National Prescribing Service Limited

Case study 32: Drugs in the elderly

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The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decision based on this information should be made in the context of the individual clinical circumstances of each patient.

Case study 32: Drugs in the elderly

Scenario

Lois is a 77-year old woman who has been your patient for a number of years. Over the last two years, she has had a gradual decline in her cognitive function, primarily manifesting as difficulty with names and memory impairment. Two months ago, she started risperidone 0.5 mg twice daily because of increased agitation and nocturnal wandering. Lois is cared for by her daughter, Anne, who now lives with her. Anne works evenings three days per week and on those days, Lois is at home by herself.

Anne brings Lois to see you today for review after she was seen in the local emergency department two days ago. Lois had a pre-syncopal episode at home and sustained a left Colles' fracture in the fall. This was treated conservatively and she was discharged from the department with analgesia (tramadol 50 mg four times daily, as needed). No underlying cardiac or neurological event was identified as the cause of the fall. Lois' other medical problems are insomnia, hypertension and depression. Her current medications are: aspirin 150 mg in the morning, risperidone (Risperdal) 0.5 mg twice daily, diltiazem CR (Cardizem CD) 180 mg at night, metoprolol (Betaloc) 50 mg twice daily, paroxetine (Aropax) 20 mg in the morning, temazepam 20 mg at night, tramadol (Tramal) 50 mg four times daily as needed.

On examination, Lois is alert and interactive. She is afebrile. Her BP is 150/70 mmHg and her pulse rate is 65 (regular). Her MMSE score is 22/30 (unchanged from previous visit). Her gait is steady and her visual acuity is 6/6 in each eye. Her left wrist is in a backslab and there appears to be good distal perfusion of her left hand with no loss of sensation. The remainder of the physical examination is normal.

Anne's three main concerns are:

- the cause of the fall and that it may happen again, saying that she 'can't be there all the time'
- the current complex medication regimen. When Anne is at work, she lays out Lois' tablets with written instructions. Anne is worried about possible misadventure associated with this
- Lois still has episodes of agitation. Anne feels that this has been reduced but not ameliorated by the addition of risperidone.

1. List three potential causes for Lois' fall (excluding cardiac or cerebrovascular event).

i _____

ii _____

iii _____

2. Identify at least two possible drug interactions (and potential effects) with Lois' current medication.

Interacting drugs	Possible effect/s

3. What specific advice would you offer Anne about non-drug measures to help with Lois' agitation?

i _____

ii _____

iii _____

4. List any changes you would consider making to Lois' medication regimen. (Please list in order of importance, starting with most important.)

_____

_____

5. List up to three reasons why the elderly are more prone to adverse effects of drugs and drug interactions.

i _____

ii _____

iii _____

Summary of results

At the time of publication 895 responses had been received from doctors, and 200 of these have been compiled for feedback.

Potential causes of Lois' fall

- The majority of respondents listed medication adverse effects as the most likely cause
- 43% of respondents suggested postural hypotension
- 23% of respondents suggested environmental hazards (including trips)

Possible drug interactions and potential effects

- Respondents reported
  - diltiazem and metoprolol 74%. Potential effects include bradycardia 29%, heart block/arrhythmia 17%
  - paroxetine and tramadol 64%. Potential effects include serotonin syndrome 58%
  - temazepam and risperidone 33%. Potential effects include enhanced sedative effect/drowsiness 22%

Non-drug measures

- Respondents would recommend
  - increased supervision/carer 28%
  - maintaining a well-defined routine 23%
  - adequate lighting and use of a night-light 18%

Changes to current medication

- All respondents would make at least one change to the medication regimen
  - cease tramadol 75%
  - substitute paracetamol for pain relief 58%
  - cease temazepam 57%
  - review the use of temazepam or reduce the dose 13%
  - review antihypertensive regimen 64%

Factors contributing to adverse effects in the elderly

- Respondents reported
  - decreased renal function 87%
  - decreased liver function 68%
  - polypharmacy 56%
  - poor compliance 32%
  - increased sensitivity to drugs 26%

Key points

- Modify dosage of drugs to allow for age-related physiological changes, pathological processes and altered drug handling ('start low and go slow').[1,2]
- Regularly review chronic treatment regimens. It may be possible to stop medications or reduce the dose in some cases.[1–3]
- Prescribe from a limited range of drugs and be familiar with their adverse effects in older people.[4]
- Provide the patient or carer with a written record of their medication regimen including the name of the medication, what the medication has been prescribed for, when the medication is to be taken, the dose and duration of therapy and possible adverse effects.[1]
- Modify risk of falls by identifying people at high risk, creating a safe environment, promoting physical activity and minimising the risk associated with medication use.[5]
- Promote supportive environmental measures (i.e. environmental modifications, familiar surroundings, orientation cues, glasses, hearing aids, maintaining activity, light therapy, music, pets and ensuring that basic physical measures are met) to assist prevention of behavioural disturbances.[2,6–8]

Results in detail

Question 1. List three potential causes for Lois' fall (excluding cardiac or cerebrovascular event).

Table 1: Potential causes of Lois' fall

Potential cause of fall	Percentage of respondents* (n=200)
Medication adverse effects	
Over sedation/drowsiness	28
Hypotension	23
Drug interactions/adverse effects	20
Undefined (listed drugs)	16
Medication errors	14
Confusion	9
Polypharmacy	6
Dizziness	5
Anaemia	4
Serotonin syndrome	2
Postural hypotension	43
Environmental hazards (including trips)	23
Muscle weakness/frailty	10
Problems with gait/ataxia/balance disorder/vasovagal	11
Dementia/decreased cognitive function	6
Dehydration	4
Age	3
Agitation	3
Other**	12

* Respondents may have more than one response.
** Includes depression, compliance, delirium, seizure, hyponatremia, hypoglycaemia, drug misuse, recent hospital discharge and unspecified organic causes.

Practice points

- Prescribe the smallest number of medications with the simplest drug regimens.[2,4]
- Consider reviewing current medication regimen. Presenting symptoms may be the result of existing medications.[1,4]
- Psychotropic drugs such as antipsychotics, antidepressants and benzodiazepines are associated with increased risk of falls and increased risk of fractures.[5]

Question 2. Identify at least two possible drug interactions (and potential effects) with Lois' current medication.

Table 2: Clinically significant drug interactions

Potentially interacting drugs	Potential effects	Percentage of respondents* (n=200)
Diltiazem and metoprolol		74
	Bradycardia	29
	Heart block/arrhythmia	17
Paroxetine and tramadol		64
	Increased risk of serotonin syndrome	58
Temazepam and risperidone		33
	Enhanced sedative effect	22
Temazepam and tramadol		21
	Enhanced sedative effect	16
Paroxetine and risperidone		14
	Inhibits metabolism of risperidone	3
Tramadol and risperidone		13
	Increased risk of seizures	4

* Respondents may have more than one response.

Practice points

- When combining a beta-blocker and a calcium channel blocker there is a risk of bradycardia and heart block: avoid combined use with verapamil and monitor heart rate with diltiazem.[3]
- Consider the possibility of serotonin syndrome when prescribing tramadol in combination with selective serotonin reuptake inhibitors (SSRIs).[3] If the combination is necessary increase the dose carefully and monitor the patient for adverse effects.[2] Clinical features of serotonin syndrome include: confusion, agitation, hypomania, hyperactivity, restlessness, hyperthermia, hypertension or hypotension, sweating, tachycardia, flushing, shivering, clonus, hyperreflexia, tremor, decreased co-ordination and diarrhoea.[2,3,9]

Question 3. What specific advice would you offer Anne about non-drug measures to help with Lois' agitation?

Table 3: Non-drug measures

Non-drug measures	Percentage of respondents* (n=200)
Supervision/carer	28
Develop and maintain a routine	23
Adequate light/night-light	18
Increase social support	18
Familiar surroundings/re-orientation	18
Physical exercise	14
Medication review	13
Webster pack/Dosette box	12
Avoid stimulants	9
Increase community support	7
Promote good sleeping habits	7
Respite care	7
Other**	15

* Respondents may have more than one response.
** Includes maintaining a safe environment, counselling, music therapy, call alert system, physiotherapy/ occupational therapy, residential care, behavioural therapy, education and support for Anne and avoiding organic causes of confusion.

Practice points

- Use non-drug measures whenever possible for agitation and do not substitute a drug for effective social care measures.[3]
- Explain cognitive and behavioural abnormalities to family members, carers and advocates.[2]
- Encourage a stimulating environment with personal belongings and orientation cues, and use of glasses and hearing aids, to assist in preventing behavioural disturbances.[2,7,8]
- Counselling, social support, occupational therapy, respite care, general nursing, environment and behaviour therapy are all important aspects of non-drug therapy which should be explored.[4]

Question 4. List any changes you would consider making to Lois' medication regimen.

All respondents would make at least one change to the medication regimen, mostly involving tramadol, temazepam and antihypertensives.

Table 4: Medication changes

Medication change	Percentage of respondents* (n=200)
Cease tramadol	75
Substitute paracetamol for pain relief	58
Cease temazepam	57
Review/decrease dose of temazepam	13
Review antihypertensives	64
– cease metoprolol	6
– decrease dose metoprolol	5
– change to another beta-blocker	2
– cease diltiazem	9
– decrease dose of diltiazem	2
– change to morning dose	2
– consider ACE inhibitor	7
– consider thiazide	3
Paroxetine	
– cease paroxetine	15
– decrease dose of paroxetine	5
– review paroxetine	12
– change antidepressant	3
Risperidone	
– cease risperidone	19
– decrease dose of risperidone	8
– review risperidone	11
– change to night-time dose	5
Other changes**	16

* Respondents may have more than one response.
** Includes Webster packs, home medicines review (HMR), cease aspirin, decrease dose of aspirin, cease all drugs.

Practice points

- Medication reduction/rationalisation should be carried out slowly to avoid rebound of symptoms except when serious adverse effects are likely or have already developed.[1]
- Depression and anxiety are often associated with persistent pain. When ceasing tramadol if pain persists consider regular paracetamol (to a maximum daily dose of 4 g in divided doses over 24 hours).[10]
- Long-term use of benzodiazepines may result in tolerance or dependence. Gradual dose reduction can prevent withdrawal symptoms.[3] Tablets can be halved, quartered or taken intermittently to minimise withdrawal effects.[3,4]
- Lois remains hypertensive in spite of her current drug therapy, which also has the potential to cause heart block. Replacement of either of her current antihypertensives with another first-line antihypertensive drug is warranted. There is good evidence that combination therapy which includes a low-dose thiazide provides effective blood pressure control.[3]

Question 5. List up to three reasons why the elderly are more prone to adverse effects of drugs and drug interactions.

Table 5: Age-related changes

Age-related changes	Percentage of respondents* (n=200)
Pharmacokinetics	
Decreased renal function	87
Decreased liver function	68
Decreased body mass	7
Decreased total body water	3
Pharmacodynamics	
Increased sensitivity	26
Compensatory mechanisms	2
Other factors	
Polypharmacy	56
Poor compliance	32
Confusion	10
Decreased cognitive function	10
Co-existing disease	4

* Respondents may have more than one response.

Practice points

- Check creatinine clearance before prescribing any drug that requires dose modification in renal impairment.[4] Serum creatinine levels may not accurately reflect declining renal function with age, as creatinine turnover falls with a decline in lean body mass.[1]
- Assess older people for factors which may contribute to drug interactions and adverse effects (e.g. hearing difficulties, poor eyesight, ability to read instructions, reduced motor skills, co-existing disease and polypharmacy).[1]
- Simplify treatment regimens where possible by regularly reviewing chronic medication management and using the lowest effective maintenance dose.[4]

Commentary 1

Dr Shanthi Kanagarajah
Geriatrician
Melbourne

Key points

- Consider existing medical problems, potential drug interactions and environmental hazards when assessing falls risk.
- Implement changes to medication regimen gradually.
- Exclude all acute medical causes of behavioral changes.
- Limited evidence exists on the efficacy of using antipsychotic drugs for the treatment of behavioral disturbances in the elderly.

Possible causes of Lois' fall (excluding cardiac or cerebro-vascular event)

As the respondents have identified, medicinal mishaps are very likely causes for falls in the elderly. These include those identified by the respondents, but given that the fall appears to be a new phenomenon and Lois was commenced on risperidone two months ago, I would be very carefully examining the possible adverse effects of this drug and balancing it against the good it might be doing.

Of the atypical antipsychotic agents, risperidone appears to have the greatest propensity to cause extrapyramidal symptoms, resembling Parkinsonism. This often has insidious onset and may be easily missed in someone who has difficulties with communication and is unable to describe subtle early symptoms easily. The physical examination should therefore carefully exclude any presence of rigidity, resting tremor, bradykinesia and increased postural imbalance (including postural hypotension).

It is worth looking at predisposing factors for falls as well as more acute factors. In Lois' case she may have already been at risk for postural hypotension because of her multiple antihypertensive drugs – the postural hypotension caused by antipsychotics may have been the catalyst for the fall. Respondents correctly identified their concerns about environmental hazards. We are not told about the time of the fall but it may have been in the evening when there is more visual difficulty. As Lois is likely to have a dementia, she may also suffer motor dyspraxia and have difficulty with gait and balance. She may also be quite de-conditioned with limited exercise and activity, thus further predisposing her to falls.

Potential drug interactions and potential effects

The responses indicate a strong concern about interactions between tramadol and paroxetine. Neither drug is commonly associated with sedation but there is certainly concern about provoking serotonin syndrome. As Lois is likely to have reduced renal clearance, the 'standard' dose of tramadol may in fact be excessive.

Paroxetine is often implicated in drug interactions that involve inhibition of cytochrome P450 2D6 and this further increases the risk of serotonin syndrome, used in conjunction with tramadol.

Non-drug measures for agitation

Prescribing Practice Review 26: Drug use in the elderly provides some simple advice on an approach to managing behavioural problems in the elderly. Foremost is ensuring that there is no acute medical cause (delirium) – common problems are urinary infection, constipation and recently commenced psychoactive drugs. A thorough history (including corroborative information from Anne) and examination, with simple investigations to exclude common causes, is of most use here.

It is often difficult to identify environmental and other triggers and often useful to request an Aged Care Assessment from the local Aged Care Assessment Team (ACAT). If available, assessment by specialist staff trained in dementia care is invaluable. Staff are able to assess Lois in her own environment and may suggest useful feasible techniques for

managing her symptoms. These may include the suggestions that respondents recommended.

A full functional assessment by the ACAT would provide some advice about general care and may include reducing the environmental triggers for falls (loose rugs, poor lighting etc) and obtaining community services to increase Lois' level of activity during the day in a safe and supervised manner.

Finally, it is worth emphasising that while antipsychotic drugs are commonly used for managing behavioural disturbances, there is very limited evidence on efficacy and increasing concern about safety.

Changes to medication regimen

The tramadol dose should certainly be questioned. I would agree with respondents that it should be stopped. Once a fracture has been adequately immobilised, the requirements for analgesic medication should be much reduced. If risperidone-induced problems are suspected it is best to try drug withdrawal and monitor the effects of both improvement and effect on behavioural management. I would suggest ceasing the morning dose of risperidone and if there is no behavioural deterioration, then ceasing the evening dose.

The concern about the interaction of diltiazem and metoprolol is justified but changes to medications should only be done gradually. If Lois does not show any evidence of heart block, I would defer this alteration and monitor for changes in heart rate/conduction until other more urgent changes are completed and Lois is in a more stable state. A similar reasoning would apply to ceasing temazepam. It is likely that Lois has become tolerant to this benzodiazepine, and while it would be optimal to cease its use, this should be done when everything else is relatively stable.

Strategies to minimise adverse drug reactions

Respondents identified several important causes of drug adverse effects. Anne's concern about Lois' complex medication regimen is very justified. I would probably list this as an important cause of medicinal mishaps.

If tramadol is ceased, then the regimen is more easily managed – perhaps assisted by blister pack or Dosette boxes. It is important to remember that as multiple medication changes are attempted there is increased potential for mistakes. It is very important for Anne to understand and be an active partner in supervising the care of Lois. In doing this, it is also important to recognise that Anne may be finding the care very stressful and that this may impede the medical plans significantly. Once again, the ACAT should be able to assist in assessing this issue, balancing both Lois' and Anne's needs and helping to access options such as respite care, if considered suitable.

Commentary 2

Dr Beres Wenck
General Practitioner
Medical Director Team Care Health 2
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Milton, QLD

Key points

- Careful thought needs to be given to selection of drugs in the elderly. Know the side-effect profile. Start low and increase slowly. Review regularly.
- Always useful to calculate the estimated glomerular filtration rate (GFR) using the Cockcroft and Gault formula in older patients regardless of their serum creatinine.
- Use of the Enhanced Primary Care (EPC) items such as a health assessment (especially if done at home), care plan (which includes a medication plan) and Home Medicines Review are useful management tools.
- Be mindful of falls prevention strategies.
- Remember to do blood tests at appropriate intervals to assist monitoring of chronic conditions and medication.

Possible causes of Lois' fall (excluding cardiac or cerebro-vascular event)

Most respondents mentioned medication and postural hypotension as causes of falls. Paroxetine and risperidone are two medications which particularly have this adverse effect. Patients with dementia may forget to eat and drink, contributing to hypotension, hypoglycaemia and other nutritional deficits that contribute to muscle weakness. Both the above medications are associated with a low risk of seizures, which may be triggered by cerebral hypoperfusion.

Gait and balance instability could be a factor despite Lois' gait being described as 'steady'. Age-related factors include increased sway and slowed reaction time, reduced balance (impaired posterior column and cerebellar function). All older people with falls should be observed as they stand up from a chair (without using their arms if possible), walk several paces, and return (the Get Up and Go test). Any tendency to age-related motor deficits will be aggravated by extrapyramidal side-effects potentially related to risperidone use and rarely also associated with paroxetine, and reduced balance from temazepam.

Dementia is associated with reduced executive function, leading to impulsivity and impaired motor planning, as well as failure to take care with environmental hazards such as stairs and loose carpets. This can be aggravated by sedation and confusion related to combination of benzodiazepine or SSRI-induced hyponatremia. Dementia is also a contributor to poor medication compliance, including repetitive dosing when patients forget that they have recently taken medication, with obvious sequelae.

Potential drug interactions and potential effects

The majority of respondents mentioned serotonin syndrome followed by cardiovascular and sedative adverse effects. Increased confusion and agitation can be caused by paroxetine, temazepam, risperidone and tramadol. Extrapyramidal side-effects can be associated with risperidone and rarely paroxetine. Postural hypotension can occur with metoprolol, diltiazem, risperidone and paroxetine. Serotonin syndrome is linked with paroxetine and tramadol.

Paroxetine is a potent inhibitor of cytochrome P450 2D6 and will influence metabolism of risperidone, metoprolol and tramadol. Even though the dose of 0.5 mg risperidone twice daily is not excessive, the potential for drug interaction means that this could translate into a higher risperidone dose. Metoprolol adverse effects, particularly bradycardia and hypotension, may be increased due to interaction with paroxetine. Seizures and serotonin syndrome have been reported in patients taking tramadol and paroxetine.

This combination should be avoided.

Non-drug measures for agitation

The main non-drug measures mentioned by respondents were the importance of developing and maintaining a routine and more supervision. Agitation may be related to dementia, depression or delirium. Accurate diagnosis of Lois' cognitive impairment and associated agitation is essential. This lady most likely has Alzheimer's disease but factors that may be aggravating her condition such as delirium, urinary tract infection, anaemia, constipation, pain, ongoing anxiety and depression, thyroid dysfunction and B_{12} deficiency need to be excluded. Some of these may be medication induced (e.g. constipation related to diltiazem).

It is important to understand Lois' needs and value systems to respond to her preferences where reasonable and possible. Identify environmental triggers for agitation and minimise these. Simplify daily regimens and avoid over stimulation and strange or threatening situations, including some television programs. Ideally have someone at home with her who understands dementia. Package medications to avoid overdosing. Trial a personal medical alarm so Lois can get assistance if she falls when alone. Enhance carer support and education through the Alzheimer's Association of Australia which also offers respite services.

Changes to medication regimen

All respondents would make at least one medication change. Tramadol should be ceased and regular paracetamol substituted. Weaning Lois' temazepam may decrease her confusion and risk of falls. Switching paroxetine to mirtazapine may improve sleep and also reduce anxiety, as well as minimising cytochrome P450 interaction. The underlying diagnosis needs confirmation. If Alzheimer's-type disease is suspected, referral to a specialist for assessment and a trial of a cholinesterase inhibitor (ChEI) is regarded as standard care.[11] Such treatment may reduce agitation and reduce the need for phenothiazines and antidepressants. Paroxetine has an inhibiting effect on metabolism of ChEI and should be avoided. Because Lois is on the diltiazem and metoprolol, the addition of a ChEI may aggravate any tendency for bradycardia and associated arrhythmias thus a prior electrocardiogram is advisable. Don't forget to treat her underlying osteoporosis.

Reasons why the elderly are more prone to adverse effects of drugs and drug interactions

Most respondents identified polypharmacy and age-related changes in drug pharmacokinetics, such as decreased renal function with age and decreased hepatic blood flow (reduced metabolism of drugs with high first-pass extraction). In the older person there is normal drug absorption except if disease is present. Distribution of drugs is altered by age with decreased total body water and lean body mass and a relative increase in body fat. Reduced albumin from acute or chronic disease or malnutrition can contribute to adverse effects of drugs in the elderly. Drug-disease interactions are more common because of the increased number of chronic diseases in older people and ageing affects target-organ responsiveness to medications (e.g. increased sensitivity to opiates, decreased beta-receptor sensitivity).

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