Psychiatric Options in the Treatment of Seniors

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Alzheimer's is an incurable but treatable disease. The use of medications is increasing, and clinicians and healthcare organizations should realize that supportive care must extend beyond prescriptions. Caregiver education and emotional support are essential elements of the treatment package. Medications can be combined with behavioral and environmental interventions. Treatment goals that set realistic expectations and treatments that enhance cognition and improve behavior lead to symptomatic improvement. One can expect initial improvement and the progression of the disease to be slowed, but should not anticipate arrest. Stabilization or a temporary delay in progression is the most notable outcome of treatment for Alzheimer's Disease (AD).

It is ideal to start anti-dementia medications as soon as the diagnosis of dementia is made. This is particularly important since recent research shows that donepezil (Aricept) begun early is beneficial in preventing frontal lobe cortical atrophy. Also, it is important to use both anti-cholinesterase inhibitors and memantine (Namenda) since each improves functioning in a different part of the brain. Anti-cholinesrase inhibitors in general improve cognitive function, including memory, whereas memantine improves social and emotional functioning.

Cognition Enhancers

The brain of a person suffering from (AD) exhibits damaged neurons and reduced levels of the neurotransmitter acetylcholine (ACh) as well as the enzyme that synthesizes ACh. This is an essential finding in the cholinergic hypothesis, which states that cognitive function may be preserved if levels of ACh are maintained, although increasing the level of ACh is not yet possible. The main cognitive enhancement therapies today are cholinesterase (AChE) inhibitors donepezil and rivastigmine (Exelon). These medications and AChE inhibitors, such as galantamine (Razadyne), are the most thoroughly studied medications used to treat AD. Tacrine (Cognex) is an older, less selective agent in that class, but is now rarely used. Stabilization from treatment with AChE inhibitors may persist for up to a year.

Donepezil was first marketed in 1997 and is the preeminent drug in its class. During a half-year trial, more than 4 of 5 patients receiving treatment showed improvement or no decline in cognitive function. Treatment with donepezil produced improvements in secondary outcomes such as on the Mini-Mental State Examination (MMSE) and the Clinical Dementia Rating Scale Sum of the Boxes.

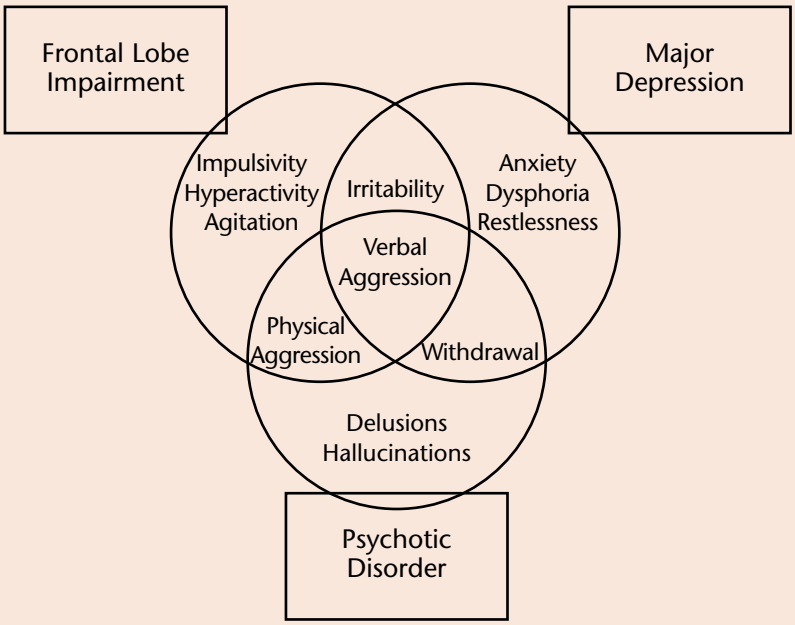
Rivastigmine is the second selective AChE inhibitor. Its duration lasts about 10 hours and is administered twice daily; unlike donepezil, which is administered only once. The side effects (usually transient and generally mild) from this treatment are similar to donepezil.

Galantamine, an AChE inhibitor has shown improved cognitive function. Early initiation of treatment is beneficial and has been shown to modulate nicotinic cholinergic activity. How this relates to the efficacy of the drug is unknown. The use of AChE inhibitors can provide a significant improvement in cognitive and functional performance of persons with AD. The drugs are well tolerated; and though the target is a secondary degenerative effect of the disease, they are one of the few pharmacologic tools for delaying

the cognitive decline of persons with AD.

Memantine is approved by the FDA for the treatment of moderate to severe dementia. A nonpharmacologic 6-week study evaluated improvements in mental ability and daily functioning in elderly, independent-living adults who were randomized to memory training, reasoning training, speed of processing training, or a control group. Of those evaluated, 87% who were speed-trained, 74% who were reasoning-trained, and 26% who were memory-trained demonstrated reliable cognitive improvement immediately after the intervention period. Thus, older patients may benefit from keeping mentally active. Recent research suggests that taking memantine has a positive effect on cognition, mood, behavior, and the ability to perform activities of daily living in persons with moderate to severe AD. The review also demonstrated a small reduction in the incidence of agitation in patients with moderate to severe dementia.

Figure 1. Causes of Psychiatric Symptoms and Behavior Can Overlap



Antioxidants

Other therapeutic strategies also have been used in the treatment of AD through reduction of oxidative stress within the brain. Agents in various antioxidant neuroprotective strategies for the treatment of AD have included vitamin E; selegiline (Emsam), a selective monoamine oxidase inhibitor; ascorbic acid; coenzyme Q; ginkgo biloba; and estrogen.

Vitamin E and selegiline currently are used by many clinicians, based partly on the results of a large clinical trial. The administration of selegiline or Vitamin E delayed progression in all endpoints. The most interesting finding of the study was that Vitamin E delayed the placement of patients into long-term-care facilities by approximately 7 months. Because Vitamin E is safer and usually less expensive than selegiline, that finding has prompted widespread clinical use of Vitamin E in patients with AD. Patients that have bleeding problems or are taking heparin must use Vitamin E with caution.

In addition to its potential antioxidant properties, estrogen is thought to possess other properties that possibly could inhibit the progression of AD although it did not improve cognitive or functional outcomes.

Prednisone has been of particular interest as a potential agent, but recent published results involving its use as a treatment of AD also were negative. AChE inhibitors will continue to offer early-stage patients the best hope for slowing the progression.

Managing the Behavioral Problems Associated with AD

Behavioral disabilities are closely linked to the functional impairments of AD. Figure 1 illustrates the ways in which psychiatric symptoms and behavior can overlap, and caregivers need to monitor symptoms closely and adjust medications as needed. Some behavioral impairments can be ameliorated to a degree with medications.

Classes of medication that have been used in the management of specific symptom clusters in patients have been reviewed and summarized in Table 1.

Risperidone (Risperdal): Despite a lack of formal sanction, compelling evidence now supports the use of risperidone or olanzapine (Zyprexa) in patients with AD who exhibit significant delusions, hallucinations, or aggressive behavior.

Olanzapine: A key study evaluating the efficacy of olanzapine for the treatment of psychosis and agitation in patients with AD recently indicated results similar to those of risperidone. The main side effects of treatment were somnolence and change in gait.

Quetiapine (Seroquel) has been introduced recently. Because of sedative effects, it is preferred for agitation. Other atypical anti-psychotics are expected to be available soon.

Ziprasidone (Geodon) should be used with caution because of the risk of cardiac arrhythmias.

Ariprazole (Abilify) is a recently

Table 1. Preferred Medication for Subtypes of Agitation

Subtype	Treatment
Delirium (other than medication toxicity)	Treat underlying medical condition. If medication is needed, consider typical antipsychotic
Depression	Without psychosis: antidepressants excitalopram (Lexapro), venlafaxine (Effexor), or duloxetine (Cymbalta) for retarded depression With psychosis: antidepressant plus antipsychotic, or electroconvulsive therapy
Psychosis	Acute: atypical antipsychotic, primary risperidone (Risperdal) or quetiapine (Seroquel) Long-term: atypical antipsychotic
Anxiety	Acute: benzodiazepine such as lorazepam (Ativan) or oxazepam (Serax) Long-term: buspirone (Buspar) or excitalopram (Lexapro)
Insomnia	Acute: trazodone (Desyrel); consider zolpidem (Ambien), eszopiclone (Lunesta), or ramelteon (Rozerem) Long-term: trazodone (Desyrel)
"Sundowning"	Acute: trazodone (Desyrel) Long-term: trazodone (Desyrel); consider typical or atypical antipsychotic.
Aggression or anger	*Severe* Acute: typical or atypical antipsychotic Long-term: divalproex sodium (Depakote) or atypical antipsychotic *Mild* Acute: trazodone (Desyrel) Long-term: divalproex sodium (Depakote), SSRI, trazodon (Desyrel), or buspirone (Buspar)
Osteoarthritic pain	Long-term: tricyclic antidepressant, SSRI, or trazodone (Desyrel), venlafaxine (Effexor), duloxetine (Cymbalta) for neuropathy associated with diabetes
Weight Loss	mirtazapine (Remeron) and psychotherapy

approved atypical anti-psychotic. The primary advantages of aripirazole are that it does not cause weight gain and it lowers triglycerides by 30-40 mgs. It does not create a risk for diabetes. In addition, it is effective with the negative symptoms of schizophrenia. It is inhibited by carbamazepine (Tegretal), paroxetine, and fluoxetine (Prozac). The main side effects are headaches, insomnia, anxiety, severe agitation, and assaultive or aggressive behaviors.

Antidepressants

These psychotropics are of some value in treating patients with AD who have depression, dysphonic agitation, anxiety, and maybe apathy. The use of the selective serotonin reuptake inhibitor (SSRI) citalopram (Celexa) in patients with dementia reported significant efficacy. Sertraline (Zoloft) had positive results after administration to patients with AD who had dysphonic affect and agitation. Among the antidepressants, excitalopram oxalate (Lexapro) or citalopram often are chosen first because they have fewer side effects (occasionally insomnia or nausea) and are usually safe to combine with other medications an older person is likely to be taking. They are given once a day (usually in the morning).

If these do not work, an alternative tailored to the needs of the individual can be chosen. For example, mirtazapine (Remeron), bupropion (Wellbutrin), duloxetine hydrochloride (Cymbalta), and venlafaxin (Effexor) tend to be energizing and might be chosen for someone who is very withdrawn or apathetic. Care must be exercised in the use of duloxetine hydrocholoride in persons with substantial alcohol use and those with chronic liver disease. The tricylic antidepressants tend to have more troublesome side effects, such as dry mouth, constipation, and dizziness if a person stands up too quickly. When used by experienced doctors and carefully monitored, they are sometimes quite effective in severe depression, but should be used with caution because of the risk of cardiac arrhythmia.

Bupropion should not be used in individuals with central nervous system problems because of a high rate of seizures. Clearly, there are many antidepressants to choose from. There often is a need to try several medications before finding the best one. Patience is important since it often takes several weeks to tell if a medicine is working. During the waiting period, a person's spirits can be kept up with activities, a day program, or a support group.

People with depression also can have delusions, such as a fear that

body organs are not working, that they have been abandoned by everyone, or that they have no more money (when in fact they have). Delusional depression can be life threatening because of the possibility of suicide, or because of refusal to eat and drink, which can cause severe weight loss and dehydration. Agitation and trouble sleeping also often are very prominent. Although these symptoms can be very upsetting to witness, there are effective treatments. Usually, the first strategy is to combine the antidepressant with an anti-psychotic medication. If severe depression or delusional depression does not respond to medications, electro convulsive therapy can be lifesaving. Although there are many negative myths surrounding shock treatment, it is very safe when given by experts and is an important tool for the severely depressed person.

Mirtazpine

Mirtazpine is the first drug in a new class of antidepressants with a unique ability to target specific serotonin receptors. Along with its efficacy in the treatment of moderate to severe depression, mirtaxapine has proven to be effective for treating anxiety, motor retardation, and cognitive and sleep disturbances associated with depression.

Mirtazpine has a tetracyclic chemical structure that causes it to act differently from other common antidepressants such as SSRIs, monoamine oxidase inhibitors (MAOIs) and tricyclics. While stimulating norepinephrine and serotonin release, mirtazpine also has the unique ability to block two specific serotonin receptors, thus causing fewer serotogergic side effects (decreased interest in sex, nausea, nervousness, insomnia, and diarrhea). In studies, the use of mirtazpine, compared with tricyclic antidepressants, also resulted in fewer anticholinergic symptoms (blurred vision, dry mouth, indigestion, and constipation), cardiovascular symptoms, and cognitive disturbances. In addition, mirtazpine has a relatively high safety margin in case of overdose and a low tendency to cause seizures. It causes no significant changes in vital signs although in some people mirtazpine tends to raise cholesterol levels. Mirtazpine should be used with caution if the patient has active liver or kidney disease, or heart or blood pressure problems. The doctor should be alert to any history of seizures, mania, hypomania, drug use, or any other physical or emotional problems.

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Some antidepressants, especially the SSRIs, can help with anxiety. Tricyclics and SSRIs also are used for pain relief in arthritis and certain types of nerve pain if over-the-counter medicines like Tylenol or Advil haven't worked. Trazodone (Desryel), a relative of nefazodone (Serzone), is sold as an antidepressant but usually is too sedating for this purpose. We discuss it later as a sleeping aide.

Use of Antidepressants with Medical Problems

Pain Management and Depression

Although significant literature supports the analgesic effects of traditional tricyclic antidepressant (TCA) medications in chronic pain, studies of the analgesic response to SSRIs have demonstrated conflicting results. Recently, duloxetine hydrochloride has been FDA-approved for neuropathic pain.

Persons failing to respond to initial conservative pain management measures may exhibit depressive symptoms, including associated sleep disturbance, loss of appetite, weight loss, and effective distress. Early interventions should include the use of antidepressant medications for mood and sleep. Low-dose TCAs and tricyclic-like antidepressants may help augment serotonin levels in the brain and improve the quality of sleep. These dual mechanisms of action may be more efficacious than short-acting sleep medications, including over-the-counter preparations. Tricyclics should be used only in low dosages or not at all with geriatric patients because of the high incidents of arrhythmias.

Those who fail to respond to medication and individual physical therapy may be candidates for multidisciplinary rehabilitation pain treatment. Multidisciplinary programs may include rehabilitation specialists; physical, occupational, and therapeutic recreational specialists; pain psychologists; biofeedback specialists; and nursing and vocational counselors. This interdisciplinary team approach relies heavily on coordinated services with the goal of improving psychosocial functioning.

Trazodone

If zolpidem tartrate (Ambien) is used, it should be alternated with trazadone. Trazodone is a relatively safe, non-habit-forming medication that technically is considered to be an antidepressant, but actually is used more often simply to help the individual get a good night's sleep. It also is a good short-term alternative treatment for anxiety or when a mild sedative is needed. It should be started in very small amounts at first and adjusted upward until the right dose is found. To help with sleep it should he given about 1 hour before bedtime. The main side effect is drowsiness if the dose is

Essential Steps in Managing Psychiatric Behavior Disturbance

1. Help the caregiver recognize and characterize the psychiatric symptoms of AD
2. Help the caregiver recognize what triggers these symptoms
3. Know what can be done to relieve symptoms
4. Use simple, clear terminology when describing symptoms to clinicians
5. Design a treatment plan after a behavior has been recognized
6. Include in treatment plan:
   a. medication
   b. behavioral techniques
   c. environmental changes

too high. Other side effects include dizziness when standing up and, very rarely, painful erections in men. In addition, sun exposure may help with sleep problems and light therapy should be considered.

Toxic Effects-Serotonin Syndrome

Residents with depression and pain frequently benefit from dual treatment with serotogenic antidepressants and opioid analgesics. However, these drugs can sometimes interact and cause serotonin syndrome, a potentially fatal condition caused by excess serotonin at postsynaptic serotonin receptors. It is a severe systemic reaction to serotonin excess, with symptoms of confusion, hypertension, restlessness, agitation, muscle rigidity, myoclonus, increased deep tendon reflexes, diaphoresis, shivering, and tremor. It can result from the combination of an MAOI with an SSRI, the combination of an MAOI with tryptophan, and less commonly with other drug combinations such as paroxetine (Paxil) and dextromethorphan (Touro), or with lithium augmentation of SSRI or MAOI antidepressants.

In a recent case report, 4 long-term care residents with possible serotonin syndrome were examined. All were taking serotonergic antidepressants and opioid analgesics, and all developed serotonin syndrome symptoms within weeks of having those medications altered. Each resident exhibited symptoms including hallucinations, myoclonus, and hypertension, although none had symptoms in all three clinical criteria categories. In all cases the symptoms resolved when at least one of the two medications was stopped, and resolution generally occurred within a day or two.

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Stimulants

The diagnosis and treatment of depression may be more difficult in older people, who usually present with somatic complaints rather than dysphoric mood and who, due to altered metabolism, experience a more brittle course on antidepressants. Once treated, older patients still have a higher and more rapid rate of recurrence.

Despite significant improvements in treatment, prominent limitations of conventional antidepressant therapy remain. They include the delayed onset of therapeutic response and the partial or lack of response in as many as 50% of patients who complete an adequate trial. Examples of stimulants include modafinil (Provigil) and methylphenidate (Ritalin).

Anticonvulsants

Divalproex (Depakote) is best known as a treatment for brain disorders such as epilepsy and seizures, and as a mood stabilizer for bipolar disorder. It also can help with behavioral symptoms in older persons with dementia, especially in a person showing aggression, anger, or hypersexual behavior. It is often combined with an anti-psychotic. The side effects of divalproex are nausea and sedation, which usually can be controlled by starting at small doses, making gradual adjustments, and monitoring the level of medication in the bloodstream.

Managing Psychosis in the Treatment of Parkinson's Diseases and Parkinsonism

Parkinson's Disease

Typical antipsychotics work by blocking the D2 subtype of dopamine receptors. Atypical agents act differently because of a different pattern of dopamine receptor-binding, with reduced activity on receptors that influence motor function. Sertonergic blockade is also believed to be important for producing an antipsychotic effect. Among the atypicals, risperidone is the most potent dopamine blocker and, thus, has been shown frequently to worsen motor function in PD.

Lewy Body Disease

Dementia with Lewy body disease (LBD) is a variant of Parkinson's disease that is significantly associated with psychosis. Visual hallucinations, fluctuating level of consciousness, and Parkinsonism are typical

Related Discussion: The Role of Psychotherapy

Research conducted on the outcome of mental health services delivered by specialists who are not full-time staff in nursing homes has shown improved clinical outcomes and less use of acute services.

The preferred practice includes the routine presence of qualified mental health clinicians in the facility. Optimal services are interdisciplinary and multidimensional, with the most effective interventions blending innovative approaches to training and education with consultation and feedback on clinical practices.

Psychiatric symptoms secondary to dementia usually begin in the first year of the disease, and progression, while gradual, is erratic. The level of agitation suggests the more severe symptoms. This usually occurs after 5 years, and is related to more severe psychiatric symptoms of paranoia, delusions, and hallucinations.

These symptoms can be controlled with a combination of medications in the form of mood stabilizers, anti-psychotic, anti-anxiety, and anti-depressants as well as psychotherapy, behavioral management, and frequent (rather than less) family contact.

Research shows that psychotherapy reduces the use of medications by 50% and 100% of those who received psychotherapy (counseling) did better than those who received medication alone. They also had a significant decrease in behavioral problems sooner and a better quality of life for longer. Psychotherapy should be recommended for all patients with psychiatric problems if they have the cognitive ability to benefit from it.

symptoms. Use of risperidone is recommended. Typical anti-psychotics make the symptoms worse.

The atypical anti-psychotics in widest use now are risperidone and olanzapine. There is a high risk of diabetes and glucose must be monitored closely.

Treatment of Anxiety and Panic Disorder

Antianxiety Medication

Benzodiazepines are a group of about a dozen medications that cause sedation and can relieve anxiety. They are best used only in temporary situations—once in a while for sleep or for a daytime crisis of anxiety or agitation when someone needs to be calmed down quickly. In an emergency, benzodiazepines sometimes are combined with an anti-psychotic; they also can be combined for a week or more with other medicines that may take longer to start working, such as divalproex.

Some benzodiazepines are preferred by for use in older people because they are cleared from the body relatively quickly. Those include lorazepam (Ativan), the primary choice because of its short half life; temazepam (Restoril); and oxazepam (Serax). The effects of others, such as flurazepam (Dalmane) and clonazepam (Klonopin), can last 24 hours or longer; these longer-acting agents usually are best avoided because they may cause daytime sedation or falling.

Benzodiazepines are habit-forming if used steadily for more than a few weeks; even single doses can cause unsteady gait and can interfere with memory. Fall precautions or a wheelchair should be considered for the first 48 hours.

Because of the disadvantages of benzodiazepines, it usually is best to avoid using them for the long-term treatment of insomnia, anxiety, or agitation unless other choices have failed. See *Better Ways to Fall Asleep: The Danger of Benzodiazepines* on page 29.

Buspirone (Buspar)

Buspirone is an anti-anxiety medication that is not habit-forming and does not cause sedation. Buspirone is an excellent choice for someone who is very nervous or worried but does not have psychotic delusions. It can be helpful for someone who gets angry too easily. It also is very safe to combine with other medications that an older person may be taking. Side effects of headache, dizziness, or nausea can occur if the dose is too strong: once in a while it also can cause over stimulation. Buspirone works gradually, and the dose usually needs to be adjusted over 2 to 6 weeks before beneficial effects can be judged.

Treatment of Panic Disorder

Selective Serotonin Reuptake Inhibitors

Systematic reviews and randomized clinical trials have found that selective serotonin reuptake inhibitors improve symptoms in panic disorder compared with placebo. One subsequent review found the discontinuation of sertraline in people with a good response increased exacerbation of symptoms. A second subsequent review found that paroxetine plus cognitive behavioral therapy improved symptoms compared with placebo plus cognitive behavioral therapy. Divalproex has been found effective in the geriatric population when SSRIs and lorazepam are not effective.

In closing, increased initial data collection, documentation, ongoing observation and assessment, and enhanced communication among treatment professionals can all result in less frustration in our respective jobs working with geriatric patients. More importantly, we can optimize the effective level of care for our patients and, consequently, their quality of life. ALC

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