated with hypoglycaemia. In addition, there appears to be a relationship between sulphonylurea use and increased risk of cardiovascular events.[28]

Some of these medicines are contraindicated or listed as inappropriate in established medicines lists such as Beers Criteria.[29] Warfarin 33.3%, insulin 13.9%, oral antiplatelet medicines 13.3% and GLMs 10.7% used alone or in combination are associated with most

Table 2 Strategies and process that help reduce medicine-related errors and AEs.

HPs
- Ensuring their medicine knowledge and competence are current and reflecting on their medicine-related beliefs and behaviours and whether they adhere to guidelines and prescribing algorithms when relevant to the individual
- Engaging people with diabetes and carers in conversations about medicines self-management using open neutral questions, choosing words carefully, avoiding ambiguity and actively listening to answers
- Understanding the risk factors for non-adherence, discussing them with the individual and/or their carers to develop strategies to reduce the risk of errors and AEs
- Providing timely personalised medicine education to older people with diabetes and/or family carers, see Table 4
- Using non-medicine options where possible and stopping unnecessary medicines to reduce polypharmacy

Governance and policy
- Implementing medicine safety standards and guidelines e.g. Australian National Commission on Safety and Quality in Health Care; UK Department of Health and the US Institute of Safe Medicine Practice standards
- Undertaking regular comprehensive medicine reviews and medicine reconciliation programmes for people most at risk. Medicine reviews might be indicated at each consultation when older people are prescribed >4 medicines
- Establishing technology programmes to minimise errors and AEs such as computerised dispensing checking programmes and automated alert systems that alert HPs to the need to ask the individual about medicine allergies

Sources: Rommers *et al*.[24]; Dooley *et al*.[25]; Fowler *et al*.[26]

emergency hospital admissions for AEs ($n = 99.628$).[30] Significantly, a prescribing cascade can occur if AEs are not recognised as the cause of symptoms. Many older people use complementary and alternative medicines and other therapies (CAM) in addition to conventional medicines.

CAM and therapies

The frequency of CAM use (medicines and other CAM therapies) varies among and within countries: 9–65%.[31] Many people with diabetes use CAM medicines and therapies[32–34] and CAM use is often self-initiated, but it is sometimes used on the advice of a CAM or conventional practitioner. People with diabetes use CAM for many reasons including to enhance well-being and quality of life, manage pain and stress and to treat inter-current illness such as colds and 'flu'.

Some CAM therapies can be useful non-medicine options for some people with diabetes; but CAM medicines must be included in the overall medicine regimen, because they can contribute to poplypharmacy. CAM, used alone or with other medicines and treatment options, can confer benefits, but the associated risks and contribution to polypharmacy must be considered. HPs must ask people with diabetes about CAM use in a non-judgmental way and document it.

Appropriate CAM education for people with diabetes and HPs may contribute to safe use. However, people with diabetes self-prescribe CAM and do not receive education; therefore, they can be at an increased risk of errors and AEs. Many HPs also lack sufficient knowledge to decide benefit and risk and to provide CAM education and should consider referring appropriately qualified CAM practitioners.

Medicine self-management

Medicine self-management is complex and requires the individual to have appropriate information about medicine to use them safely. Older people often have complications and comorbidities that affect their medicines and other self-care capability. The more complications the individual has the more difficult it is for them to manage self-care.

Self-efficacy[35] older age, female gender and belief in the treatment/medicine predict medicine adherence.[36] Inappropriate medicine use influences outcomes such as blood glucose, lipids, blood pressure, function and quality of life. Risk factors associated with medicine non-adherence are shown in Table 3. It is important to remember that medicine management is a complex relentless burden for many older people with diabetes and is time consuming for staff in care homes.

Compliance, adherence and concordance

'Compliance' is no longer regarded as an acceptable term: adherence or sometimes concordance, are preferred. The three terms are often used interchangeably, but they actually have different meanings and they can all be positive or negative. Adherence refers the extent to which people follow HPs' recommendations[36]; however, that definition does not encompass shared decision-making or the current focus on personalising care.

Concordance, a more recent term, is used to denote agreement about medicine use decided in a partnership between people with diabetes and prescribers.[36] The 'ban' on using the term 'compliance' misses the point that 'compliance' encompasses three inter-related concepts that are all important to and need to be monitored as part of effective medicine management:

- The individual's informed choice to use medicines to improve or maintain their health (acceptance).[37].
- The extent to which the individual follows agreed medicine regimens (adherence).[38]
- The duration of using the medicine from commencement to discontinuation (persistence).[38]

Compliance can refer to shared decisions between individuals and their HP prescribers (positive)[39,40]: it is negative if it is used to mean people with diabetes must follow HPs' directions.

Table 3 Risk factors for non-adherence to medicines.

- Expected outcomes such as lower HbA$_{1c}$, lipids and/or blood pressure are not as significant as expected.
- People who
    - do not have their prescriptions filled
    - miss appointments, especially after being in hospital
    - are forgetful, cognitively impaired or are distressed or depressed
    - have a difficult life situation, live alone and have limited support
    - develop a new problem including medicine side effects such as nausea, bloating and hypoglycaemia
    - have several diabetes complications, other comorbidities and geriatric syndromes, especially if they cause difficulty undertaking self-care such as opening medicine containers
    - who do not experience usual symptoms e.g. myocardial infarction, hypoglycaemia, foot ulcers, urinary tract infections
    - have low income
    - have difficulty coping, solving problems and low self-esteem
    - low literacy and numeracy
    - do not believe the medicine will be beneficial or that the medicines are not appropriate to their culture
    - who report they miss doses, inappropriately adjust doses or stop medicines

The more risk factors present the more likely the individual is to be non-adherent.

Diabetes is a lifelong disease. Some people are concerned about taking medicines for long periods of time and 'take a rest' from some or all of their medicines from time to time.[6,41] Some GLMs are required for life e.g. insulin for T1DM. HPs advise people with T1DM not to stop taking insulin, even temporarily, without the advice of their doctor or diabetes educator because of the risk of ketoacidosis. Personalised diabetes care and education can improve adherence and outcomes.

Personalised medicine education and care

HP and older people with diabetes, and often their carers, need access to information about medicines they can understand. Importantly, the information needs to be personalised to the individual's unique risk and benefit profile. A key aspect of personalising medicine education and making shared decisions likely to enhance adherence is understanding the individual's beliefs, attitudes and preferences concerning medicines

If agreement cannot be reached, optimal outcomes are unlikely to be achieved.[38] Significantly, HPs' and older people with diabetes's perspectives about medicines and other treatments often differ, as does the way they decide benefit and risk.[42] People do not use 50% of the medicines prescribed for chronic diseases,[43] one-fifth of people do not commence using prescribed medicines, another one-fifth stop using medicines before they complete the full course, and a further 40% do not use their medicines according to directions. It is not clear whether 100% compliance/adherence is necessary or whether an individually determined 'appropriate' compliance/adherence rate is acceptable.

One hundred per cent compliance is important for medicines with a narrow therapeutic index such as digoxin and warfarin to maintain therapeutic blood levels and consequently benefit. Therefore, optimal outcomes and compliance rates must be examined for each medicine and from the perspectives of the person with diabetes and the HP to decide an agreed medicine plan. In some cases, family carers' perspectives might need to be considered, especially when the carer works and cannot be available to assist the individual at all times.

Obviously, if people do not take use medicines, they will not 'work'. However, there is little understanding about the relationship between people's medicine compliance/adherence rates and the effects on health outcomes. Adherence appears to have a positive effect on treatment outcomes and reduces the risk of no or poor outcomes by 26% compared with non-adherence.[44,45] The DCCT[3] and UKPDS[4] demonstrated improvements in HbA$_{1c}$ and other parameters, which were partly due to medicine adherence as well as the effects of regular monitoring, support and encouragement from the research team.

Outcomes also depend on the pharmacodynamics and pharmacokinetics of the particular prescribed medicines and are, in turn, influenced by individual factors, such as age and gender, and complications such as renal and liver disease. Altering medicine dose forms can affect the duration of action; for example, crushing long-acting dose forms of metformin and inappropriately cutting medicines in half, which affect medicine bioavailability.

Identifying people at risk of non-adherence is an important component of comprehensive personalised medicine management.[46] Factors that affect people with diabetes' adherence include

- A good relationship between the individual and the HP enhances adherence.[47]
- HP's knowledge and competence to prescribe and educate, proactively monitor and identify older people with diabetes at risk of non-adherence, errors and AEs.
- Age, health literacy, medicine beliefs, physical and mental functioning, social factors including resources, support and problem-solving capacity.
- The effects of medicine side effects such as hypoglycaemia.
- Forgetting, which occurs for many reasons including cognitive changes associated with inter-current illness, dementia and hyper- and hypoglycaemia.
- The complexity and burden of the medicine regimen and difficulty fitting medicine management into the daily routine.
- Cultural factors, for example, Chinese people may stop medicines on Chinese New Year to avoid inviting bad luck into the New Year.[48]
- Diabetes complications and other comorbidities that contribute to sensory changes, swallowing difficulties and changes in fine motor skills, which can make tasks such as opening medicine containers and testing blood glucose difficult.
- People often stop medicines or find creative ways to cope because of medicine costs including setting up 'a medicine buying co-operative' with 'mates who take the same medicines'.

Factors that influence HPs' medicine behaviours include previous experience with medicines and diabetes and its management. Research shows physician compliance with care standards decreases as physicians gain experience and that older physicians are less likely to use new 'proven' therapies.[49] Availability of current information and evidence-based decision aides, such as online medicine handbooks and diabetes guidelines, is important.

HPs are also influenced by information supplied by pharmaceutical representatives, which could represent a conflict of interest. AE risks increase when multiple prescribers are involved in the individual's care. Timely, adequate communication among the person with diabetes/family, prescribers and dispensers can help reduce the risk.

Measuring medicine adherence

Usually a combination of parameters such as HbA$_{1c}$, blood glucose and lipids, blood pressure and sometimes

Table 4 Information about medicines that can help people with diabetes use their medicines safely and effectively.

It is important that written information meets readability and design standards to enhance readability and usefulness. Information to provide
- How to read the medicine label
- The name of the medicine
- What the medicine is for and what it does (action/s)
- When to take the medicine in relation to food, exercise other medicines and any specific precautions that apply
- How to take it and how long to take it for
- How and where to store the medicines and how to dispose of unused medicines and related equipment
- The *individual's* likelihood of experiencing common side effects, how to recognise when they have side effect and what to do if about a side effect
- Special precautions, for example interactions with foods and other medicines
- Some people might benefit from hints to help them remember to take their medicines
- Information about what to do if they miss a dose or doses
- Information about the Hon Code to help them decide whether information about medicines on the Internet is accurate and reliable (conforms to the Hon Code). Information about the Hon Code can be accessed from: http://www.healthconnect.org/HONcode?conduct.html

blood and/or urine medicine levels are measured to monitor medicine adherence. Other factors include the presence or absence of symptoms such as pain, thirst and polyuria indicating hyperglycaemia.

Self-report needs to be maintained using diaries/record books and Adherence Monitoring System such as Medsindex that compares actual and expected prescription refills according to the dose regimen can be used.[50] A number of questionnaires are also used including the Brief Medicines Questionnaire (BMQ), The Morisky Scale, Medicines Adherence Report Scale (MARS) and Beliefs about Medicines Questionnaire (BaMQ), but they are used in research projects more frequently than in clinical practice.

Family carers

Family members and unrelated paid carers often help older people with diabetes undertake activities of daily living, diabetes self-care and medicine management when the individual can no longer perform these tasks unaided. These carers often do not have relevant medicine knowledge and skills to manage medicines safely or to undertake other self-care tasks such as monitoring blood glucose, which increase the risk of AEs and places considerable stress on the carer.[7]

Many family carers are also old, have health problems and use medicines. The burden and stress often means the carers neglect their own health and medicine adherence. Carers are also an important source of information and can provide valuable information about their relative's medicine history, beliefs and behaviours that might not otherwise be available.

Strategies that can help people with diabetes use their medicines safely and effectively

Fewer than 50% of strategies used to improve medicine compliance are effective.[37] As indicated, the HP-individual relationship makes a significant difference to safe medicine use and adherence. Multiple, individualised strategies involve actively discussing medicines with the person with diabetes, including the factors that make it

difficult/easier to adhere, and providing the information the individual needs in a format that suits their learning style[51] (see Table 4).

Summary

Medicine self-management is complex and challenging. HPs can play a key role in helping people with diabetes manage their medicines appropriately by engaging with the individual to determine and understand their beliefs about experience of medicines, which will help put their medicine-related behaviours into perspective. Compliance and non-compliance are accepted HP terminology. They are descriptors that mean many different things to people with diabetes and their carers. However, the terms should not be used as judgmental labels.

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