DRUG & THERAPEUTICS LETTER

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Treating dementia

The variation in presentation can make diagnosis of cognitive impairment or early dementia difficult. However, early diagnosis may enable planning for the future, decrease anxiety with appropriate education and allow consideration of treatment.

The diagnosis of dementia is made on clinical assessment using formal criteria. These include a history of the gradual onset of impairments in two or more cognitive domains, which cause difficulty in everyday function. These impairments should not be attributable to another cause, such as a drug effect or depression. Cognitive domains which are commonly impaired include memory, language and decision-making ability.

A detailed history with a collateral history from family and friends is essential in making the diagnosis, determining a pattern of progression and assessing any impact on daily living.

It is worth deliberately excluding other conditions that may appear to cause cognitive impairment such as delirium, depression and the adverse effects of some drugs such as antipsychotics. The clinical features of these conditions are usually different from those of dementia when considered closely . Blood tests to help exclude illnesses mimicking dementia would include measurement of full blood count, biochemistry, thyroid stimulating hormone, vitamin B12 and folate. A CT scan of the brain is useful in excluding conditions that may be amenable to treatment, such as subdural haemorrhage and normal pressure hydrocephalus. Although there may be reversible elements for many with abnormal tests, reversible causes of dementia are extremely rare (less than 1.5%).

There is no 'cure' for most dementias. However, if the diagnosis includes information about the subtype of dementia it allows a patient and their family to:

- access information that may help them deal with functional difficulties
- benefit from specific treatments (for example cholinergic therapies)
- avoid drugs known to aggravate problems (for example, anticholinergics, and antipsychotics in dementia with Lewy bodies)
- make plans for the future.

There is a good correlation between the clinical diagnosis of Alzheimer's disease and the neuropathology at autopsy. This association is less certain with other subtypes of dementia, but even a

putative diagnosis may allow a patient and carer to make sense of the patient's symptoms. An example is the severe fluent aphasia seen in a younger patient with frontotemporal dementia.

Non-drug therapy

Monitor the patient's general health and other chronic conditions, especially vascular risk factors, to optimise health and independence. Should there be unexpected changes in cognition or behaviour, reconsider the possibility of incident delirium or depression. Other problems that can cause aggravated behaviours or distress in patients with dementia include pain, constipation, reduced vision and hearing loss.

Psychosocial interventions for carers, such as teaching them specific problem-solving skills, are more effective if the patient is also involved. Other factors that appear to be important include structured individual counselling, involvement of the extended family and consistent professional long-term support. These interventions can help to reduce the psychological burden and can reduce the need for institutional care of the patient. However, there is little impact on the carer's overall burden. Interventions that do not improve outcomes include single interviews and interventions not associated with long-term contact such as short educational programs and support groups alone.

There is some evidence for the cost-effectiveness of community-based occupational therapy aimed at improving the patient's daily function. Cochrane reviews have found no supportive evidence for the use of aromatherapy, music therapy, transcutaneous electrical nerve stimulation (TENS) or bright light therapy.

In practice, maintaining cognitive, physical and social activity appears to help in improving quality of life for the patient and reducing the burden of care. This burden is also improved by education about symptom progression, burden management and enabling appropriate access to services including respite care.

Drug therapy

Dementia is a progressive disease. Drug treatment at best only slows the decline in cognitive function.

The drugs available are donepezil, galantamine and rivastigmine.

There is a statistical benefit of cholinesterase inhibitors in mild to moderate Alzheimer's disease, however the clinical benefit remains uncertain and all the studies are short term. There is no evidence that one drug has a benefit over another. Many specialists switch to another cholinesterase inhibitor if there is no efficacy or tolerance of the first.

There is also some evidence for the efficacy of cholinesterase inhibitors in vascular dementia and dementia with Lewy bodies. The drugs have not been approved for these indications.

Common adverse effects include nausea, vomiting and diarrhoea. These are less troublesome with dose titration. Other adverse effects include bronchoconstriction (particularly in patients with asthma), bradycardia, cramps and vivid dreams.

Memantine is a non-competitive antagonist of the N-methyl D-aspartate (NMDA) receptor.

Placebo-controlled trials have shown benefit in patients with moderate to

severe Alzheimer's disease. Memantine has been used in combination with cholinesterase inhibitors in clinical trials. As with the cholinesterase inhibitor studies, the outcomes measured do not translate easily into clinical practice.

Memantine requires dose titration over a month to minimise the adverse effects of agitation, hallucination and headache. It may also increase the risk of seizure activity. Memantine is excreted in the urine and is probably not suitable for use in those with renal impairment.

Hundreds of different drugs are currently in various stages of clinical testing including vaccines and monoclonal antibodies against amyloid protein. There is no consistent evidence of efficacy or safety for drugs such as vitamin E, selegiline, vitamin B12 or ginkgo biloba.

Timing of cessation of drug therapy for dementia is controversial, but should be considered if the patient is completely dependent in their care needs. Cessation should be discussed with the patient's family, particularly as they may notice some deterioration in the patient's functional abilities.

Conclusion

Most cases of dementia are diagnosed on clinical assessment. Excluding treatable causes of cognitive impairment is vital. Management of the patient and their care needs should be individualised. The needs of the carers as well as the patient themselves should be considered. Early education and planning for future events can assist both the patient and their support network.

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Brief Information

Drug-associated macular oedema - latanoprost and rosiglitazone

Macular oedema causes blurred or distorted vision due to painless swelling of the macula. The condition is relatively common and is frequently associated with various ocular conditions including cataract surgery and age-related macular degeneration; and, rarely, drug toxicity. Chronic macular oedema or multiple recurrences may result in macular photoreceptor damage with permanent

impairment of central vision.

Drug associated macular oedema has been reported with the use of latanoprost and rosiglitazone.

Latanoprost is a prostaglandin F2α analogue used as eye drops for the treatment of open angle glaucoma or ocular hypertension either alone or in combination with the beta-blocker timolol.

Macular oedema is identified as a potential adverse effect, more commonly occurring in patients with aphakia or pseudophakia with anterior chamber lenses and/or torn posterior lens capsule, or in patients with known risk factors for macular oedema such as diabetic retinopathy and retinal vein occlusion.

The association between the hypoglycaemic agent rosiglitazone and macular oedema is also known. There is evidence that withdrawal of rosiglitazone is followed by resolution of macular oedema.

Macular oedema should be suspected with any loss of visual acuity not correctible by by pin-hole refraction.

Drug Monitoring and Toxicology Laboratory

Total number of patients who utilized the services from October 2008 to June 2009 was 642.The summary of samples received by this laboratory during these nine months are as follows:

S.N.	Drug/Enzyme	Reference Range	Total samples	Results within normal limits	Results beyond normal limits
1	Paracetamol	10-20 µg/ml	119	68	51
2	Cholinesterase	4260-11250 U/L	523	136	387
		Total samples	642	204	438

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