While dementia is marked by such cognitive deficits as disorientation, memory loss and changes in intellectual functioning, these are not the symptoms that cause the most distress to caregivers. In the middle and later stages of the illness, as many as 50% of patients with dementia will exhibit agitation. Of the approximately 4 million people in the United States who suffer from dementia, 70% will become psychotic within the first six or seven years of the illness (Sunderland, 1995, 1996). The term agitation refers to a range of behavioral disturbances including aggression, combativeness, shouting, hyperactivity and disinhibition (Small et al., 1997). It is the symptoms of agitation such as uncooperativeness with necessary care, motoric hyperactivity, verbal abuse and disinhibition that are the most stressful aspect of caring for the demented person.

The nonspecific neuropsychiatric symptoms of agitation can generate feelings of frustration, fear and helplessness in both the patients and their caregivers. Coping mechanisms may fail and give way to intolerance as family members try to deal with these problems day after day. Caring and concern can quickly turn to annoyance, outright anger and even elder abuse. Caregivers' lack of understanding and unrealistic expectations compound the problem. Demented people, having lost their mental powers, may not be able to communicate the exact problem. Some caregivers may see the affected elderly people as manipulative rather than as victims of unavoidable central nervous system changes. Professionals working with the elderly are also not immune to these feelings. The first line of defense in addressing agitation in the elderly is a careful diagnostic evaluation for medical conditions, psychiatric problems or social/environmental disturbances that can underlie behavioral disturbances. The medical model, making use of a thorough history, with physical examination and laboratory tests, may offer clues to reverse underlying physical disorders, such as infections, medication side effects, neurological diseases, metabolic disorders or pain. Polypharmacy, very common in the elderly, and the possibility of drug-drug interactions must be considered as a cause of agitation. Medications such as benzodiazepines, beta-blockers, selective serotonin reuptake inhibitors (SSRIs), neuroleptics and diphenhydramine can cause problems. Malingering and factitious disorder also must be differentiated from dementia. Here, the cognitive deficits are inconsistent over time (American Psychiatric Association, 1997).

Physical discomfort such as hunger, constipation and sleep deprivation also can contribute to agitated behavior (Streim, 1997). If the medical evaluation is unremarkable, psychiatric diagnostic issues need to be explored. Underlying psychiatric problems such as an anxiety disorder or psychosis with delusional thinking and hallucinations can be treated. A major depressive disorder can masquerade as pseudodementia. Substance abuse, a hidden disorder in the elderly, needs to be ruled out, since drug-alcohol interactions as well as the long-term toxic effects of chronic substance abuse may underlie agitated behavior. The next step is the assessment of the patient's overall psychosocial/environmental situation. Historical factors, involving psychosocial stressors, such as a death in the family, a change in personnel or roommate, or recent surgery need to be identified. Behavioral and environmental modification can be helpful in producing positive change. Settings can be altered to adjust for noise, temperature, the patient's routine or other aggravating factors. Often, the elderly person may be trying to communicate boredom, frustration or loneliness. Increased contact between patient and caregiver can be helpful. A supportive psychotherapeutic approach, handled by a calm, reassuring and confident professional, can offer comfort and education, and can fulfill unmet needs. Even a demented person will remember a sincere, soft voice and a gentle touch long after the visitor has left the room.
If the troublesome symptoms are still present after the medical, psychiatric and psychosocial causes of the mental status changes have been either ruled out or treated, then a trial of behavioral modification and/or medication can be offered for symptomatic relief and management.

In compliance with the Nursing Home Reform Amendments of the 1987 Omnibus Budget Reconciliation Act (OBRA), professionals often seek to reduce the inappropriate use of psychotropic medications among nursing home patients (Sunderland, 1995). However, pharmacological treatment (See Table) is needed if behavioral agitation places the patient or others in danger or interferes significantly with either the individual’s care or the care of other patients (American Psychiatric Association, 1997; Jung and Grossberg, 1993).

The U.S. Food and Drug Administration has not approved any medication for the treatment of behavioral agitation in dementia. However, the first line of defense is usually a traditional major tranquilizer such as haloperidol (Haldol), thioridazine (Mellaril), thiothixene (Navane) or perphenazine (Etrafon, Trilafon). These agents do not always produce good results and are most useful if the agitation is associated with psychotonic features (Alexopoulos et al., 1998). They should only be used for short-term intervention, at the lowest effective dose. Patients need to be monitored closely due to the possibility of sedation, worsening of perception, dry mouth, constipation, postural hypotension, extrapyramidal side effects (especially akathisia), tardive dyskinesia and neuroleptic malignant syndrome. *(If an underlying psychotic disorder is the basis for the agitation, however, then long-term treatment with conventional high-potency antipsychotics or atypical antipsychotics may be needed (Alexopoulos et al., 1998)-Ed.)*

The newer atypical antipsychotic agents, such as risperidone (Risperdal), clozapine (Clozaril), olanzapine (Zyprexa) and quetiapine (Seroquel) offer the promise of treatment with an improved side-effect profile (Raskind, 1998; Kumar, 1997).

The benzodiazepines with shorter half-lives, such as lorazepam (Ativan), oxazepam (Serax) and alprazolam (Xanax) can be useful, particularly if anxiety and tension are a major component of the agitation. The benzodiazepines stay in the body a short period of time, and can be ordered on an as-needed basis. Side effects include sedation, amnesia, confusion and a paradoxical response. They can intensify cognitive slowing, cause dependence and produce changes in equilibrium that can contribute to increased risk of falls and fractures. Long-term use can lead to habituation and dependence.

Withdrawal symptoms can occur, particularly if the patient goes into the hospital or nursing home, and doesn't reveal all of the medications that he or she has been taking. Buspirone (BuSpar), a serotonergic azapirone anxiolytic, also has been used for agitation (Cantillon et al., 1996). It is an alternative to the benzodiazepines and does not produce their undesirable side effects. It has a slower onset of action, but shows little or no sedation and few drug-drug or drug-alcohol interactions. It does not impair psychomotor performance. Unlike benzodiazepines, it is not associated with withdrawal reactions and lacks dependence/abuse potential as evidenced by studies of drug discrimination and withdrawal in animals and clinical experience with patients, especially known substance abusers (Ayd, 1995). *(It should be noted, however, that there have been case reports of serotonin syndrome when buspirone is combined with SSRIs. Buspirone, a 5-HT1A partial agonist, affects serotonin even though it is not an SSRI-Ed.)*

The serotonergic antidepressant trazodone (Desyrel) has been used to treat agitation (Houlihan et al., 1994). Its principal side effects include postural hypotension, sedation and dry mouth (American Psychiatric Association, 1997).

SSRIs, such as sertraline (Zoloft), paroxetine (Paxil), fluvoxamine (Luvox), fluoxetine (Prozac) and citalopram (Celexa) are useful if symptoms of depression, anxiety or irritability are prominent (Alexopoulos et al., 1998; Nyth and Gottfries, 1990). In a multicenter Scandinavian study (Nyth and Gottfries, 1990), citalopram was more effective than placebo for the target symptoms of irritability, fear and panic, depressed mood, and restlessness. Improvement was limited to patients with Alzheimer's disease. No significant effects of citalopram were noted in patients with vascular dementia. *(The SSRIs, themselves, however, may occasionally be associated with akathisia-like reactions [Perry et al., 1997]-Ed.)*

Other medications that have been tried for chronic agitation include beta-blockers such as propranolol (Inderal) and pindolol (Visken) (Weiler et al., 1988), antihistamines and lithium carbonate (Eskalith, Lithobid). With antihistamines, however, there is a risk of anticholinergic confusion. Sexually inappropriate behavior can be very upsetting to caregivers. But most of what is seen in the demented elderly is really sexually ambiguous behavior such as disrobing, and involves no sexual arousal. It is caused by disorganization secondary to cognitive impairment. Hypersexualy can occur, but is infrequent (Redinbaugh et al., 1997). Medroxyprogesterone (Amen, Cynrin,
Depo-Provera) and related hormonal agents have been used for the treatment of intrusive disinhibited sexual behavior (American Psychiatric Association, 1997).

The anticonvulsants, such as carbamazepine (Epitol, Tegretol) and valproate (Depakene, Depakote), appear to show promise in the management of the behavioral complications of dementia. They may work by facilitating a brain chemical, GABA, deficient in dementia. If the behavioral agitation in dementia represents a form of organic mania, anticonvulsants may be effective based on their mood-stabilizing properties. The effectiveness of carbamazepine has been variable, showing improvement of up to 50% in patients with agitation associated with mood lability, aggression or anxiety (Chambers et al., 1982; Gleason and Schneider, 1990; Lemke, 1995; Tariot et al., 1994). Carbamazepine has potential for drug-drug interactions, effects on the white cell blood count and toxicity. Its principal side effects include unsteadiness, drowsiness, dizziness and confusion. Valproate may be as effective and a safer treatment for the behavioral complications of dementia, particularly of the Alzheimer's type. It is most helpful with symptoms of physical aggression. Valproate appears to be better tolerated due to a more benign side effect profile and fewer drug-drug interactions. It may reduce behavioral agitation without sedation or other cognitive or neurological side effects (Lott et al., 1995; McElroy et al., 1996). Gastrointestinal distress, such as nausea, dyspepsia and diarrhea, and weight gain are possible but infrequent. These effects can be further minimized by the use of divalproex sodium, a delayed-release tablet. Published studies show no significant laboratory abnormalities. The rare occurrence of hepatic transaminase elevations and thrombocytopenia are both reversible (American Psychiatric Association, 1997; McElroy et al., 1996; Sanborn et al., 1995).

The treatment of behavioral symptoms is complex and difficult. The preceding options may improve the quality of life, maximize functioning and diminish the need for custodial care in agitated demented patients. They can reduce suffering and stress, as well as increase the comfort and safety of patients and caregivers. Etiologies may be multifactorial requiring both nonpharma-cological and pharmacological interventions. A biopsychosocial approach is best. More work is still needed in this important clinical area.

However, even if these therapies are successful, the physician's job is not complete unless he or she also focuses on the caregivers. They need to be educated about the dementia, available treatments and sources of care and support; given empathetic help in making informed decisions symptoms of; and given hope. Their physical health and emotional resiliency are essential to the successful management of agitation in the elderly.


References


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