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Alzheimer's and Non-Alzheimer's Dementia: A Critical Review of Pharmacological and Nonpharmacological Strategies

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Objective. Dementia is an age-related progressive neurodegenerative disorder afflicting about 5% of the world's population, and it is expected to grow dramatically in the future keeping in view our ageing society. Currently available medications appear to be able to produce moderate symptomatic benefits but do not to stop disease progression. In this article, the management of the disorder, including the currently available drugs as well as psychosocial strategies, is discussed. *Methods.* A computerized search on Pubmed from 1980 to 2006 was carried out and all articles evaluated and graded on NICE guidelines. *Results and conclusions.* Currently evaluated and accepted medications only bring about a reduction in the deteriorating course. A combination of pharmacotherapy and psychosocial management is the need of the hour.

Keywords: dementia; Alzheimer's dementia; non-Alzheimer's dementia; psychosocial management; current trends in management

Introduction

Dementia is defined as a progressive impairment of cognitive functions occurring in clear consciousness (ie, in the absence of delirium).[1] It is a progressive, degenerative disease characterized by cognitive decline and impaired memory, thinking, and behavior. Global impairment of intellect is the essential feature, manifested as difficulty with memory, attention, thinking, and comprehension. Other mental functions may often be affected, including change in mood, personality, and social behavior. Nevertheless, the diagnosis of dementia should not be made without evidence of memory deficits and at least one other cognitive deficit (eg, language or visual–spatial skills).

It has been observed that the prevalence of dementia is increasing as more and more people live to advanced age, with increasing life expectancy, because it is primarily the illness of old age. Worldwide estimates of the number of people suffering from dementia vary from 15 to 18 million, and it is estimated that by 2025, 34 million people will have the disease, 71% of whom will live in developing countries.[2] The prevalence of dementia increases with age and doubles every 5 years, starting from 1% at 60 years of age to about 30% to 40% by 85 years of age.[3] The spread of HIV infection and the prolonged survival of patients with AIDS and other chronic diseases will further increase the number of cases of dementia.[4] Although several medications and therapies exist, not all of them are effective. This article aims to review the operational diagnosis and management of dementia—both pharmacological and nonpharmacological.

Methods

A computerized search on Pubmed/MEDLINE was performed from 1980 to December 2006 for all articles in English using combinations of the following terms: dementia, Alzheimer's disease, non-Alzheimer's disease, treatment, pharmacology, management,

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Table 1. Diagnostic Criteria for Dementia (DSM IV TR)[6]

Memory
One or more of language, praxis, gnosis, and executive functioning
Significant impairment and decline in social or occupational functioning
Gradual onset and continuing cognitive decline
Other central nervous system or substance-induced conditions are excluded
Deficits not exclusively during course of delirium and not better accounted for by depression

behavioral therapy, cognitive therapy, pharmacological therapy, and psychotherapy. Subsequently, bibliographies of articles selected via the first strategy were searched. Full-text articles were retrieved with the help of institutional online access and, if required, by writing personally to the authors. Assessment of this literature led to pertinent articles, which were weighted according to a rating scheme based on NICE guidelines. The articles were then evaluated in a nonquantitative manner, collated, and treatment regimens conceptualized after summarization of the results.

Diagnosis of Dementia

The diagnosis of dementia is important as it is a syndrome for which several diagnostic criteria have been proposed, with each criterion emphasizing different aspects of the condition. The most commonly accepted definitions are the ones by *International Classification of Diseases 10* (ICD-10)[5] and the *Diagnostic and Statistical Manual for Mental Disorders*, 4th edition, Text Revision (DSM IV TR).[6] However, the American Academy of Neurology (AAN) 2001 guideline to diagnose dementia follows the DSM IIIR, which is equivalent to the DSM IV TR criteria (Table 1).

A complete medical team consisting of several health professionals is required for the assessment and management of a person with dementia. The assessment of a person's cognitive state is influenced by many factors, including level of education and culture. A screening tool such as the Mini-Mental State Examination is brief and simple to use, although other instruments are also available for use either singly or in combination.[7,8] Neuropsychological assessment provides a comprehensive profile of cognitive function that can help determine the presence, degree, and pattern of deficits but is time consuming and expensive and is not uniformly available everywhere. Basic investigations including computed tomography san and/or magnetic resonance imaging of brain to exclude B_{12} deficiency, hypothyroidism, and structural abnormality are important to exclude any potentially reversible cause or coexisting condition that may not be clinically apparent.[8,9] Brief cognitive assessment instruments that focus on limited aspects of cognitive function[10] (ie, Clock Drawing Test, Time and Change Test) may be considered when screening for dementia.

Table 2. Mild Cognitive Impairment

Memory complaint, preferably corroborated by an informant
Objective memory impairment
Normal general cognitive function
Intact activities of daily living
Not fulfilling criteria for dementia

Dementia should be, however, differentiated from normal aging and mild cognitive impairment (MCI). There has been recent interest in MCI, with reports of annual conversion rates of MCI to Alzheimer's disease (AD) of 6% to 25%[11] and increasing with older age. A recent study indicated a conversion rate of 11% at 3 years.[12] MCI may be indicated by any of the conditions indicated in Table 2.

Patients with MCI should be recognized and monitored for cognitive and functional decline because of their increased risk for subsequent dementia.

Management

Current clinical practice encourages open discussion of the diagnosis with patients and their families to allow treatment strategies to be implemented as early as possible and to allow families to plan for the future.[9] An integrated approach involving both psychosocial and pharmacological strategies is essential for better care, which includes community and support services, professional groups (such as the Alzheimer's Association), memory-clinic services, and geriatric services. The general practitioner plays a pivotal role in directing and managing care.[12]

Behavioral and psychological symptoms of dementia are common, occurring in 90% of those with dementia at some point in their course. These include hallucinations, delusions, misidentifications, agitation,

depression, anxiety, aberrant motor behavior, and aggression.

Medications such as antipsychotics (including atypical ones) and mood stabilizers are used for these symptoms[13] although the evidence for their use is not strong. Ongoing review is essential because the need for medication is likely to vary throughout the course of the disease. There is increasing evidence for the efficacy of atypical antipsychotics in those with behavioral and psychological symptoms of dementia,[13] with cholinesterase inhibitors showing positive outcomes with regard to these symptoms.[13,14]

Cognitive and intellectual problems are the main targets of both pharmacological and psychosocial strategies.

Treatment Strategies

Pharmacotherapy for Alzheimer's dementia includes the use of the following:

1. Cholinesterase inhibitors (ChE-Is): the drugs under this category include tacrine, donepezil, rivastigmine, and galantamine. Metrifonate, another drug in this category, has fallen out of favor.
2. Acetylcholine precursors: the only drug in this category is CDP-choline or citicoline.
3. *N*-Methyl-D-aspartic acid (NMDA) receptor antagonist: this is a relatively new category and includes only one drug, memantine.

Pharmacotherapies for non-Alzheimer's dementia are given below.

1. Vascular dementia can be treated by the use of aspirin or warfarin for the prevention of stroke; pharmacologic enhancement of acetylcholine levels using donepezil,[15] rivastigmine,[16] and galantamine[17]; and neuroprotective strategies using memantine,[18] statins,[19] nimodipine,[20] antioxidants,[21] and propentophylline.[22]
2. Dementia with Lewy bodies is, however, not easily treatable. Rivastigmine has shown some improvement,[23] whereas low-dose clonazepam has been used for sleep disturbances.[24] The main focus should be on avoidance of drugs such as typical antipsychotics, which may precipitate Parkinsonism.
3. Frontotemporal dementia is another area where the management strategies have been bleak so far. Selective serotonin reuptake inhibitors, such as paroxetine (up to 20 mg/day), reduce behavioral symptoms,[25] whereas selegeline (1.25 mg/day), a selective monoamine oxidase B inhibitor, causes decreased agitation and aggressiveness and improved executive-attention performance.[26]
4. HIV-associated dementia, whose incidence is reduced by highly active antiretroviral therapy, unfortunately does not provide complete protection. Potential therapies for HIV-associated dementia include the use of memantine, nimodipine, minocycline, selegiline, lexipafant (a platelet-activating factor antagonist), prinomastat, and CN-1189 (inhibitor of tumor necrosis factor-α).[27]
5. Dementia associated with prion diseases, such as Creutzfeldt–Jakob disease, Gerstmann–Straüssler–Scheinker disease, fatal insomnia, new variant CJD, and kuru, have no treatment so far, although quinacrine and chlorpromazine in cell cultures hold promise.[28]
6. Parkinson's disease with dementia (PDD) has no effective treatment so far.
7. Dementia with Huntington's disease has also evaded any effective treatment; however, a few drugs such as minocycline and creatine have shown efficacy in animal models.[29]

The various drugs used, their pharmacodynamics, indications, and dosages along with adverse reactions and level of evidence are detailed in Table 3.

Other Drugs and Investigational Treatments

Physostigmine was poorly tolerated and is not yet licensed.[45]

Eptastigmine was withdrawn from the market because it led to the development of neutropenia.[45]

Linopirdine, an acetylcholine releaser, showed no advantage over placebo.

Besipirdine, a similar drug, developed by Hoechst, was a selective M-channel blocker (a potassium channel inactivated by muscarinic agonist) and was not found to be an effective acetylcholine releaser, and trials have been unremarkable.[45]

The use of xanomeline, an acetylcholine agonist, was stopped because of unacceptable side effects.[46]

Sabcomeline is a partial agonist of M_1 receptors. A significant improvement on Alzheimer's Disease Assessment Scale Cognitive Subscale was seen in a randomized placebo-controlled trial in 364 patients over 14 weeks.[46]

Antioxidants target the prevention of dementia and its progression by reducing oxidative injury. Part of the injury from amyloid-β deposition in AD is through free radicals and the resultant oxidative cellular damage.[47]

Table 3. Characteristics of the Various Drugs Used for Alzheimer's Disease and Vascular Dementia

Drug	Pharmacodynamics	Therapeutic Indication	Adverse Reactions	Dosage	Level of Evidence
Tacrine	Reversibly inhibits AChE and BuChE, making more acetylcholine available It inhibits BuChE activity slightly more than AChE	Mild to moderate AD	Increased liver alanine transaminase in 40% to 50% of treated patients Gastrointestinal problems, for example, nausea, diarrhea, vomiting, appetite loss, increased gastric acid secretion, dyspepsia, weight loss	Initiated at 40 mg/day in 4 divided doses; maintained for 4 weeks; then increased to 80 mg/day in 4 divided doses; additional titration can be made at 4-week intervals if tolerable to a maximum dose of 160 mg/day. Available as 10-, 20-, 30-, or 40-mg capsules	Meta-analysis has shown that 80 mg/day was effective and that lower doses of 40 and 20 mg/day appeared not significantly beneficial[30]
Donepezil	Reversible, noncompetitive inhibitor that is highly selective for AChE than BuChE	Mild to moderate AD Vascular dementia	Diarrhea, nausea, insomnia, vomiting, muscle cramps, fatigue, and anorexia	Initiated at 5 mg/day; may be increased to 10 mg/day after 4-6 weeks, depending on tolerability. Available as 5- and 10-mg tablets	Six RCTs[26,27] found both the 5-mg and 10-mg doses of the drug to be effective in improving cognitive and global functioning after 6 months of treatment. Meta-analysis has, however, shown the higher dose to be more effective[31]
Rivastigmine	Inhibitor of both AChE and BuChE; a noncompetitive, pseudo-irreversible ChE-I	Mild to moderate AD Vascular dementia	Diarrhea, nausea, vomiting, insomnia, muscle cramps, fatigue, and anorexia	Initiated at 1.5 mg twice daily; increased by 3 mg every 2 weeks and titrated according to tolerability to a maximum dose of 6 mg twice daily. Available as 1.5-, 3-, 4.5-, and 6-mg capsules	High-dose rivastigmine (6-12 mg/day) has been shown to be superior to placebo in cognition, functioning, and overall lesser deterioration[32]
Galantamine	Reversibly and competitively inhibits centrally active AChE, making more acetylcholine available Modulates nicotinic receptors, which enhances actions of acetylcholine Nicotinic modulation enhances the actions of other neurotransmitters	Mild to moderate AD Vascular dementia	Increases hepatic transaminase Gastrointestinal problems can occur in a dose-dependent manner Dizziness, headache, nausea, vomiting, diarrhea, anorexia, weight loss	Initiated at 4 mg twice daily, which may be increased to a dose of 8 mg twice daily after 4 weeks to a maximum of 32 mg/day at an interval of at least 4 weeks depending on the patient's tolerability Available as 4-, 8-, and 12-mg tablets	Both 16 and 24 mg/day galantamine has been shown to be superior compared with placebo in cognition and functioning although the 24 mg group did not differ significantly from the 16 mg/day group[33]

(*continued*)

Table 3. (continued)

Drug	Pharmacodynamics	Therapeutic Indication	Adverse Reactions	Dosage	Level of Evidence
	by increasing the release of dopamine, norepinephrine, serotonin, GABA, and glutamate				
Metrifonate[34]	Irreversible inhibitor of both AChE and BuChE	Behavioral problems associated with AD. Reports of improvement in depression, dysphoria, agitation, aggression, and aberrant motor behavior	Diarrhea, vomiting, and intestinal discomfort. Leg cramps and reduction of heart rate	Dose range is 60-80 mg/day, once daily	Pooled data from various studies have shown efficacy on cognition, significant changes in behavior and function, and significant improvements in career burden[35-37]
CDP-Choline (citicoline)	It promotes the activity of phosphocholine-cytidyltransferase, the rate-limiting enzyme in the phosphatidylcholine synthesis pathway in brain cells Citicoline attenuates phospholipase A2, which helps maintain healthy arachidonic acid metabolism Citicoline may help moderate the formation of reactive oxygen species, lipid peroxidase, and leukotrienes within cerebral tissue	Mild to moderate AD	Gastrointestinal upset, headache	Available in 250-mg capsules given as 2-4 capsules/day in divided doses with or without meals	Failed to show evidence of any positive results[38]
Memantine	Selective uncompetitive blocker of the NMDA receptors, which is involved in the excitatory gluteminergic neurotransmitter system Blocks the binding of glutamate to the receptor and blocks the ion current (Ca^{2+}, Na^{+}) through the receptor channel	Moderate to severe AD HIV-associated dementia and vascular dementia	Constipation, dizziness, headache, and confusion	Starting dose is 5 mg/day, and can be increased by 5 mg each week. A dose of more than 5 mg should be administered in 2 divided doses. The recommended target dose is 20 mg/day. Available as 5- and 10-mg tablets	Memantine has shown better outcome than those receiving placebo in the domains of cognition, general functioning, and increased autonomy.[39-41] However, all studies are limited by the short duration of evaluation (24-28 weeks)

(continued)

Table 3. (continued)

Drug	Pharmacodynamics	Therapeutic Indication	Adverse Reactions	Dosage	Level of Evidence
	activated by glutamate	Mild to moderate	Hypotension, headache, nausea, and bradycardia	Dosage is 60-mg tablets four hourly	Evidence of some short-term benefit mainly in cognitive function and global impression, but not in activities on daily living, for patients with degenerative and multi-infarct dementia, and mixed dementia across 14 RCTs[42]
Nimodipine	An isopropyl calcium channel blocker that readily crosses the blood–brain barrier Its primary action is to reduce the number of open calcium channels in cell membranes, thus restricting influx of calcium ions into cells	AD, vascular dementia, or mixed Alzheimer's and vascular dementia			
Propentophylline	Acts by inhibiting the uptake of adenosine and blocking the enzyme phosphodiesterase It inhibits the production of free radicals and reduces the activation of microglial cells	Mild to moderate AD and vascular dementia	Headaches, dizziness, gastrointestinal pain, and nausea	300-mg tablets thrice daily (eg, 900 mg/day), taken 1 hour before meals orally or given in the dosage of 20 mg/kg/day intravenously	Limited evidence that it might benefit cognition, global function, and activities of daily living in AD and/or vascular dementia[43]
Lexipafant	Inhibits PAF, a bioactive lipid produced by HIV-infected monocytes taht has been detected at high levels in the CSF of immunosuppressed HIV-infected patients with CNS dysfunction	HIV-associated dementia	Very rarely myocardial infarction and pulmonary emboli. Common adverse events are nausea, vomiting, and gastrointestinal pain	Dosage of 250 mg every 12 hours	Limited evidence did not improve neurologic outcome[44]
Prinomastat	A matrix metalloproteinase inhibitor and belongs to the family of drugs called angiogenesis inhibitors				
	Blocks the action of metalloproteinase-2 or MMP2, which destroys brain nerve cells	HIV-associated dementia	None reported so far as it still in research		No evidence of any favorable outcome

Abbreviations: AChE, acetylcholineesterase; BuChE, butyrylcholinesterase; AD, Alzheimer's disease; RCT, randomized control trial; ChE-I, cholinesterase inhibitor; CNS, central nervous system.

Vitamin E: studies have shown that vitamin E in a large daily dose of 2000 IU (1000 IU 2 times a day) is an effective antioxidant for delaying the rate and progression of AD.[48,49] An alternative to supplementation is high intake of foods containing vitamin E. A diet rich in this vitamin can reduce the rate of cognitive decline in the elderly.[50] Some foods with high vitamin E content include

nuts (almonds, hazelnuts, and peanut butter), sunflower seeds, shrimp, plain wheat grain, and fortified cereals. Vitamin E (1000 IU orally 2 times a day) should be considered in an attempt to slow the progression of AD.[8]

Selegiline, a selective MAO-B inhibitor, was found to be superior to placebo in delaying time to death and decline in activities of daily living. There was no benefit to cognition, no significant effect on institutionalization, and no additive effect with vitamin E.[48]

Melatonin: there is insufficient evidence to support the effectiveness of melatonin in managing the cognitive and noncognitive sequelae of dementia.[51]

Nicergoline is an ergot derivative that has shown positive effects on cognition and behavior with mild to moderate Alzheimer's dementia and vascular dementia. However, there was an increased risk of adverse effects, limiting the use of this drug.[52]

Anti-inflammatory drugs may slow the process of AD and provide a degree of neuronal protection.[53] A 6-month trial of the nonsteroidal anti-inflammatory drug diclofenac for treatment of AD reported a slightly slower, but not statistically significant, decline in cognition,[54] but treatment with corticosteroids has failed to show improvement in cognition or behaviour.[55] Trials with rofecoxib and other selective COX-2 inhibitors, however, have not yet shown these agents to affect the progression of established AD. These trials are ongoing, and COX-2 nonsteroidal anti-inflammatory drugs may prove beneficial in the prevention or treatment of AD.

Clinical trial suggests that patients receiving estrogen replacement therapy may respond better to ChE-Is.[56] Estrogen also demonstrates effects on oxidation by stimulating the peroxidase reaction. Estrogen affects the genes that inhibit the production of pathological proteins.[57] Additionally, estrogen appears to promote the nonamyloidogenic processing of the amyloid precursor protein.[58] However, the long-term use of estrogen has been limited because of the risk of development of breast, uterine, or ovarian cancer. Guidelines state that estrogen should not be prescribed to treat AD.[8]

Statins: tetrospective epidemiological studies show a decreased risk of developing AD and dementia among those taking statin drugs to lower blood lipids, particularly in those aged less than 80 years.[59,60] The cholesterol-lowering agents simvastatin and lovastatin reduce intracellular and extracellular levels of Aβ42 and Aβ40 peptides in primary cultures of hippocampal neurons and mixed cortical neurons[61]; in addition, simvastatin also reduces cholesterol turnover in the brain.[62] More studies are needed to determine whether the lowering of serum cholesterol with statins may retard the pathogenesis of AD or other dementias.[63]

Glycogen synthase kinase-3β (GSK-3β) is involved in the phosphorylation of tau, an event in the pathway leading to tangle formation through presumed cytoskeletal changes in microtubules.[64,65] Valproate is an inhibitor of GSK-3β[66] and may be a therapeutic target in AD. Additionally, other GSK-3β inhibitors are being developed.[67]

Ginseng is the most widely used of all herbal remedies. People have used ginseng for thousands of years as an ergogenic for the restoration of strength, mental work capacity, and resistance to stress. Studies, however, have not found significant effects on work performance or differences with placebo in concentration, memory, and cognition.[68]

Huperzine A, derived from the moss *Huperzia serrate*, is a Chinese herbal remedy for the treatment of dementia. Its cognitive effects may be comparable to that of the acetylcholineesterase inhibitors (AChE-Is).[69] It is a reversible AChE-I and should not be taken if the patient is on an AChE-I drug. Compared with tacrine and donepezil, huperzine A has a longer duration of action and a higher therapeutic index.[69] In addition, huperzine A may improve working memory via an adrenergic mechanism and protect against glutamate-induced toxicity.[70] The side effects of this herbal remedy are generally mild and similar to other AChE-Is.[71]

Immunization therapy using Aβ-42 (AN-1792) in conjunction with the T helper (Th) 1 adjuvant QS-21 has shown slower rates of cognitive decline; however, increased incidence of microhemorrhages in mice after passive Aβ immunotherapy has been reported.[72]

Another novel approach based on intracellular expression of single-chain antibodies (intrabodies) specific to the β-site is of therapeutic significance if appropriate delivery mechanisms, such as delivery by intranasal administration of phage-expressing anti-β site-directed antibodies, are shown to be safe in humans.[73,74]

Preliminary data suggest that members of the sortin nexin family of proteins can reduce the rate of APP endocytoses and increases APP production, possibly by exposing the APP substrate to ADAM-10 (a disintegrin and metalloproteinase) for an extended period of time.[75]

Chelation therapies using hexadentate chelators, such as desferrioxamine (DFO), and a synthetic aminocarboxylate ligand, DP-109,[76] have been investigated. DFO treatment led to a significant reduction in the rate of decline of daily living activities, whereas DP-109 has been demonstrated

to possess a strong inhibition activity on plaque formation and deposition in female hAbPP-transgenic Tg 2576 mice.[77,78] Tridentate chelators, such as aroyl hydrazone ligands, are currently under investigation; bidentate chelators, such as clioquinol, has entered clinical trial.

Epidemiological studies have suggested that groups of people who consume diets high in omega-3 fatty acids may experience a lower prevalence of certain neurological conditions, particularly cognitive impairment and dementia disorders; thus, consumption of diets rich in omega-3 fatty acids holds promise in the treatment of dementia.[79]

Although all the above-mentioned strategies are being evaluated, none of them are recommended as there is insufficient evidence to support the use other antioxidants, anti-inflammatory agents, or other putative disease-modifying agents specifically to treat AD because of the risk of significant side effects in the absence of demonstrated benefits.[8]

Psychosocial Management of Dementia

Over the past 3 decades, interest has grown in the use of psychosocial interventions for people with dementia. Empirical studies and systematic reviews have been undertaken on a range of such interventions to examine their effectiveness. However, little account has been taken of the appropriateness of psychosocial interventions for people in different stages of the illness.[80] It has to be understood that the aim of the psychological or psychosocial approach is to improve the quality of life of the patient.

Behavioral Intervention

It is used as an intervention in the management of challenging behaviors in a dementia patient. Emerson[81] has pointed out certain challenging behaviors that these patients exhibit:

1. Repetitive screaming
2. Scratching self
3. Outburst of temper
4. Hitting own head by hand or by object
5. Biting self or others

Literature suggests that wandering behavior and some stereotyped behaviors can successfully be reduced using this technique.[82,83]

Cognitive Strategies

These strategies can be used to reduce the cognitive load on the patient with dementia. A point of caution is that these strategies should be used after taking into account the status of cognitive functioning. In reducing cognitive overload, spoken words may be supplemented with relevant pictures and objects to provide a context for what is said,[84] which helps in increasing the social interaction of these patients. Teri and Gallagher-Thompson[85] have reported positive findings with people in the early stages of AD. Individual and group cognitive therapy has also been used by other researchers with some favorable results.[86]

Reality Orientation

It is very widely used[85] and consists of 2 parts:

1. Verbal orientation: it is the ability to answer questions relating to time, place, and person orientation.
2. Behavioral orientation: it is the ability to find the way from place to place without getting lost.

Studies have also shown that that reality orientation is an effective intervention in improving cognitive ability, as measured using the Mini-Mental State Examination.[87,88] Furthermore, follow-up data of Baldelli et al[87] show that improvement in cognitive ability, even after taking into account a decline after the end of the intervention period, is maintained 3 months after the collection of posttest data. However, neither study demonstrated that reality orientation is effective in improving well-being. Finally, no evidence was found that reality orientation is effective in improving communication, functional performance, and cognitive ability measured in terms of memory recall. Despite these concerns, the debate concerning efficacy has been largely settled following the favorable review by Spector et al[89] of 6 randomized controlled trials of this therapy.

Formal Psychotherapy

There are no controlled outcome studies of formal psychotherapy in persons with dementing illnesses.[90] Persons who are cognitively handicapped (ie, those with low IQ or those who are educationally deprived) or those who have mild static cognitive impairment can be treated in groups with techniques such as paradoxical intervention, task assignment,

promoting identification, reinforcement, education, and advice.[91]

Validation Therapy

This therapy was developed by Naomi Feil[92] in 1960s in the United States. Originally called as fantasy therapy, it is based on the fact that some of the features associated with dementia were active strategies on the part of the patient to avoid stress, boredom, loneliness, and so on, and as reality is often too painful for the patient, he or she retreats into an inner reality (fantasy). Hitch[93] noted that validation therapy promotes contentment, results in less negative affect and behavioral disturbance, produces positive effects, and provides the individual with insight into external reality. However, Neal and Briggs[94] felt that one still had to be convinced with respect to its efficacy.

Reminiscence Therapy

It includes helping the patient to think about and review positive past experiences,[95] for example, birthdays, family holidays, and so on. The aim is to provide pleasure and cognitive stimulation by focusing on happy memories.

Although Spector et al[96] concluded that there was little evidence of a significant impact of the approach, other studies indicate that this may lead to improvement in certain behaviors such as self-care.[97,98]

Life Review Therapy

It is concerned with correction of negative memories.[99] According to Buechal[100] it is a process of reevaluation, resolution, and reintegration of past conflicts, giving new significance to one's life.

Although evidence is only suggestive, some patients may benefit from the following:

- Simulated presence therapy,[101] such as the use of videotaped or audio taped family member[102]
- Massage[103]
- Comprehensive psychosocial care programs
- Pet therapy[104]
- Commands issued at the patient's comprehension level
- Bright light, white noise[105]
- Cognitive remediation

Conclusions

Medications for the treatment of dementia—both Alzheimer's and non-Alzheimer's—that are available today include cholinesterase inhibitors and the NMDA receptor antagonist memantine. These drugs are safe, and they have been reported to produce moderate symptomatic benefits in several large and independent studies. At present, however, there is no treatment available that can stop the progressive deterioration of cognitive functions in patients suffering from dementia. The development of novel drugs with strong disease-modifying properties, therefore, represents one of the biggest unmet medical needs today. Regarding psychosocial management, although evidence is only suggestive, therapies are useful adjuncts to pharmacotherapy.

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