PHA-7001B Central Nervous System

Alzheimer's Diseases

Learning objectives

- Use the appropriate criteria to ensure the acetylcholinesterase inhibitors are used within their license
- Consider the ethical issues around autonomy when prescribing for patients with disorders that affect cognition and respond appropriately
- Identify and manage adverse drug reactions associated with the treatment of dementia
- Identify appropriate pharmacological and non-pharmacological interventions for disturbing neuropsychiatric behaviours

Mr TP is a 74 year old man. His wife has approached the pharmacy, accompanied by Mr TP, while out shopping as she is worried about his memory and would like to buy a supplement to help. You invite them into you consulting room to find out more.

Mr TP is a pleasant man who chats easily to you and doesn't share his wife's concerns. He does concede that he is a bit more forgetful but puts this down to advancing age and isn't concerned. Mrs TP explains that her husband forgot to pick the grandchildren up from school 3 times last month and when he collected her from the hairdressers last week, he forgot where he left the car. She also reports that, despite being very easygoing usually, he is more snappy and short-tempered lately. Mr TP smiles when his wife tells you this, and rolls his eyes at you. He tells you that this is because he gets told off a lot more than he used to and smiles at his wife.

Mrs TP has read that fish oil is good for memory and would like to buy it for him.

You probe further and find that there is a history of Alzheimer's disease in the family. Mr TP's own father died from AD when he was 81 years old. In asking about his general health, you find out that Mr TP has had a persistent cough recently and is a bit chesty following a cold, but otherwise is well with regular medication for blood pressure only. He does not drink alcohol or smoke.

You reassure them but explain that memory changes such as these need to be investigated by the GP in case there is a simple cause that is easily taken care of and refer them on. What tests will the GP undertake to determine the likely cause of his current symptoms?

Question 1

Will need to rule out organic causes of cognitive decline before considering Alzheimer's disease e.g.
Electrolyte imbalances- all U&Es (renal failure or hyperuraemia can ppt confusion)

Metabolic disturbances-
 Vit B12 and folate (low levels can cause memory impairment and mood changes),
 TFTs (rule out hypothyroidism as a cause of dementia-like presentation)
 Blood glucose (diabetes is a risk factor in itself but too stringent control can lead to confusion in the elderly i.e. hypos)
 LFTs (rule out any metabolic dysfunction e.g. hyperammonaemia in liver cirrhosis)

Infective screen- CRP, FBC, temperature, urine MSU (dipstick no longer recommended as diagnostic tool for UTI in patients >65years),
FBC
Imaging (not realistic in GP surgery but may refer)- CT brain to rule out stroke/tumour can also help identify cause i.e. small vessel disease suggestive of vascular dementia.
Full medical history- identifying any risk factors e.g. FH, genetic component, alcoholism etc
When all organic causes have been ruled out formal behavioural and cognitive assessment and potential referral to a specialist memory service e.g. specialist psychiatrist/old age psych.

The severity of Alzheimer's disease can be assessed using several methods, depending on the setting for example research utilises ADAS-cog **or** clinical practice and the outcome being assessed.
Clinical practice uses a variety of measures, often along with clinically based assessments such as biographical interview e.g.
 AMTS (abbreviated mental test score) is often used acutely to determine whether memory problems present (10 questions).
 Severity is frequently defined by Mini Mental State Examination (MMSE) score:
o mild Alzheimer's disease: MMSE 21–26
o moderate Alzheimer's disease: MMSE 10–20
o moderately severe Alzheimer's disease: MMSE 10–14
o severe Alzheimer's disease: MMSE less than 10

A few days later, Mrs TP returns to your pharmacy. She has a prescription for co-amoxiclav 625 mg TDS (21). She thanks you for your referral and says that, after asking lots of questions and listening to Mr TP's chest, the doctor gave him this prescription. She asks you whether this is to help his memory, and how long will it take to work. What do you tell her?

Question 2

The doctor may have found signs of a chest infection and given a course of antibiotics is to treat. Acute infection can, especially in older people, lead to changes in memory and behaviour (older people do not have the in-built reserve to fight off infection as well as younger people therefore even the smallest of insults can knock them back and precipitate confusion/induce delirium).
That is why it is important to treat infection and rule out other organic causes before embarking upon treatment to help with cognition.
After asking whether Mr TP is allergic to penicillin (he's not), you explain that his chest

should start sounding better after a few days, but that he should complete the course even if his symptoms disappear completely before the end of 7 days

You are on duty 3 weeks later when a prescription comes over from the surgery for Mr TP. It requests:

Ebixa® treatment initiation pack (op) MDU

According to this drug's license, what has Mr TP been diagnosed with and would you like to clarify the prescriber's intentions?

Question 3

According to this drug's license, Mr TP has been diagnosed with moderate to severe dementia of the Alzheimer's type. This suggests that he has significant cognitive impairment and does not fit with your impression of Mr TP a few weeks ago, who was independent with his ADLs and responding appropriately to conversation, with only mild memory impairment and behavioural symptoms.
You should contact the GP to ensure that he has selected the correct treatment. Only acetylcholinesterase inhibitors are licensed for the treatment of mild-moderate dementia of the Alzheimer's type and the GP may have selected the wrong product in error.

The doctor thanks you for you call and says that the memory clinic recommended 'pharmacological memory support' in their letter to her and she hadn't been aware of the different licenses. However she agrees with you that an acetylcholinesterase inhibitor would be more appropriate given the severity of his symptoms and would be happier with that. She asks you to make a recommendation. What do you recommend?

Question 4

Mr TP has no cardiovascular issues of note, and no swallowing difficulties that suggest he would need a non-solid formulation. He takes an antihypertensive each day without problems and so a cost effective, once daily formulation would seem sensible.

While donepezil, rivastigmine or galantamine are all clinically fine, NICE endorse that "treatment should normally be started with the drug with the lowest acquisition cost (taking into account required daily dose and the price per dose once shared care has started i.e. between memory specialist potentially and GP)".

The most cost effective choice is donepezil tablet 5 mg OD (considering OD administration and acquisition- now that they are all available in generic this is not as much of a problem).

NICE recommendation and licencing for memantine:

Memantine monotherapy is recommended as an option for managing Alzheimer's disease for people with:

- moderate Alzheimer's disease who are intolerant of or have a contraindication to AChE inhibitors **or**
- severe Alzheimer's disease.

The doctor supplies you with a prescription the following day and Mr TP comes to collect it. He asks you if he can speak to you privately. You invite him into the consultation room.

He tells you that he knows that the memory specialist thinks he has lost his mind but he doesn't agree and has no intention of taking this medication. He

claims that the specialist asked a lot of silly questions and just because he didn't have the answers on the tip of his tongue and needed to think about them, they have claimed him to be senile and started this medication.

He acknowledges that his wife really wants him to take the medication and so he tells that he is going to keep collecting the prescription so that his wife doesn't suspect anything but that he is going to throw the tablet away each day. That way, everyone is happy. He expects you to be complicit in this and not tell his wife or the GP. What do you tell him?

Question 5

You may not reveal anything about his medical condition or medication to a third party without his consent unless you consider there to be a real and imminent danger to his health or the health of the public.
However, it is not ethical to continue to dispense a prescription that you know that the patient is not taking. It breaches a number of bioethical principles including fidelity and justice.
Mr TP is not lacking in capacity and is currently capable of making his own decision about how he would like his health to be managed. He is able to refuse to take the medication if he wants to and is able to understand the consequences of both taking and not taking it.
Explain to him that the medicine is proposed to improve his memory and slow down the disease. It works well in some people, and not at all in others. **On average, about half of the patients that take it tend to decline slower that it's thought they would without it.**** (3rd improve,3rd non decline, 3rd no response)
Tell him that it is his choice about whether he takes the medication or not and that the GP would support him in any decision he made, as would you, but that it would not be ethical for you to continue to supply it to him knowing that he did not intend to take it. In this situation, you would need to inform the GP of his intentions.
Suggest he involves his wife- it is likely he will need her support further down the line as the disease progresses.

Mr TP decides not to accept the medication and thanks you for your support.

A year later, you receive a prescription for

Donepezil 5 mg OD (28)

It is collected by Mrs TP. She explains that his condition has deteriorated over the last year and he now accepts that medication may be helpful. She is keen to ensure Mr TP gets the best from this medication. What information do you give her about the use of donepezil?

Question 6

The tablet should be taken in the evening. At least a month at 5mg OD will be needed to determine whether there is any effect and that it is well tolerated. A higher dose can then be trialled after 1 month (4 weeks)
Mr TP will continue to be reassessed to see if there is any benefit (approx. every 3 months).
Common side effects include nausea, diarrhoea and headache. Advice you could provide to combat these nausea- Stick to simple foods - avoid fatty or spicy meal, diarrhoea- ensure you drink plenty of fluid and headache- simple analgesia may help.
He may also experience some changes in his mood or behaviour and experience strange dreams. If any of these things happen and are distressing, they will go away if the medicine is stopped.
Manufacturer information:
"Therapy with donepezil should only be started if a caregiver is available who will regularly monitor drug intake for the patient. Maintenance treatment can be continued for as long as a therapeutic benefit for the patient exists. Therefore, the clinical benefit of donepezil should be reassessed on a regular basis. Discontinuation should be considered when evidence of a therapeutic effect is no longer present. Individual response to donepezil cannot be predicted"

Mrs TP asks you if this will stop Mr TP ending up like his father, who spent the last few years of his life very unwell in a nursing home, with no recognition of family and friends and this was very hard on every one. What do you tell her?

Question 7

It is important that expectations of treatment are realistic to ensure that over-

reliance on drugs doesn't limit social interventions that are also helpful.
It is ok to explain to Mrs TP that Alzheimer's Disease is neurodegenerative and that patients do deteriorate over time. However it is impossible to predict the rate of decline and so Mr TP may yet experience years of reasonable health.

8 months later Mrs TP returns with an FP10 HP prescription for

Oxybutynin 5 mg TDS

You ask to speak to Mrs TP and enquire about the health of her husband. She says he is doing ok, still on the donepezil but not as well as he was. He needs to be supervised a lot of the time and is having increasingly angry outbursts. He had minor op recently and the ward staff noticed that he was a bit incontinent which was upsetting for him, and the hospital prescribed this to help.

Should you dispense this? What could be the cause of his urinary symptoms and what action should you take?

Question 8

Due to pro-cholinergic effects, urinary incontinence is a common side effect of acetylcholinesterase inhibitors. It would resolve upon withdrawal of donepezil but then any benefits Mr TP may be experiencing would be lost.
An anticholinergic such as oxybutynin would counteract the pro-cholinergic effects of the donepezil on his urinary tract. However, oxybutynin crosses the blood brain barrier and will also counteract any effects that the donepezil is having in supporting Mr TP's cognition. (mechanism of action of oxybutynin= anticholinergic action in blocking the muscarinic effects of acetylcholine on smooth muscle)
Options include:
If you dispense the oxybutynin, it will render the donepezil useless
If you don't dispenser oxybutynin, urinary incontinence could hinder daily activities including sleep, and unmanaged urinary incontinence which could lead to further complications.
Mirabegron, Mirabegron is a β-3-adrenergic drug with less cholinergic burden, less risk of confusion, it helps with urinary incontinence as well and does not interact with donepezil

6 years after your first contact with Mr TP and his wife, his PMR is flagged to you while undertaking an audit of appropriate antipsychotic medication prescribed in elderly patients. You see that for the last 4 months, on days you weren't on duty, the following medication has been dispensed:

Ebixa® 20 mg OD
Risperidone 0.5 mg prn
Lorazepam 1 mg up to QDS prn for aggressive behaviour
Amlodipine 10 mg OD
Senna ii ON
Fybogel I BD

Does anything concern you about this record? What other information would you like to find out? How would Mr TP's neuropsychiatric symptoms be measured?

Question 9

Ebixa® 20 mg OD -(max, S/E constipation)
Risperidone 0.5 mg prn-(see below review, max dose, S/E constipation common)
Lorazepam 1 mg up to QDS prn for aggressive behaviour- (see below, check dose taking, must not be stopped suddenly, max dose in elderly usually 2mg/24 hr and susceptibility of S/E greater with A/D, can cause paradoxical effect of aggression)
Amlodipine 10 mg OD- S/E constipation common
Senna ii ON- Laxatives to be reviewed, constipation common with current meds prescribed, stool chart, lifestyle, diet, fluids etc
Fybogel I BD

The use of antipsychotics is challenging in patients with dementia because it increases their risk of stroke significantly. As a result, only risperidone is licensed to treat persistent aggression in in patients with moderate to severe AD but **only for 6 weeks**, up to a maximum of 1mg BD.
You would like to ring Mrs TP and ask how Mr TP is getting on, and ask the following:
What are his symptoms are like at the moment?
What is the normal daily dose of risperidone being used?
How is she using the lorazepam and risperidone – in what order and for what type of behaviour? . If Lorazepam considered to be weaned off, talk here how to do it safely (patient currently could take max recommended adult dose)
Is the issue worse at night time or during the day? – Sundowning?
Is Mrs TP getting enough rest to allow her to cope with Mr TP's symptoms?
Does Mrs TP have enough support at home to continue to care for Mr TP? – Day-care Centre ?
Assessment of the severity of Mr TP would be via the Neuropsychiatric Inventory (NPI)

which is a validated test administered to Mrs TP to find out how she distressing perceives his behaviour to be. Also consider conducting carer givers distress test with Mrs TP.

You find Mrs TP in reasonable spirits. She explains that the hospital, during Mr TPs last admission for a UTI, started risperidone as his behaviour on the ward became very disturbing indeed and he slapped a healthcare assistant. The GP must've thought it good to carry on as it's on his repeat. She gives a dose of 0.5 mg at night to help him get off to sleep and doesn't use the lorazepam as the label says it's for aggressive behaviour, which he doesn't exibit.

Why do you think his behaviour deteriorated so much in hospital?

What should you next course of action be?

Question 10

The UTI itself may have contributed to worsening symptoms of dementia. The unfamiliar hospital environment may have also caused Mr TP to feel anxious and worried, which manifested in symptoms of disturbing behaviour. This can often happen when a patient is placed in an unfamiliar environment.
Risperidone is only licensed for 6 weeks use and so is now being used off license. It also increases the risk of stroke in Mr TP.
You explain to Mrs TP that it is likely that the Risperidone was prescribed to manage his unsafe behaviour in hospital and that it isn't really the right choice to just get him settled. You can discuss alternative methods to help with sleep, such as sleep hygiene methods and non-pharmacological approaches. Potentially a low dose short-term sleeping aid may be an option, such as Zopiclone, however, should be used with caution and regularly monitored as there is an increased risk of falls in elderly and AD patients.
You communicate this to his GP

Mrs TP is worried that her husband might show some aggressive behaviour in the future while at home and asks for your advice if there are any non-pharmacological management that might help. What advice do you give?

Question 11

Non Pharmacological Therapies

- **Cognitive/Emotion-oriented Interventions:**
  - *Reminiscence Therapy*
  - *Simulated Presence Therapy (SPT)*
  - *Validation Therapy*
  - *Reality Orientation Therapy*
- **Sensory Stimulation Interventions:**
  - *Acupuncture*
  - *Aromatherapy*
  - *Light Therapy*
  - *Massage and Touch Therapy*
  - *Music Therapy*
  - *Snoezelen Multisensory Stimulation Therapy*
  - *Transcutaneous Electrical Nerve Stimulation (TENS)*
- **Behavior Management Techniques:**
- **Other Psychosocial Interventions:**
  - *Animal-assisted Therapy (AAT)*
  - *Exercise*
- **Various Interventions Targeting a Specific Behavioral Symptom**
  - *Wandering*
  - *Agitation*
  - *Inappropriate Sexual Behavior*

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Nonpharmacological treatment of isb

Behavioural modifications

For public behaviours:

- Sensitive explanation of inappropriateness and gentle redirection
- Avoid confrontation
- Do not ignore these behaviours
- Distraction
- Single rooms for patients
- Avoid inappropriate external cues like over-stimulating television or radio programs.
- Modified clothing: trousers which open in the back or are without zippers may be helpful.
- Provide adequate social activity.
- Encourage family and friends to visit.
- Provide simple and repeated explanations of why such behaviours are unacceptable.

Mrs TP asks you what support services are available for Patients and their Carers. What support services are available and how would you signpost Mrs TP?

Question 12

Dementia friend- learning abut dementia to help the community
Dementia UK
Alzheimer’s Society
Pilgrim friends- care homes and residential homes
NHS website
Age UK
Young Dementia UK
Alzheimer’s research UK

Charities and voluntary organisations provide valuable support and advice on their websites and via their helplines:

- Alzheimer's Society's National Dementia Helpline on 0300 222 1122
- Age UK's Advice Line on 0800 055 6112 (free)
- Independent Age on 0800 319 6789 (free)
- Dementia UK Admiral Nurse Dementia helpline on 0800 888 6678 (free)
- Carers Direct helpline on 0300 123 1053 (free)
- Carers UK on 0800 808 7777 (free)

Talk to other carers

Sharing your experiences with other carers can be a great support as they understand what you're going through. You can also share tips and advice.

If it's difficult for you to be able to attend regular carers groups, join one of the online forums:

- Carers UK forum
- Alzheimer's Society Talking Point forum