Chapter 3

Treatment

A | Overview of Treatment

CQ 3A-1

How should interventions and support be given following a diagnosis of dementia?

Answer

To improve the quality of life (QOL) of people with dementia and their families, it is necessary to provide post-diagnostic support from the early stage after dementia is diagnosed, which involves giving advice on ways to live with dementia, guidance to connect to social resources, and help with making future plans. Different countries adopt various approaches of post-diagnostic support, including education on dementia and participation in peer support groups such as dementia café, with some countries even considering to prepare written informed decision and future care plan according to each person's wishes. Careful discussions are required to find the approaches of post-diagnostic interventions and support which are appropriate to Japan.

Comment and evidence

Until now, medical care for dementia has focused on early diagnosis and treatment initiation. However, it has been pointed out that these approaches alone are not sufficient to mitigate the psychological impact on the patients and their families or their fear of a future without hope. The current view is that to help persons affected by dementia prepare their future with confidence, post-diagnostic support is necessary from the early stage following the diagnosis, by providing useful advice on living with dementia and information on social resources, and helping them plan the future. Such approaches have already been started in some countries [1].

Regarding the future approaches of post-diagnostic intervention and support in Japan, careful discussions from various perspectives are needed, taking into consideration the unique cultural characteristics and actual circumstances in Japan.

■ References

1) Innes A, Szymczynska P, Stark C. Dementia diagnosis and post-diagnostic support in Scottish rural communities: experiences of people with dementia and their families. Dementia (London). 2014; 13(2): 233-247.

■ Search formula

PubMed search: July 7, 2015 (Tuesday)

#1 "Dementia/therapy" [Majr] OR "Cognition Disorders/therapy" [Majr] OR "Memory Disorders/therapy" [Majr] OR ((dementia [TI] OR cognition disorder* [TI] OR cognitive disorder* [TI] OR memory disorder* [TI]) AND (therapy [TI] OR therapeutic [TI] OR treatment [TI])) OR("Dementia/diagnosis" [Mesh] OR (dementia [TI] AND post [TI] AND (diagnosis [TI] OR diagnostic [TI] OR diagnoses [TI]))) AND ("Social Support" [Majr] OR support* [TI]) OR (("Dementia" [Mesh] OR dementia [TI]) AND post-diagnostic) OR post-diagnostic support*

Ichushi search: July 7, 2015 (Tuesday)

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CQ 3A-2

How should pharmacotherapy, non-pharmacologic interventions and care be provided during treatment of dementia?

Answer

Use a combination of pharmacotherapy and non-pharmacologic interventions to treat dementia with the goal to improve cognitive function and quality of life (QOL). For behavioral and psychological symptoms of dementia (BPSD), in principle, non-pharmacologic interventions should take priority over pharmacotherapy. When using psychotropic drugs, continuously monitor for adverse events and whether medication is necessary.

Comment and evidence

In the treatment of dementia, the target symptoms include cognitive impairment, which is called the core symptom, as well as BPSD including delusion and irritability. Treat these symptoms by a combination of pharmacotherapy and non-pharmacologic interventions. When BPSD are observed, investigate whether there are physical diseases causing these symptoms and whether care is appropriate; and for treatment, give priority to non-pharmacologic interventions over pharmacotherapy [1, 2].

1. Treatment for cognitive impairment

For Alzheimer's disease dementia, cholinesterase inhibitors and NMDA receptor antagonist are recommended. Cholinesterase inhibitors are recommended for dementia with Lewy bodies. After medication is started, evaluate cognitive function regularly by psychological tests such as the Mini-Mental State Examination.

2. Treatment for BPSD

For BPSD, evaluate changes in physical conditions that may have caused the symptoms, and whether care and environment are appropriate [1]. For environmental modification, consider using long-term care insurance services such as day service. Non-pharmacologic interventions mitigate BPSD [3]. Care for patients with dementia, whether at home or in an institution, should be based on person-centered care that respects the will and hope of individual patients [4]. Giving guidance to caregivers regarding appropriate care delays admission to institution [5]. Occupational therapy using sensory stimulation is reported to improve BPSD [6].

After starting psychotropic drugs, continuously evaluate efficacy and adverse effects. If the demerits outweigh the benefits, consider dose reduction or discontinuation of the drug, while paying attention to the possibility of relapse of psychiatric symptoms following drug withdrawal [1].

■ References

1) Kales HC, Gitlin LN, Lyketsos CG, et al. Management of neuropsychiatric symptoms of dementia in clinical settings: recommendations from a multidisciplinary expert panel. J Am Geriatr Soc. 2014; 62(4): 762-769.
2) Gauthier S, Cummings J, Ballard C, et al. Management of behavioral problems in Alzheimer's disease. Int Psychogeriatr. 2010; 22(3): 346-372.
3) Brodaty H, Arasaratnam C. Meta-analysis of nonpharmacological interventions for neuropsychiatric symptoms of dementia. Am J Psychiatry. 2012; 169(9): 946-953.
4) Kitwood T (translated by Takahashi S). Person-centered Care for Dementia. Tokyo: Tsutsui Shobo; 2005: 5-37. (In Japanese)
5) Olazaran J, Reisberg B, Clare L, et al. Nonpharmacological therapies in Alzheimer's disease: a systematic review of efficacy. Dement Geriatr Cogn Disord. 2010; 30(2): 161-178.
6) Kim SY, Yoo EY, Jung MY, et al. A systematic review of the effects of occupational therapy for persons with dementia: a meta-analysis of randomized controlled trials. NeuroRehabilitation. 2012; 31(2): 107-115.

■ Search formula

PubMed search: July 7, 2015 (Tuesday)

#1 (("Dementia/drug therapy" [Majr] OR (dementia [TI] AND ("drug therapy" [TI] OR chemotherapy [TI] OR pharmacotherapy [TI] OR "pharmacological therapy" [TI]))) OR ("Cognition Disorders/drug therapy" [Majr] OR ((cognition disorder* [TI] OR cognitive disorder* [TI]) AND ("drug therapy" [TI] OR chemotherapy [TI] OR pharmacotherapy [TI] OR "pharmacological therapy" [TI]))) OR ("Memory Disorders/drug therapy" [Majr] OR (memory disorder* [TI] AND ("drug therapy" [TI] OR chemotherapy [TI] OR pharmacotherapy [TI] OR

"pharmacological therapy" [TI])))) OR (("Dementia/rehabilitation" [Majr] OR (dementia [TI] AND rehabilitation [TI]))OR("Cognition Disorders/rehabilitation" [Majr]OR((cognition disorder* [TI]OR cognitive disorder* [TI]) AND rehabilitation [TI])) OR ("Memory Disorders/rehabilitation" [Majr] OR (memory disorder* [TI] AND rehabilitation [TI])))) OR (("Dementia/therapy" [Majr] AND "Rehabilitation" [Mesh]) OR ("Cognition Disorders/therapy" [Majr] AND "Rehabilitation" [Mesh]) OR ("Memory Disorders/therapy" [Majr] AND "Rehabilitation" [Mesh])) OR (("Dementia/nursing" [Majr] OR (dementia [TI] AND nursing [TI])) OR ("Cognition Disorders/nursing" [Majr] OR ((cognition disorder* [TI] OR cognitive disorder* [TI]) AND nursing [TI])) OR ("Memory Disorders/nursing" [Majr] OR (memory disorder* [TI] AND nursing [TI])) OR (("Dementia/diet therapy" [Majr] OR (dementia[TI] AND "diet therapy" [TI])) OR ("Cognition Disorders/diet therapy" [Majr] OR ((cognition disorder* [TI] OR cognitive disorder* [TI]) AND "diet therapy" [TI])) OR ("Memory Disorders/diet therapy" [Majr] OR (memory disorder* [TI] AND "diet therapy"[TI])))) OR (("Dementia/surgery" [Majr] OR (dementia[TI] AND (surg* [TI] OR operation* [TI])))) OR ("Cognition Disorders/surgery" [Majr] OR ((cognition disorder* [TI] OR cognitive disorder* [TI]) AND (surg*[TI] OR operation* [TI])))) OR ("Memory Disorders/surgery" [Majr] OR (memory disorder* [TI] AND (surg* [TI] OR operation* [TI])))) OR (("Dementia/radiotherapy" [Majr] OR (dementia [TI] AND radiotherapy [TI])) OR ("Cognition Disorders/radiotherapy" [Majr] OR ((cognition disorder* [TI] OR cognitive disorder* [TI]) AND radiotherapy [TI])) OR ("Memory Disorders/radiotherapy" [Majr] OR (memory disorder* [TI] AND radiotherapy [TI])))) OR (((("Dementia/therapy" [Majr] AND "Psychotherapy" [Mesh]) OR (dementia [TI] AND psychotherapy [TI])) OR ("Cognition Disorders/therapy" [Majr] AND "Psychotherapy" [Mesh]) OR ((cognition disorder* [TI] OR cognitive disorder* [TI]) AND psychotherapy [TI]) OR ("Memory Disorders/therapy" [Majr] AND "Psychotherapy" [Mesh]) OR (memory disorder* [TI] AND psychotherapy [TI])) OR ((("Dementia/therapy" [Majr] AND "Social Support" [Mesh]) OR (dementia [TI] AND social support* [TI])) OR ("Cognition Disorders/therapy" [Majr] AND "Social Support" [Mesh]) OR ((cognition disorder* [TI] OR cognitive disorder* [TI]) AND social support* [TI]) OR ("Memory Disorders/therapy" [Majr] AND "Social Support" [Mesh]) OR (memory disorder* [TI] AND social support* [TI])) OR (("Dementia/therapy" [Majr] AND "Patient Care" [Mesh]) OR (dementia [TI] AND "patient care" [TI])) OR ("Cognition Disorders/therapy" [Majr] AND "Patient Care" [Mesh]) OR ((cognition disorder* [TI] OR cognitive disorder* [TI]) AND "patient care" [TI]) OR ("Memory Disorders/therapy" [Majr] AND "Patient Care" [Mesh]) OR (memory disorder* [TI] AND "patient care" [TI]) OR (("Dementia/therapy"[Majr] AND "Quality of Life" [Mesh]) OR (dementia [TI] AND quality of life* [TI])) OR ("Cognition Disorders/therapy" [Majr] AND "Quality of Life" [Mesh]) OR ((cognition disorder* [TI] OR cognitive disorder* [TI]) AND quality of life* [TI]) OR ("Memory Disorders/therapy" [Majr] AND "Quality of Life" [Mesh]) OR (memory disorder* [TI] AND quality of life* [TI]) OR (("Dementia/therapy" [Majr] AND "Informed Consent" [Mesh]) OR (dementia [TI] AND "informed consent" [TI]) OR ("Cognition Disorders/therapy" [Majr] AND "Informed Consent" [Mesh]) OR ((cognition disorder* [TI] OR cognitive disorder* [TI]) AND "informed consent" [TI]) OR ("Memory Disorders/therapy" [Majr] AND "Informed Consent" [Mesh]) OR (memory disorder* [TI] AND "informed consent" [TI]) OR (("nonpharmacological therapy" OR "non pharmacological therapy") AND ("Dementia/therapy" [Majr] OR dementia [TI] OR "Cognition Disorders/therapy" [Majr] OR cognition disorder* [TI] OR cognitive disorder* [TI] OR "Memory Disorders/therapy" [Majr] OR memory disorder* [TI]))

Ichushi search: July 7, 2015 (Tuesday)
#1 (Dementia/MTH OR Dementia/TI OR Cognitive impairment/MTH OR Cognitive impairment/TI OR Cognitive function impairment/TI OR Memory disorder/MTH OR Memory Disorder/TI) AND ((SH = Pharmacotherapy, Rehabilitation, Nursing, Surgical therapy, Transplantation, Dietary therapy, Psychiatric therapy, Radiotherapy) OR Pharmacotherapy/MTH OR Pharmacological action/MTH OR Pharmacotherapy/TI OR Pharmacotherapy/TI OR Medication/TI OR Rehabilitation/MTH OR Rehabilitation/TI OR Nursing/MTH OR Nursing/TI OR Surgery/MTH OR Surgical operation/TI OR Surgery/TI OR Transplantation/TI OR Dietary therapy/MTH OR Dietary therapy/TI OR Therapeutic diet/TI OR Psychiatric therapy/TH OR Psychiatric therapy/TI OR Radiotherapy/MTH OR Radiological treatment/TI OR Radiotherapy/TI OR Social support/MTH OR Social support/TI OR Patient management/MTH OR Patient management/TI OR Patient care/TI OR Informed consent/TH OR "Informed Consent"/TI OR QOL/TH OR QOL/TI OR "Quality of Life"/TI)

CQ 3A-3

What are the principles and precautions of pharmacotherapy in older people with dementia?

Answer

Older people with dementia tend to develop adverse events during pharmacotherapy. (1) Consider starting with a low dose, such as one-half to one-quarter of the dose used in young adults, depending on the type of drug to be prescribed. (2) Evaluate drug efficacy after a short period of treatment. (3) Simplify the method of drug taking. (4) Avoid taking multiple drugs as far as possible, while paying attention to adverse events specific to older people. Periodically evaluate the type of drug, the dosage, and the necessity of long-term prescription. (5) Confirm adherence to drug-taking with family members, caregivers, pharmacists, and others.

Comments and evidence

Many older people are affected by multiple diseases and the symptoms tend to be atypical. In addition, they show large individual differences in symptoms and response to drugs. For these reasons, they tend to use multiple drugs in combination for prolonged periods. The frequencies of adverse events are also high in older people; 15% of those aged 75 years or above have adverse events [1].

In view of the physiological deterioration of liver and renal functions in older people, consider starting with a low dose, such as one-half to one-quarter of the dose used in young adults, depending on the type of drug used.

Evaluate efficacy after a short period of treatment.

Simplify the method of drug taking.

Avoid using multiple drugs.

Confirm adherence to drug-taking with both the patient and also the caregiver.

■ References

1) Toba K, Akishita M, Mizuno Y, et al. Adverse drug reaction in the elderly. Japanese Journal of Geriatrics (Nippon Ronen Igakkai Zasshi) 1999; 36(3): 181-185. (In Japanese)

■ Search formula

PubMed search: July 7, 2015 (Tuesday)

#1 ("Dementia/drug therapy" [Majr] OR (dementia [TI] AND ("drug therapy" OR chemotherapy)) OR "Cognition Disorders/drug therapy" [Majr] OR ((cognition disorder* [TI] OR cognitive disorder* [TI]) AND ("drug therapy" OR chemotherapy)) OR "Memory Disorders/drug therapy" [Majr] OR(memory disorder* [TI] AND ("drug therapy" OR chemotherapy))) AND "Aged, 80 and over" [Mesh]

Ichushi search: July 6, 2015 (Monday)

#1 (Dementia/MTH OR Dementia/TI OR Cognitive impairment/MTH OR Cognitive impairment/TI OR Cognitive function impairment/TI OR Memory disorder/MTH OR Memory disorder/TI) AND (CK = Elderly (80~)) AND ((SH = Pharmacotherapy) OR Pharmacotherapy/MTH OR Pharmacological effect/MTH OR Drug treatment/TI OR Pharmacotherapy /TI OR Therapeutic drug/TI)

CQ 3A-4

What are the adverse events of psychotropic drugs [such as falls, declined activity of daily living (ADL), cognitive impairment, and aspiration pneumonia]?

Answer

Adverse events of antipsychotic drugs include over-sedation, hypotension, falls, dysphagia, constipation, and neuroleptic malignant syndrome. Antipsychotic drugs are also associated with increased risk of death. Pay special attention to impaired glucose tolerance when using olanzapine and quetiapine. Selective serotonin reuptake inhibitor (SSRI) and serotonin-norepinephrine reuptake inhibitor (SNRI) may cause nausea, loose stools, and serotonin syndrome. Benzodiazepine anxiolytics and hypnotic drugs may cause falls, aspiration, somnolence, and respiratory depression. A

Comments and evidence

Older people with dementia are prescribed drugs under the situations of impaired walking function and judgement ability together with increased susceptibility to developing adverse events. Adverse events of antipsychotics include over-sedation, falls, fracture, dysphagia, constipation, urinary tract infection, cerebrovascular disease, cardiovascular event, venous thrombosis, edema, gait disturbance, neuroleptic malignant syndrome, and increased risk of death [1].

Olanzapine and quetiapine are contraindicated in patients with diabetes and those with a history of diabetes. Risperidone and aripiprazole should be administered with caution in patients with diabetes or a history of diabetes, and patients with risk factors of diabetes including a family history of diabetes, hyperglycemia, and obesity. For olanzapine, quetiapine, and aripiprazole, warning has been issued regarding the need to monitor blood glucose and explain to patients what to do when adverse effects occur.

The antidepressant SSRI and SNRI may cause gastrointestinal symptoms such as nausea and loose stools, and serotonin syndrome (including tremor, sweating, tachycardia, anxiety, and agitation). Among anxiolytics and hypnotic drugs, benzodiazepines is the main drug class that may cause weakness, falls, aspiration, dysphagia, somnolence, and respiratory depression, etc.

■ Reference

1) Huybrechts KF, Gerhard T, Crystal S, et al. Differential risk of death in older residents in nursing homes prescribed specific antipsychotic drugs: population based cohort study. BMJ. 2012; 344: e977.

■ Search formula

PubMed search: July 7, 2015 (Tuesday)

#1 ("Dementia/drug therapy" [Mesh] OR (dementia [TI] AND ("drug therapy" OR chemotherapy)) OR "Cognition Disorders/drug therapy" [Mesh] OR ((cognition disorder* [TI] OR cognitive disorder* [TI]) AND ("drug therapy" OR chemotherapy)) OR "Memory Disorders/drug therapy" [Mesh] OR (memory disorder* [TI] AND ("drug therapy" OR chemotherapy))) AND ("Psychotropic Drugs/adverse effects" [Mesh] OR ((psychotropic drug* [TI] OR psychotropic agent* [TI]) AND (side effect* [TI] OR adverse effect* [TI] OR adverse reaction* [TI])) OR "Psychopharmacology/adverse effects" [Mesh] OR (psychopharmacology [TI] AND (side effect* [TI] OR adverse effect* [TI] OR adverse reaction* [TI])) OR ((antipsychotic agent* [TI] OR antipsychotic drug* [TI]) AND (side effects* [TI] OR adverse effect* [TI] OR adverse reaction* [TI])))

Ichushi search: July 6, 2015 (Monday)

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CQ 3A-5

What are the treatment procedures when using pharmacotherapy for dementia?

Answer

Before starting pharmacotherapy for dementia patients, consider carefully whether such therapy is necessary. If pharmacotherapy is required, confirm adherence to drug taking and the indications of the drug, give sufficient explanations to patients and caregivers, and then start treatment. B

Comments and evidence

Since older people already have other physical illnesses, they may be using a combination of multiple drugs. Before starting pharmacotherapy for dementia, consider carefully the necessity of the therapy, and initiate treatment if the treatment is judged to be necessary.

Before initiating pharmacotherapy, explain the general benefits and risks of pharmacotherapy using language that is easy to understand even for the patient with dementia, and give due consideration also to respect the will of the patient. Despite these explanations, if the patient's intention cannot be confirmed, or if the patient lacks the ability to make a judgment, explain to family members or other proxies and obtain consent.

People with dementia have difficulties managing medication from a relatively early stage of the disease due to cognitive impairment. Accidents such as unintentional overdose may occur due to the inability to manage medication. When prescribing medications for patients with dementia, it is necessary to simplify the method of drug taking such as minimizing the number of drug-taking, to facilitate visual medication management by dispensing drugs together in one package or using a pill box, and to modify the environment so that it can be shared between the patient and caregiver. Depending on the severity of dementia, the caregiver may need to fully manage the medication. It is desirable to start pharmacotherapy after making the above preparations and confirming that the environment allows maintenance of good adherence.

Behavioral and psychological symptoms of dementia (BPSD) can appear at any stage of dementia. Parallel to pharmacotherapy for cognitive impairment, start treatment (non-pharmacological interventions or pharmacotherapy) for BPSD any time when the need arises. Also provide concomitant treatments for neurological symptoms associated with the primary disease, coexisting conditions specific to older people (including delirium, dysphagia, falls/fractures, pneumonia, urinary disorder, and constipation), and physical complications (including hypertension, diabetes, and dyslipidemia).

Regardless of the drugs used, pay close attention to adverse events. When adverse events are observed, consider changing or discontinuing the drug promptly.

■ Further reading

1) Toba K. Dementia (second volume): Pharmacotherapy for dementia: compliance and adherence to drug taking. Japanese Journal of Clinical Medicine (Nihon Rinsho) 2011; 69: 22-25 (In Japanese)
2) Japan Geriatrics Society, Japan Agency for Medical Research and Development / Study Group on Safety of Medical Treatment in the Elderly (Ed.) Guidelines for Medical Treatment and its Safety in the Elderly 2015. Tokyo; Medical Tribune; 2015. (In Japanese)

■ Search formula

PubMed search: July 4, 2015 (Saturday), July 18, 2015 (Saturday)

#1 "Dementia/drug therapy" [Majr] OR (dementia[TI] AND ("drug therapy" OR chemotherapy)) OR "Cognition Disorders/drug therapy" [Majr] OR ((cognition disorder* [TI] OR cognitive disorder* [TI]) AND("drug therapy" OR chemotherapy)) OR "Memory Disorders/drug therapy" [Majr] OR (memory disorder* [TI] AND ("drug therapy" OR chemotherapy))

Ichushi search: July 4, 2015 (Saturday)

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CQ 3A-6

What are the adverse events due to cholinesterase inhibitors and NMDA receptor antagonists, and what should be done in case of these events?

Recommendation

The common adverse events of cholinesterase inhibitors are gastrointestinal symptoms including nausea/vomiting and diarrhea.

The common side effects of NMDA receptor antagonists include somnolence, dizziness, constipation, and headache.

In principle, these adverse events are managed by dose reduction or discontinuation of the responsible drug.

1B

Comments and evidence

Regarding serious adverse events of medications used to treat Alzheimer's disease dementia, cholinesterase inhibitors have been reported to cause adverse effects of the cardiovascular system such as syncope, bradycardia, and QT prolongation [1]. The NMDA receptor antagonist memantine has been reported to cause serious adverse events including syncope and psychiatric symptoms [2].

Cholinesterase inhibitors are associated with high frequencies of adverse events of the gastrointestinal system such as diarrhea, nausea/vomiting, and headache [3]. Gastrointestinal symptoms are more likely to appear when administration is initiated or when the dose is increased, and the incidence increases as the dose becomes higher. The rates of syncope [1, 4], fracture [1, 4], accidental injury [4], bradycardia [1], pacemaker implantation [1] have been shown to be higher under administration of cholinesterase inhibitors compared to controls [3]. Rivastigmine patch is a transdermal formulation that achieves relatively stable blood level. While the frequency of gastrointestinal symptoms associated with the patch formulation is lower than that of the oral formulation [5], skin reaction may occur at the site of application.

Although dizziness, somnolence, headache, and constipation have been reported to be relatively frequent adverse effects of memantine [2], one meta-analysis finds no significant difference compared with placebo [6].

Since the frequencies of occurrence of common adverse events differ depending on the disease, attention is required.

There is little evidence on how to manage adverse effects. Domperidone may be effective for gastrointestinal symptoms [7]. A moisturizer may be used to prevent inflammation at the site of application of the rivastigmine patch. If inflammation persists, consider using topical steroids [8].

In all cases, including those mentioned above, if adverse events are serious, consider reducing the dose or discontinuing the causative drug.

There is little evidence on the treatment of acute intoxication due to overdose or mistaken administration. Since acute intoxication may sometimes lead to death, caution is required.

References

1) Howes LG. Cardiovascular effects of drugs used to treat Alzheimer's disease. Drug Saf. 2014; 37(6): 391-395.
2) Honma A, Ozawa M, Shiosakai K, et al. Safety and efficacy of memantine hydrochloride in patients with Alzheimer's disease: Interim results of specified drug use survey on long-term use of memantine hydrochloride. Journal of Geriatrics(Nippon Ronen Igakkai Zasshi) 2014; 25(4): 419-433. (In Japanese)
3) Ihl R, Frolich L, Winblad B, et al. WFSBP Task Force on Treatment Guidelines for Alzheimer's Disease and other Dementias. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the biological treatment of Alzheimer's disease and other dementias. World J Biol Psychiatry. 2011; 12(1): 2-32.
4) Kim DH, Brown RT, Ding EL, Kiel DP, Berry SD. Dementia medications and risk of falls, syncope, and related adverse events: meta-analysis of randomized controlled trials. J Am Geriatr Soc. 2011; 59(6): 1019-1031.
5) Birks JS, Grimley Evans J. Rivastigmine for Alzheimer's disease. Cochrane Database Syst Rev. 2015; (4): CD001191.
6) Matsunaga S, Kishi T, Iwata N. Memantine monotherapy for Alzheimer's disease: a systematic review and meta-analysis. PLoS One. 2015; 10(4): e0123289.
7) Kano O, Urita Y, Ito H, et al. Domperidone effective in preventing rivastigmine-related gastrointestinal disturbances in patients with Alzheimer's disease. Neuropsychiatr Dis Treat. 2013; 9: 1411-1415.
8) Tahira T. Pharmacotherapy–core symptom. Tahira T: ABC of New Diagnosis and Treatment 22; Neurology 3; Alzheimer's Disease Dementia 2nd Edition. 138-145, Osaka: Saishin Igakusha; 2014. (In Japanese)

Search formula

PubMed search: July 4, 2015 (Saturday)

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Ichushi search: July 4, 2015 (Saturday)

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CQ 3A-7-1

What are the non-pharmacological therapies for dementia?

Answer

Non-pharmacological interventions for persons with dementia include cognitive function training, cognitive stimulation, exercise therapy, reminiscence, music therapy, and activities of daily living (ADL) training. C

Comment and evidence

Among the treatments for dementia, all the therapies other than pharmacotherapy are grouped together as non-pharmacological therapies. Non-pharmacological therapies aim to improve not only cognitive impairment but also behavioral and psychological symptoms of dementia (BPSD) as well as functions of daily living. Non-pharmacological therapies for dementia are broadly divided into interventions for patients with dementia and interventions for the caregivers. In practice, however, the two kinds of interventions are conducted in combination.

It should be noted that non-pharmacological therapies are intended not only for mitigating psychiatric symptoms and behavioral disorders but also for other benefits. For example, methods such as music therapy and reminiscence therapy are highly significant as means to engage dementia patients in active communication and involve them in daily living. Therefore, the validity and importance of these therapies cannot be judged solely based on whether mental symptoms are improved. In the clinical setting, it is necessary to consider intervention methods also for the purpose of maintaining the patients' quality of life (QOL) and their motivation in daily living.

Caregivers also should receive care. Appropriate interventions for caregivers are effective to preventive burnout. Structured psychological education for caregivers (a combination of learning knowledge, communication skills, behavior management, cognitive behavioral therapy, etc.) has been shown to reduce caregiver burnout and depression [1].

■ Reference

1) Jensen M, Agbata IN, Canavan M, et al. Effectiveness of educational interventions for informal caregivers of individuals with dementia residing in the community: systematic review and meta-analysis of randomised controlled trials. Int J Geriatr Psychiatry. 2015; 30 (2):130-143.

■ Further reading

1) Olazaran J, Reisberg B, Clare L, et al. Nonpharmacological therapies in Alzheimer's disease: a systematic review of efficacy. Dement Geriatr Cogn Disord. 2010; 30(2): 161-178.
2) Brodaty H, Arasaratnam C. Meta-analysis of nonpharmacological interventions for neuropsychiatric symptoms of dementia. Am J Psychiatry. 2012; 169(9): 946-953.

■ Search formula

PubMed search: July 4, 2015 (Saturday), August 3, 2015 (Sunday)

#1 ("Dementia/therapy" [Majr] OR (dementia [TI] AND (therapy [TI] OR therapeutic [TI] OR treatment [TI])) OR "Cognition Disorders/therapy" [Majr] OR ("cognition disorder*" [TI] AND (therapy [TI] OR therapeutic[TI] OR treatment [TI])) OR "Memory Disorders/therapy" [Majr] OR (memory disorder* [TI] AND (therapy [TI] OR therapeutic [TI] OR treatment [TI]))) NOT ("Dementia/drug therapy" [Mesh] OR (dementia [TI] AND ("drug therapy" OR chemotherapy)) OR "Cognition Disorders/drug therapy" [Mesh] OR ("cognition disorder*" [TI] AND ("drug therapy" OR chemotherapy)) OR "Memory Disorders/drug therapy" [Mesh] OR (memory disorder* [TI] AND ("drug therapy" OR chemotherapy))) OR ("Dementia/therapy" [Mesh] OR (dementia [TI] AND (therapy [TI] OR therapeutic [TI] OR treatment [TI])) OR "Cognition Disorders/therapy" [Mesh] OR ("cognition disorder*" [TI] AND (therapy [TI] OR therapeutic [TI] OR treatment [TI])) OR "Memory Disorders/therapy" [Mesh] OR (memory disorder* [TI] AND (therapy [TI] OR therapeutic [TI] OR treatment [TI]))) AND (neuropsychiatric symptom* OR behavioral symptom* OR behavioural symptom* OR psychological symptom*) OR "neuropsychiatric symptoms of dementia" OR "behavioral and psychological symptoms of dementia"

Ichushi search: July 4, 2015 (Saturday)

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CQ 3A-7-2

What are the symptoms that respond to non-pharmacological therapies for dementia?

Recommendation

Non-pharmacological therapies and exercise therapy that exert effects on cognitive function, such as cognitive stimulation, are effective in improving cognitive impairment in dementia. Exercise therapy may be effective in improving activities of daily living (ADL), and music therapy may be effective to treat behavioral and psychological symptoms of dementia (BPSD). 2C

Comments and evidence

Non-pharmacological therapies that are effective for cognitive impairment in Alzheimer's disease dementia include cognitive stimulation [1, 2]. A meta-analysis shows that interventions using cognitive stimulation improves the Mini Mental State Examination score by 1.74 points (95% confidence interval 1.13 to 2.36) and ADAS-cog by 2.27 points (95% confidence interval 0.99 to 3.55) compared to the no intervention group, and the effect remains evident during the follow-up period of 1 to 3 months [3]. Multi-component interventions have also been shown to improve ADL, quality of life (QOL), as well as behavior and mood [1]. When cognitive stimulation is used, participants' self-evaluation for QOL and well-being improves [1]. However, little evidence is available for other non-pharmacological interventions including transcutaneous electrical stimulation therapies (transcranial, peripheral), exercise therapy, music therapy, reminiscence therapy, ADL training, massage, recreational therapy, light therapy, multisensory stimulation therapy, supportive psychotherapy, validation therapy, acupuncture, transcranial magnetic stimulation, and muscle relaxation. Future reports with high-quality evidence are awaited. In the actual clinical setting, it is important to select an intervention method that matches the individuality of the patient.

Providing multi-component interventions including psychological education for caregivers delays institutionalization of home-care patients, reduces BPSD, and improves caregiver outcomes.

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■ Search formula

PubMed search: July 4, 2015 (Saturday), August 3, 2015 (Sunday)

#1 ("Dementia/therapy" [Majr] OR (dementia [TI] AND (therapy [TI] OR therapeutic [TI] OR treatment [TI])) OR "Cognition Disorders/therapy" [Majr] OR ("cognition disorder*" [TI] AND (therapy [TI] OR therapeutic [TI] OR treatment [TI])) OR "Memory Disorders/therapy" [Majr] OR (memory disorder* [TI] AND (therapy [TI] OR therapeutic [TI] OR treatment [TI]))) NOT ("Dementia/drug therapy" [Mesh] OR (dementia [TI] AND ("drug therapy" OR chemotherapy)) OR "Cognition Disorders/drug therapy" [Mesh] OR ("cognition disorder*" [TI] AND ("drug therapy" OR chemotherapy)) OR "Memory Disorders/drug therapy" [Mesh] OR (memory disorder* [TI] AND ("drug therapy" OR chemotherapy))) OR ("Dementia/therapy" [Mesh] OR (dementia [TI] AND (therapy [TI] OR therapeutic [TI] OR treatment [TI])) OR "Cognition Disorders/therapy" [Mesh] OR ("cognition disorder*" [TI] AND (therapy [TI] OR therapeutic [TI] OR treatment [TI])) OR "Memory Disorders/therapy" [Mesh] OR (memory disorder* [TI] AND (therapy [TI] OR therapeutic [TI] OR treatment [TI])) AND (neuropsychiatric symptom* OR behavioral symptom* OR behavioural symptom* OR psychological symptom*) OR "neuropsychiatric symptoms of dementia" OR "behavioral and psychological symptoms of dementia"

Ichushi search: July 4, 2015 (Saturday)

#1 (Dementia/TH OR Dementia/TI OR Cognitive impairment/TH OR Cognitive impairment/TI OR Cognitive function impairment/TI OR Memory disorder/TI OR Memory disorder/TI) AND ((SH = Therapeutic use, treatment, drug treatment, surgical treatment, transplantation, dietary treatment, psychiatric treatment, radiologic treatment) OR Treatment/TH OR Treatment /TI OR Therapy/TI) NOT ((SH = Pharmacotherapy) OR Pharmacotherapy/TH OR Drug treatment/TI OR Pharmacotherapy/TI OR Therapeutic drug/TI)

B | Treatment for behavioral and psychological symptoms of dementia (BPSD)

CQ 3B-1

What are the effective non-pharmacological therapies and pharmacotherapy for anxiety?

Recommendation

Anxiety is an important symptom that can cause or induce other behavioral and psychological symptoms of dementia (BPSD). The fundamental approach is to interact with the patient by speaking in a reassuring tone with a caring attitude. As non-pharmacological therapies for anxiety, music therapy and cognitive behavioral therapy may be effective, and they should be considered. If these treatments are not adequately effective, consider prescribing risperidone, olanzapine or quetiapine. 2C

Comments and evidence

Anxiety is an important symptom that can cause or induce other BPSD. First, the fundamental approach is to interact with the patient in a reassuring voice and attitude. Music therapy has been confirmed to be effective as a non-pharmacological therapy for anxiety [1]. Music therapy is desirably provided directly by music therapists, and is especially recommended for people with moderate to severe dementia. Cognitive behavioral therapy has been shown to be effective for persons with mild to moderate dementia [2].

If the above interventions do not provide adequate effect, consider pharmacotherapy.

A double-blind RCT comparing risperidone with haloperidol confirms the superiority of risperidone for anxiety symptoms [3]. Olanzapine has also been shown to be a safe and effective drug compared with placebo as control in a double-blind RCT for the treatment of anxiety in patients with Alzheimer's disease dementia [4]. In an open-label study comparing quetiapine and haloperidol, quetiapine improves anxiety and is well tolerated whereas haloperidol is not effective [5]. Since these atypical antipsychotics are used off-label, it is necessary to give adequate explanations to the patients and families, and to pay attention to adverse events while using the drugs. In addition, even if a drug is effective, it should not be used casually; keep in mind to reduce the risk of adverse effects by adjusting the dose or withdrawing the drug when symptoms have improved.

Benzodiazepines have been used to mitigate mild anxiety symptoms, but there is no clear evidence. When using this drug, pay attention to adverse events such as sedation, disorientation, delirium, confusion, disinhibition, ataxia, falls, fracture, and drug dependence at usual doses.

■ References

References 3-5 on pharmacotherapy are the same as the references in the previous version of the guideline.

1) Raglio A, Bellelli G, Mazzola P, et al. Music, music therapy and dementia: a review of literature and the recommendations of the Italian Psychogeriatric Association. Maturitas. 2012; 72(4): 305-310.
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■ Search formula

Non-pharmacological therapy
PubMed search: October 2, 2015 (Friday)

#1 ("Dementia/therapy" [Majr] OR dementia [TI] OR "Alzheimer disease" [TI] OR "Alzheimer's disease" [TI] OR "vascular dementia" [TI] OR "Lewy Body" [TI] OR "frontotemporal dementia" [TI] OR "frontotemporal lobar degeneration" [TI]) AND ("nonpharmacological therapy" OR "non pharmacological therapy" OR "nonpharmacologic therapy" OR "non pharmacologic therapy" OR "nonpharmacological treatment" OR "non pharmacological treatment" OR "nonpharmacologic treatment" OR "non pharmacologic treatment" OR nonpharmacological intervention* OR non pharmacological intervention* OR nonpharmacologic intervention* OR non pharmacologic intervention* OR "nonpharmacological management" OR "non pharmacological management" OR "nonpharmacologic management" OR "non pharmacologic management" OR "validation therapy" OR "reality orientation" OR "reminiscence therapy" OR "music therapy" OR "light therapy" OR "tactile therapy" OR "aromatherapy" OR "occupational therapy" OR "exercise therapy" OR "exercise training" OR "exercise program" OR "physical exercise" OR "cognitive training" OR "rehabilitation" OR "stimulation therapy" OR "psychological therapy" OR (caregiver* AND ("psycho-education" OR intervention)) OR "dementia care service" OR "adult day service" OR "dementia day service" OR "Rehabilitation" [Mesh] OR "Phototherapy" [Mesh] OR "Exercise" [Mesh] OR "rehabilitation" [Mesh] OR "Psychotherapy" [Mesh] OR ("Caregivers" [Mesh] AND ("psycho-education" OR intervention)) OR "Touch" [Mesh] OR "Day Care" [Mesh]) AND ("Anxiety" [Mesh] OR anxiety [TI] OR indifference* [TI] OR "Aggression" [Mesh] OR aggression [TI] OR "Psychomotor Agitation" [Mesh] OR agitation [TI] OR "Irritable Mood" [Mesh] OR irritability [TI] OR "Delusions" [Mesh] OR delusion* [TI] OR "Hallucinations" [Mesh] OR hallucination* [TI] OR "Depression" [Mesh] OR depression [TI] OR dysphoria [TI] OR "Wandering Behavior" [Mesh] OR wandering [TI] OR "Inhibition (Psychology)" [Mesh] OR disinhibition* [TI] OR ("Sexual Behavior" [Mesh] AND inappropriate [TI]) OR "inappropriate sexual behaviour" [TI] OR "inappropriate sexual behavior" [TI] OR restlessness [TI] OR("Motor Activity" [Mesh]AND aberrant [TI]) OR "aberrant motor behaviour" [TI] OR "aberrant motor behavior" [TI] OR "Sleep Disorders" [Mesh] OR "nighttime insomnia" [TI] OR "sleep disturbance" [TI] OR "daytime napping" [TI] OR "daytime sleepiness" [TI] OR "Apathy" [Mesh] OR apathy [TI] OR "Delirium" [Mesh] OR delirium [TI] OR ((anxiety OR indifference OR aggression OR agitation OR irritability OR delusion* OR hallucination* OR depression OR dysphoria OR wandering OR disinhibition* OR "inappropriate sexual behaviour" OR "inappropriate sexual behavior" OR restlessness OR "aberrant motor behaviour" OR "aberrant motor behavior" OR "nighttime insomnia" OR "sleep disturbance" OR "daytime napping" OR "daytime sleepiness" OR apathy OR delirium) AND (in process [SB] OR publisher [SB])))

Ichushi search: October 2, 2015 (Friday)
#1 (Dementia/TH OR Dementia/TI OR Alzheimer/TI OR Alzheimer/TI OR frontotemporal lobar degeneration/TI OR "frontotemporal lobar degeneration"/TI) AND ((SH = Surgical therapy, transplantation, dietary therapy, radiotherapy, nursing, rehabilitation) OR Non-pharmacotherapy/TI OR Non-pharmacological treatment/TI OR validation therapy/TH OR validation therapy/TI OR "validation therapy"/TI OR Reality orientation/TH OR "Reality orientation"/TI OR Reminiscence/TH OR Reminiscence/TI OR "reminiscence therapy"/TI OR Music therapy/TH OR Music therapy/TI OR "music therapy"/TI OR Light therapy/TH OR Light therapy/TI OR "light therapy"/TI OR Aromatherapy/TH OR Aromatherapy/TI OR "aromatherapy"/TI OR Occupational therapy/TH OR Occupational therapy/ TI OR "occupational therapy"/TI OR Exercise therapy/TH OR Exercise therapy/TI OR "exercise therapy"/TI OR Exercise training/TH OR Exercise training/TI OR "exercise training"/TI OR Physical exercise/TH OR Physical exercise/TI OR "physical exercise"/TI OR "exercise program"/TI OR Cognitive training/TH OR Cognitive training/TI OR "cognitive training"/TI OR Rehabilitation/TH OR Rehabilitation/TI OR "rehabilitation"/TI OR Stimulation therapy/TI OR "stimulation therapy"/TI OR Psychological therapy/TH OR Psychological therapy/TI OR "psychological therapy"/TI OR ((Caregiver/TH OR Caregiver/TI) AND (Education/TI OR Intervention/TI)) OR (caregiver/TI) AND ("psycho-education"/TI OR intervention/TI)) OR Nursing care service/TH OR Nursing care service/TI OR "dementia care service"/TI OR Day care/TH OR Day care/TI OR "adult day service"/TI OR "dementia day service"/TI OR Therapeutic touch/TH OR "tactile therapy"/TI OR Tactile care/TI) AND (Anxiety/TH OR Anxiety/TI OR Indifference/TI OR Aggression/TH OR Aggression/TI OR Psychomotor agitation/TH OR Irritable mood/TH OR Hallucination/TH OR Hallucination/TI OR Delusion/TH OR Delusion/TI OR Depression/TH or Depression/TI or Depression/TI OR Violence/TH or Violence/TI OR Wandering/TH or Wandering/TI OR Restlessness/TI OR (Psychomotor agitation/TH AND Restlessness) OR Inappropriate sexual behavior/TI OR Sexual perversion/TH OR ((Deviation OR Abnormality) AND Sexual behavior/TH) OR Sleep disorder/TH or Sleep disorder/TI OR Sleeping disturbance/TI OR Dyssomnia/TI OR Insomnia/TI OR Sleepiness/TI OR Apathy/TH or Apathy/TI OR Delirium/TH or Delirium/TI)

Pharmacotherapy
PubMed search: June 23, 2015 (Tuesday)
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Ichushi search: June 23, 2015 (Tuesday)
#1 (Dementia/TH OR Dementia/TI) AND ((SH = Pharmacotherapy) OR Pharmacotherapy/TH OR Drug treatment/TI OR Pharmacotherapy/TI OR Therapeutic drug/TI OR Kampo medicine/TH OR Antipsychotics/TH) AND (Anxiety/TH OR Anxiety/TI OR Indifference/TI)

CQ 3B-2

What are the effective non-pharmacological therapies and pharmacotherapy for agitation?

Recommendation

Treat agitation based on person-centered care; consider the reasons and causes for the symptoms and try to resolve them. It is also effective for the caregivers to learn appropriate conversation skills with persons with dementia and to practice the skills. Other non-pharmacological interventions such as group activities, music therapy, tactile care, and massage have been shown to be effective. For pharmacotherapy, atypical antipsychotics such as risperidone and aripiprazole have been shown to be effective. Consider also to use *Yokukansan* (liver-inhibiting powder), tiapride, carbamazepine, sertraline, escitalopram, and trazodone. 2C

Comments and evidence

In a systematic review that examines the effectiveness of 33 non-pharmacological interventions for agitation, educating caregivers about personal-centered care and training them to acquire appropriate communication skills with persons with dementia improve agitation [1]. Other non-pharmacological therapies including group activities, music therapy conducted by experts based on a program, tactile care, and massage have been shown to be effective.

If non-pharmacological therapies do not provide adequate effect, consider pharmacotherapy. Note that all the drugs described below are used off-label, and should be used with caution after explaining adequately to the patients and families and paying attention to adverse events during use. In addition, even when a drug is effective, it should not be used casually, and efforts should be made to decrease the risk of adverse effects by reducing the dose or withdrawing the drug when symptoms have improved.

In a systematic review that summarizes 18 studies on atypical antipsychotics compared with placebo for agitation and aggression in Alzheimer's disease dementia, low-dose risperidone is most promising and aripiprazole can be expected to be as effective as risperidone, while the effect of olanzapine is variable, and quetiapine is not effective [2].

A systematic review on antidepressants finds little research and insufficient evidence, but the effectiveness of sertraline, escitalopram, and trazodone has been reported [3]. Carbamazepine can also be expected to be effective [2]. A multicenter study in Japan has reported the effectiveness of *Yokukansan* [4]. Tiapride is also reported to be effective for agitation and aggression [5]. Use of tiapride may be considered because it is covered by health insurance in Japan for aggressive behavior and hyperphrenia associated with the sequelae of cerebral infarction.

■ References

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■ Search formula

Non-pharmacological therapies

PubMed search: October 2, 2015 (Friday)

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Ichushi search: October 2, 2015 (Friday)
#1 (Dementia/TH OR Dementia/TI OR Alzheimer/TI OR frontotemporal lobar degeneration/TI OR "frontotemporal lobar degeneration"/TI) AND((SH = Surgical therapy, transplantation, dietary therapy, radiotherapy, nursing, rehabilitation) OR 非Pharmacotherapy/TI OR Non-pharmacological treatment/TI OR validation therapy/TH OR validation therapy/TI OR "validation therapy"/TI OR Reality Orientation/TH OR "Reality Orientation"/TI OR reminiscence/TH OR reminiscence/TI OR "reminiscence therapy"/TI OR Music therapy/TH OR Music therapy/TI OR "music therapy"/TI OR Light therapy/TH OR Light therapy/TI OR "light therapy"/TI OR Aromatherapy/TH OR Aromatherapy/TI OR "aromatherapy"/TI OR Occupational therapy/TH OR Occupational therapy/ TI OR "occupational therapy"/TI OR Exercise therapy/TH OR Exercise therapy/TI OR "exercise therapy"/TI OR Exercise training/TH OR Exercise training/TI OR "exercise training"/TI OR Physical exercise/TH OR Physical exercise/TI OR "physical exercise"/TI OR "exercise program"/TI OR Cognitive training/TH OR Cognitive training/TI OR "cognitive training"/TI OR Rehabilitation/TH OR Rehabilitation/TI OR "rehabilitation"/TI OR Stimulation therapy/TI OR "stimulation therapy"/TI OR Psychological therapy/TH OR Psychological therapy/TI OR "psychological therapy"/TI OR ((Caregiver /TH OR Caregiver/TI) AND (Education/TI OR Intervention/TI)) OR (caregiver/TI) AND ("psycho-education"/TI OR intervention/TI)) OR Nursing care service/TH OR Nursing care service/TI OR "dementia care service"/TI OR day care/TH OR day care/TI OR "adult day service"/TI OR "dementia day service"/TI OR Therapeutic touch/TH OR "tactile therapy"/TI OR Tactile care/TI) AND(Anxiety/TH OR Anxiety/TI OR Indifference/TI OR Aggression/TH OR Aggression/TI OR Psychomotor agitation/TH OR Irritable mood/ TH OR Hallucination/TH OR Hallucination/TI OR Delusion/TH OR Delusion/TI OR Depression/TH or Depression/TI or Depression/TI OR Violence/TH or Violence/TI OR Wandering/TH or Wandering/TI OR Restlessness/TI OR (Psychomotor agitation/TH AND Restlessness)OR Inappropriate sexual behavior/TI OR Sexual perversion/TH OR ((Deviation OR Abnormality)AND Sexual behavior/TH) OR Sleep disorder/TH or Sleep disorder/TI OR Sleeping disturbance/TI OR Dyssomnia/TI OR Insomnia/TI OR Sleepiness/TI OR Apathy/TH or Apathy/TI OR Delirium/TH or Delirium/TI)

Pharmacotherapy
PubMed search: June 23, 2015 (Tuesday)
#1 Dementia [Mesh] AND ("drug therapy" [subheading] OR "Drug therapy" [Mesh]) OR ("Dementia/therapy" [Mesh] AND ("Antipsychotic Agents" [Mesh] OR "Benzodiazepines" [Mesh] OR "Serotonin Uptake Inhibitors" [Mesh] OR "Antidepressive Agents" [Mesh] OR "Anticonvulsants" [Mesh] OR "Anticonvulsants" [PA] OR "Yi-Gan San" [Supplementary Concept] OR "Herbal Medicine" [Mesh] OR "Medicine, Kampo" [Mesh] OR "ramelteon" [Supplementary Concept] OR "suvorexant" [Supplementary Concept])) OR (dementia OR "alzheimer disease" OR "alzheimer's disease" OR "frontotemporal lobar degeneration") AND (pharmacological OR drug OR medicine OR antipsychotics OR benzodiazepine OR "selective serotonin reuptake inhibitors" OR "serotonin-norepinephrine reuptake inhibitors" OR antidepressant* OR "mood stabilizer" OR anticonvulsant* OR Yokukansan OR "Japanese herbal" OR "traditional herbal" OR kampo OR ramelteon OR suvorexant OR "orexin receptor antagonist" OR "melatonin receptor agonist")

Ichushi search: June 22, 2015 (Monday)
#1 (Dementia/TH OR Dementia/TI) AND ((SH = Pharmacotherapy) OR Pharmacotherapy/TH OR Drug treatment/TI OR Pharmacotherapy/TI OR Therapeutic drug/ TI OR Kampo medicine/TH OR Antipsychotics/TH) AND (Aggression/TH OR Aggression/TI OR Psychomotor agitation/TH OR Irritable mood/ TH)

CQ 3B-3

What are the effective non-pharmacological therapies and pharmacotherapy for hallucinations and delusions?

Recommendation

For persons with dementia who manifest hallucinations and delusions, the first step is to reduce their anxiety through an approach of acceptance. In addition, when a specific person is the object of delusion, consider keeping a temporal and physical distance from that person. Also consider the possibility that the drugs being taken may cause hallucinations and delusions, and investigate this possibility. In patients with Alzheimer 's disease dementia, if symptoms do not improve by anti-dementia drugs and the above methods, consider using atypical antipsychotics such as risperidone, olanzapine, quetiapine, and aripiprazole. *Yokukansan* may also be considered. 2C

Comment and evidence

For hallucinations and delusions, it is important to listen to the patients' complaint first, and then give them a sense of security in a receptive and sympathetic manner without denial or affirmation. It is also important to give them a role and something to live for.

When a specific person in the family is the subject of delusion, it is useful to utilize care services to keep a time and physical distance between the patient and that person. If such intervention does not solve the problem, pharmacotherapy has to be considered. For delusions in Alzheimer 's disease dementia, try to administer anti-dementia drug. If the symptoms do not improve, consider using antipsychotic drugs. However, since these drugs are used off-label, it is necessary to explain carefully to the patients and families and pay attention to adverse events during use. In addition, even if a drug is effective, it should not be taken casually. Bear in mind the need to reduce the risk of adverse effects by adjusting the dose or withdrawing the drug when symptoms have improved.

Regarding the use of antipsychotic drugs in persons with dementia, effectiveness has been reported in a few studies with small numbers of cases, but no large-scale randomized controlled trial (RCT) has been reported [1-3]. When using antipsychotic drugs, atypical antipsychotics (risperidone, olanzapine, quetiapine, aripiprazole) are recommended.

For drugs other than antipsychotics, *Yokukansan* has been reported to be effective in a small number of cases [2].

Regarding pharmacotherapy for visual hallucinations in Parkinson's disease with dementia (PDD) and dementia with Lewy bodies (DLB), see CQ7-6.

References

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3) Shinagawa S, Nakajima S, Plitman E, et al. Psychosis in frontotemporal dementia. J Alzheimers Dis. 2014; 42(2); 485-499.

Search formula

Non-pharmacological therapies

PubMed search: October 2, 2015 (Friday)

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Ichushi search: October 2, 2015 (Friday)
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Pharmacotherapy
PubMed search: June 23, 2015 (Tuesday)
#1 (Dementia [Mesh] AND ("drug therapy" [subheading] OR "Drug therapy" [Mesh])) OR ("Dementia/therapy" [Mesh] AND ("Antipsychotic Agents" [Mesh] OR "Benzodiazepines" [Mesh] OR "Serotonin Uptake Inhibitors" [Mesh] OR "Antidepressive Agents" [Mesh] OR "Anticonvulsants" [Mesh] OR "Anticonvulsants" [PA] OR "Yi-Gan San" [Supplementary Concept] OR "Herbal Medicine" [Mesh]OR "Medicine, Kampo" [Mesh] OR "ramelteon" [Supplementary Concept] OR "suvorexant" [Supplementary Concept])) OR ((dementia OR "alzheimer disease" OR "alzheimer's disease" OR "frontotemporal lobar degeneration") AND (pharmacological OR drug OR medicine OR antipsychotics OR benzodiazepine OR "selective serotonin reuptake inhibitors" OR "serotonin-norepinephrine reuptake inhibitors" OR antidepressant* OR "mood stabilizer" OR anticonvulsant* OR Yokukansan OR "Japanese herbal" OR "traditional herbal" OR kampo OR ramelteon OR suvorexant OR "orexin receptor antagonist" OR "melatonin receptor agonist")) AND ("Delusions" [Mesh] OR delusion* OR "Hallucinations" [Mesh] OR hallucination*)

Ichushi: June 22, (Monday)
#1 (Dementia/TH OR Dementia/TI) AND ((SH = Pharmacotherapy)OR Pharmacotherapy/TH OR Drug treatment/TI OR Pharmacotherapy/TI OR Therapeutic drug/ TI OR Kampo medicine/TH OR Antipsychotics/TH) AND (Hallucination/TH OR Hallucination/TI OR Delusion/TH OR Delusion/TI)

CQ 3B-4

What are the effective non-pharmacological therapies and pharmacotherapy for depression?

Recommendation

For depressive symptoms, consider the situation of the person with dementia and communicate with a receptive attitude. Regarding non-pharmacological interventions, utilization of social support, reminiscence therapy, and music therapy are effective. In Japan, utilization of long-term care services is a realistic measure. If no improvement is observed after the above interventions have been given for a certain period of time, consider using antidepressants such as selective serotonin reuptake inhibitor (SSRI) and serotonin-norepinephrine reuptake inhibitor (SNRI). 2C

Comments and evidence

A systematic review clarifies that social support, classified as a non-pharmacological intervention, may improve depressive symptoms in people with dementia [1].

Two randomized controlled trials (RCTs) have demonstrated the effectiveness of music therapy. Both individual therapy [2] provided by music therapists and group music activity program [3] are effective, and both singing and music appreciation are also effective. A meta-analysis also shows that reminiscence therapy has a moderate improvement effect in reducing depressive symptoms in older people with dementia [4]. For exercise therapy, a meta-analysis concludes with moderate confidence that there is no effect on depression [5].

Regarding antidepressants, a systematic review of 10 RCTs and 3 meta-analyses finds that the effect of antidepressants for depression in dementia is inconclusive [6]. In addition, a meta-analysis of 6 RCTs on SSRI also does not support the effectiveness of SSRI for depression in dementia [7]. Furthermore, mirtazapine is not effective [8]. The observation periods in most of the above studies on non-pharmacological interventions are 5-12 weeks. Therefore, if symptoms do not improve after 12 weeks of non-pharmacological intervention, consider starting antidepressants. When selecting drug options, start with SSRI and SNRI that have few adverse effects.

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Search formula

Non-pharmacological therapies

PubMed search: October 2, 2015 (Friday)

#1 ("Dementia/therapy" [Majr] OR dementia [TI] OR "Alzheimer disease" [TI] OR "Alzheimer's disease" [TI] OR "vascular dementia" [TI] OR "Lewy Body" [TI] OR "frontotemporal dementia" [TI] OR "frontotemporal lobar degeneration"[TI]) AND ("nonpharmacological therapy" OR "non pharmacological therapy" OR "nonpharmacologic therapy" OR "non pharmacologic therapy" OR "nonpharmacological treatment" OR "non pharmacological treatment" OR "nonpharmacologic treatment" OR "non pharmacologic treatment" OR nonpharmacological intervention* OR non pharmacological intervention* OR nonpharmacologic intervention* OR non pharmacologic intervention* OR "nonpharmacological management" OR "non pharmacological management" OR "nonpharmacologic management" OR "non pharmacologic management" OR

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Pharmacotherapy
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CQ 3B-5

What are the effective non-pharmacological therapies and pharmacotherapy for wandering?

Recommendation

Consider the reason or cause of wandering from the viewpoint of the patient with dementia and take preventive measures. For a person with dementia who wanders frequently, make a plan to facilitate finding of the missing person. Regarding pharmacotherapy, risperidone may be considered, but the scientific evidence is insufficient. Tiapride may also be considered, because this drug is covered by health insurance in Japan for wandering associated with the sequelae of cerebral infarction. However, if the above interventions and treatments do not solve the issue, consider using nursing care services such as institutional care service. 2C

Comments and evidence

To address wandering in patients with dementia, non-pharmacological interventions are the first choice, and when they are not effective, pharmacotherapy is selected. Many of the drugs used for these behavioral symptoms are used off-label. Therefore, it is necessary to use with caution, giving sufficient explanations to the patients and families and paying attention to adverse events during use. In addition, even if the drug is effective, it should not be used casually. Keep in mind to decrease the risk of adverse effects by reducing the dose or withdrawing the drug when symptoms have improved.

Wandering

Various actions of a person with dementia can be recognized by others as signs of wandering. First, consider the nature, reason and cause of the actions from the viewpoint of the person with dementia, and take preventive measures. While wandering, the persons with dementia are often tense and confused. It is important to listen to them and make them feel reassured. For persons with dementia who frequently wander, it is important to take precautions even while they are calm. For example, dress them in easily recognizable clothes, write contact information on the clothes and shoes they wear, and use devices such as global positioning systems (GPS). Moreover, it is useful to obtain support from neighbors and to register in programs for wandering persons in municipalities that have such mechanisms. Although there is no study that evaluates the effectiveness of pharmacotherapy focusing on wandering in dementia patients, a randomized controlled trial (RCT) that compares the effects of risperidone on behavioral and psychological symptoms of dementia (BPSD) reports significant improvement for wandering [1]. Therefore, use of risperidone may be considered. Tiapride may also be used, as its indication for wandering associated with the sequelae of cerebral infarction is covered by health insurance in Japan. In the case of wandering associated with agitation, drugs for agitation may be considered (see CQ3B-2). In addition, improvement of sleep/wake pattern has been reported to reduce wandering [2]. Therefore, if the patient also has sleep disturbance, consider treatment for sleep disturbance (see CQ3B-6). If there is no improvement despite various treatments and interventions, consider utilizing institutional care services.

■ References

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■ Search formula

Non-pharmacological therapies

PubMed search: October 2, 2015 (Friday)

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CQ 3B-6

What are the effective non-pharmacological therapies and pharmacotherapy for sleep disturbance (excluding REM sleep behavior disorder)?

Recommendation

First, assess sleep disturbance accurately and conduct differential diagnosis. If there are physical symptoms (such as pain, urinary frequency, and itchiness), psychological or social stress, stimulant-containing products, and drugs that may contribute to sleep disturbance, mitigate those factors. In addition, encourage the patient to do sunbathing and physical activities during the day, and to attempt to improve the sleep environment. If possible, consider bright light therapy. For pharmacotherapy, use of trazodone or risperidone may be considered. However, benzodiazepines as sleep inducing agents are not recommended because of the risk of adverse events such as sedation and falls. 2C

Comment and evidence

In Alzheimer's disease dementia and dementia with Lewy bodies, complex sleep disturbances such as insomnia, hypersomnia, and sleep/wake rhythm disturbances may occur [1]. In addition, the patients tend to have various conditions such as sleep apnea syndrome, restless legs syndrome (RLS), periodic limb movement disorder, nocturnal leg cramp, and REM sleep behavior disorder. Therefore, it is important to assess sleep disturbance accurately and conduct differential diagnosis. Furthermore, sleep disturbance may become chronic due to diverse underlying factors including physical symptoms (such as pain, urinary frequency, and itchiness), exacerbation of psychiatric symptoms, increased psychological and social stress, and influence by stimulant-containing products (such as alcohol, caffeine, and nicotine) and drugs. Therefore, removal of these factors is also important.

In a systematic review of 38 pharmacological or non-pharmacological intervention studies targeting sleep disturbances in patients with mild to moderate Alzheimer's disease dementia, bright light therapy gives the best results and is effective in reducing nocturnal awakening and prolonging nighttime sleep [2]. In addition, multi-faceted interventions including daytime sunlight exposure, physical activity, exercise, restriction of daytime napping, structured bedtime routines (performing certain actions in a predetermined order before going to bed), improvement of sleep environment such as reducing noise and light at night are also effective in improving sleep disturbance. The use of pharmacotherapy is limited when considering safety. In particular, although sedative-hypnotic medications represented by benzodiazepines are widely used clinically, there are few data supporting their use. Conversely, they may cause sedation, daytime somnolence, falls, confusion, and amnesia, and should therefore be used with caution. Two randomized controlled trials (RCTs) have shown the effectiveness of risperidone, and this drug may be considered.

It has been reported that trazodone given to patients with Alzheimer's disease dementia at a dose of 50 mg per day for 2 weeks prolongs total sleeping time and improves sleep efficiency. Use of this drug may be considered [3].

Regardless of which drugs are being used, even if they prove to be effective, they should not be used casually. Always remember to reduce the risk of adverse effects by reducing the dose or withdrawing the drug when symptoms have improved.

■ References

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■ Search formula

Non-pharmacological therapies

PubMed search: October 2, 2015 (Friday)

#1 ("Dementia/therapy" [Majr] OR dementia[TI] OR "Alzheimer disease" [TI] OR "Alzheimer's disease" [TI] OR "vascular dementia" [TI] OR "Lewy Body" [TI] OR "frontotemporal dementia" [TI] OR "frontotemporal lobar degeneration" [TI]) AND ("nonpharmacological therapy" OR "non pharmacological therapy" OR "nonpharmacologic therapy" OR "non pharmacologic therapy" OR "nonpharmacological treatment" OR "non pharmacological treatment" OR "nonpharmacologic treatment" OR "non pharmacologic treatment" OR nonpharmacological intervention* OR non pharmacological intervention* OR nonpharmacologic intervention* OR non pharmacologic intervention* OR "nonpharmacological management" OR "non pharmacological management" OR "nonpharmacologic management" OR "non pharmacologic management" OR

"validation therapy" OR "reality orientation" OR "reminiscence therapy" OR "music therapy" OR "light therapy" OR "tactile therapy" OR "aromatherapy" OR "occupational therapy" OR "exercise therapy" OR "exercise training" OR "exercise program" OR "physical exercise" OR "cognitive training" OR "rehabilitation" OR "stimulation therapy" OR "psychological therapy" OR (caregiver* AND ("psycho-education" OR intervention)) OR "dementia care service" OR "adult day service" OR "dementia day service" OR "Rehabilitation" [Mesh] OR "Phototherapy" [Mesh] OR "Exercise" [Mesh] OR "rehabilitation" [sh] OR "Psychotherapy" [Mesh] OR ("Caregivers" [Mesh] AND ("psycho-education" OR intervention)) OR "Touch" [Mesh] OR "Day Care" [Mesh]) AND ("Anxiety" [Mesh] OR anxiety [TI] OR indifference* [TI] OR "Aggression" [Mesh] OR aggression [TI] OR "Psychomotor Agitation" [Mesh] OR agitation [TI] OR "Irritable Mood" [Mesh]OR irritability [TI] OR "Delusions" [Mesh] OR delusion* [TI] OR "Hallucinations" [Mesh] OR hallucination* [TI] OR "Depression" [Mesh] OR depression [TI] OR dysphoria [TI] OR "Wandering Behavior" [Mesh] OR wandering [TI] OR "Inhibition (Psychology)" [Mesh] OR disinhibition* [TI] OR ("Sexual Behavior" [Mesh] AND inappropriate [TI]) OR "inappropriate sexual behaviour" [TI] OR "inappropriate sexual behavior" [TI] OR restlessness [TI] OR("Motor Activity" [Mesh] AND aberrant[TI]) OR "aberrant motor behaviour"[TI] OR "aberrant motor behavior" [TI] OR "Sleep Disorders" [Mesh] OR "nighttime insomnia" [TI] OR "sleep disturbance" [TI] OR "daytime napping" [TI] OR "daytime sleepiness" [TI] OR "Apathy" [Mesh] OR apathy [TI] OR "Delirium" [Mesh] OR delirium [TI] OR ((anxiety OR indifference OR aggression OR agitation OR irritability OR delusion* OR hallucination* OR depression OR dysphoria OR wandering OR disinhibition* OR "inappropriate sexual behaviour" OR "inappropriate sexual behavior" OR restlessness OR "aberrant motor behaviour" OR "aberrant motor behavior" OR "nighttime insomnia" OR "sleep disturbance" OR "daytime napping" OR "daytime sleepiness" OR apathy OR delirium) AND (in process [SB] OR publisher [SB])))

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Pharmacotherapy
PubMed search: June 23, 2015 (Tuesday)
#1 (Dementia [Mesh] AND ("drug therapy" [subheading] OR "Drug therapy" [Mesh])) OR ("Dementia/therapy" [Mesh] AND ("Antipsychotic Agents" [Mesh] OR "Benzodiazepines" [Mesh] OR "Serotonin Uptake Inhibitors" [Mesh] OR "Antidepressive Agents" [Mesh] OR "Anticonvulsants"[Mesh] OR "Anticonvulsants" [PA] OR "Yi-Gan San" [Supplementary Concept] OR "Herbal Medicine" [Mesh] OR "Medicine, Kampo" [Mesh] OR "ramelteon" [Supplementary Concept] OR "suvorexant" [Supplementary Concept])) OR ((dementia OR "alzheimer disease" OR "alzheimer's disease" OR "frontotemporal lobar degeneration") AND (pharmacological OR drug OR medicine OR antipsychotics OR benzodiazepine OR "selective serotonin reuptake inhibitors" OR "serotonin-norepinephrine reuptake inhibitors" OR antidepressant* OR "mood stabilizer" OR anticonvulsant* OR Yokukansan OR "Japanese herbal" OR "traditional herbal" OR kampo OR ramelteon OR suvorexant OR "orexin receptor antagonist" OR "melatonin receptor agonist")) AND ("Sleep Disorders" [Mesh] OR "nighttime insomnia" OR "sleep disturbance" OR "daytime napping" OR "daytime sleepiness")

Ichushi search: June 23, 2015 (Tuesday)
#1 (Dementia/TH OR Dementia/TI AND ((SH = Pharmacotherapy) OR Pharmacotherapy/TH OR Drug treatment/TI OR Pharmacotherapy/TI OR Therapeutic drug/TI OR Kampo medicine/TH OR Antipsychotics/TH)) AND (Sleep disorder/TH or Sleep disorder/TI OR Sleep disturbance/TI OR Dyssomnia/TI OR Insomnia/TI OR Somnolence/TI)

CQ 3B-7

What are the effective non-pharmacological therapies and pharmacotherapy for apathy?

Recommendation

As a non-pharmacological intervention for apathy, therapeutic activities customized for individual patients with dementia are suggested to be effectiveness. In Japan, incorporating this approach as a program in dementia care service seems to be a realistic measure. For pharmacotherapy, cholinesterase inhibitor is the first choice if indicated for the disease. Memantine may be considered, but antidepressants and antiepileptic drugs have not been reported to be effective.

2C

Comments and evidence

Apathy is a state of reduced spontaneity, initiative, interest, concern, motivation, and emotion. Because these are not positive symptoms such as delusion and irritability, they tend to be misunderstood as posing less burden on nursing care. However, since patients may gradually stop executing actions that should be taken in daily life, or do not respond to communication from other persons, apathy is a symptom that requires treatment.

To verify the effects of non-pharmacological interventions for apathy, a systematic review of 56 studies suggests that therapeutic activities, particularly those planned to match the level and interest of the individual, can be expected to be beneficial [1]. Specifically, these activities involve participant-led interactive discussions, and activities such as solving puzzles, making salad, sorting beads, woodwork, and catching ball are conducted while an occupational therapist provides guidance to the family caregivers. In Japan, receiving this treatment as a program in dementia care service seems to be a realistic measure.

A systematic review that summarizes the effects of pharmacotherapy confirms the benefit of cholinesterase inhibitors for apathy, and recommends these drugs as first-line drug for patients with dementia if there is no contraindication [2]. Memantine may also be effective.

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Search formula

Non-pharmacological therapies

PubMed search: October 2, 2015 (Friday)

#1 ("Dementia/therapy" [Majr] OR dementia [TI] OR "Alzheimer disease" [TI] OR "Alzheimer's disease" [TI] OR "vascular dementia" [TI] OR "Lewy Body" [TI] OR "frontotemporal dementia" [TI] OR "frontotemporal lobar degeneration" [TI]) AND ("nonpharmacological therapy" OR "non pharmacological therapy" OR "nonpharmacologic therapy" OR "non pharmacologic therapy" OR "nonpharmacological treatment" OR "non pharmacological treatment" OR "nonpharmacologic treatment" OR "non pharmacologic treatment" OR nonpharmacological intervention* OR non pharmacological intervention* OR nonpharmacologic intervention* OR non pharmacologic intervention* OR "nonpharmacological management" OR "non pharmacological management" OR "nonpharmacologic management" OR "non pharmacologic management" OR "validation therapy" OR "reality orientation" OR "reminiscence therapy" OR "music therapy" OR "light therapy" OR "tactile therapy" OR "aromatherapy" OR "occupational therapy" OR "exercise therapy" OR "exercise training" OR "exercise program" OR "physical exercise" OR "cognitive training" OR "rehabilitation" OR "stimulation therapy" OR "psychological therapy" OR (caregiver* AND ("psycho-education" OR intervention)) OR "dementia care service" OR "adult day service" OR "dementia day service" OR "Rehabilitation" [Mesh] OR "Phototherapy" [Mesh] OR "Exercise" [Mesh] OR "rehabilitation" [sh] OR "Psychotherapy" [Mesh] OR ("Caregivers" [Mesh] AND ("psycho-education" OR intervention)) OR "Touch" [Mesh] OR "Day Care" [Mesh]) AND ("Anxiety" [Mesh] OR anxiety [TI] OR indifference* [TI] OR "Aggression" [Mesh] OR aggression [TI] OR "Psychomotor Agitation" [Mesh] OR agitation [TI] OR "Irritable Mood" [Mesh] OR irritability [TI] OR "Delusions" [Mesh] OR delusion* [TI] OR "Hallucinations" [Mesh] OR hallucination* [TI] OR "Depression" [Mesh] OR depression [TI] OR dysphoria [TI] OR "Wandering Behavior" [Mesh] OR wandering [TI] OR "Inhibition (Psychology)" [Mesh] OR disinhibition* [TI] OR ("Sexual Behavior" [Mesh] AND inappropriate [TI]) OR "inappropriate sexual behaviour" [TI] OR "inappropriate sexual behavior" [TI] OR restlessness [TI] OR ("Motor Activity" [Mesh] AND aberrant [TI])OR "aberrant motor behaviour" [TI] OR "aberrant motor behavior" [TI] OR "Sleep Disorders" [Mesh] OR "nighttime insomnia"[TI] OR "sleep disturbance" [TI] OR "daytime napping" [TI] OR "daytime sleepiness" [TI] OR "Apathy" [Mesh] OR apathy [TI] OR "Delirium" [Mesh] OR delirium [TI] OR ((anxiety OR indifference OR aggression OR agitation OR

irritability OR delusion* OR hallucination* OR depression OR dysphoria OR wandering OR disinhibition* OR "inappropriate sexual behaviour" OR "inappropriate sexual behavior" OR restlessness OR "aberrant motor behaviour" OR "aberrant motor behavior" OR "nighttime insomnia" OR "sleep disturbance" OR "daytime napping" OR "daytime sleepiness" OR apathy OR delirium) AND (in process [SB] OR publisher [SB])))

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Pharmacotherapy
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C | Interventions for Coexisting Diseases

CQ 3C-1

How is delirium treated?

Recommendation

Always remember to prevent delirium. When delirium has emerged, treat or remove the direct causative or inducing factors. If symptoms do not respond to these interventions and treatments, consider treatment with atypical antipsychotics such as quetiapine, perospirone, risperidone, and olanzapine. Also consider hospitalization for the purposes of detailed investigations of the cause of delirium, smooth implementation of treatment, and ensuring safety of the patient. Clinical guidelines for delirium have been prepared by the Japanese Society of General Hospital Psychiatry, refer to the guidelines as needed. 2C

Comments and evidence

Since dementia is a risk factor for the development of delirium, it is necessary to be always vigilant for early detection and treatment of delirium. The background factors of delirium include the following: (1) predisposing factors (current or past history of organic brain disorder, old age); (2) precipitating factors (environmental factors such as hospitalization and noise; physical factors such as pain, dehydration, and malnutrition; sensory factors such as decreased vision and hearing; mental factors such as psychological stress and anxiety; sleep-related factors such as disrupted circadian rhythm; (3) direct factors that may induce delirium even as a single factor (stroke, electrolyte abnormality, infection, initiation or withdrawal of drug use) [1].

For treatment of delirium in dementia, refer to the clinical guidelines on delirium prepared by the Delirium Guideline Revision Group of Japanese Society of General Hospital Psychiatry [2]. First, always try to remove the precipitating factors. Also, treat the direct factor, if possible. If delirium does not improve after these treatments, consider atypical antipsychotics (quetiapine, perospirone, risperidone, and olanzapine). The former two are recommended from the viewpoint of short half-life. The latter two have the advantage of being a liquid formulation and an orally disintegrating tablet, respectively. Use haloperidol injection if intake of oral medication is difficult. Use the minimum required dose, and in principle administer in the evening. For treatment of delirium, also consider hospitalization for the purposes of detailed investigations of the cause, ensuring safety of the patient, smooth implementation of treatment, and provision of a calm environment.

In a multicenter randomized controlled trial (RCT) conducted in Japan, the frequency of delirium is reduced by taking ramelteon from the time of admission [3]. Therefore use of this drug may be considered. All of the drugs mentioned above are used off-label. When prescribing these drugs, it is necessary to explain in detail to the patients and families, and to be aware of adverse events.

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■ Search formula

PubMed search: June 23, 2015 (Tuesday)

#1 ((Dementia [Mesh] AND ("drug therapy" [subheading] OR "Drug therapy" [Mesh])) OR ("Dementia/therapy" [Mesh] AND ("Antipsychotic Agents" [Mesh] OR "Benzodiazepines" [Mesh] OR "Serotonin Uptake Inhibitors" [Mesh] OR "Antidepressive Agents" [Mesh] OR "Anticonvulsants" [Mesh] OR "Anticonvulsants" [PA] OR "Yi-Gan San" [Supplementary Concept] OR "Herbal Medicine" [Mesh] OR "Medicine, Kampo" [Mesh] OR "ramelteon" [Supplementary Concept] OR "suvorexant" [Supplementary Concept])) OR ((dementia OR "alzheimer disease" OR "alzheimer's disease" OR "frontotemporal lobar degeneration") AND (pharmacological OR drug OR medicine OR antipsychotics OR benzodiazepine OR "selective serotonin reuptake inhibitors" OR "serotonin-norepinephrine reuptake inhibitors" OR antidepressant* OR "mood stabilizer" OR anticonvulsant* OR Yokukansan OR "Japanese herbal" OR "traditional herbal" OR kampo OR ramelteon OR suvorexant OR "orexin receptor antagonist" OR "melatonin receptor agonist"))) AND ("Delirium" [Mesh]OR delirium)

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CQ 3C-2

How epilepsy including seizures should be treated in patients with dementia?

Recommendation

The former antiepileptic drugs may worsen cognitive function, and should be used with caution in older patients with dementia. Novel antiepileptic drugs are relatively well tolerated and effective if the drug titration is applied. 2C

Comments and evidence

In dementia patients, the risk of both generalized and partial seizures is six times higher than in the control group [1, 2]. Especially in Alzheimer's disease, the accumulation of amyloid β (Aβ) induces hyperexcitation of the cortical network in the hippocampus, resulting in cognitive impairment, and the hippocampus can be the focus of epileptic seizures at the same time [3, 4]. In patients with Alzheimer's disease, epilepsy with seizure focus in temporal lobe is common, and transient memory impairment tends to occur especially if cognitive decline occurs at a younger age [5]. In familial Alzheimer's disease, several cases with seizures and myoclonus have been reported [4]. Cheng et al. [6] compared the age-adjusted annual incidence of epilepsy between control and Alzheimer's disease, and reported that the risk of epilepsy is increased by 1.85 times in patients with Alzheimer's disease at 3.6 years after the onset of dementia [6].

Because epileptic seizures worsen the prognosis of patients with dementia due to the higher risk of falls, trauma, and death, appropriate treatment with anti-epileptic drugs is required. However, the semiology of seizures is often non-convulsive, subtle, and diverse, and often not recognized as seizures by the patient or the caregiver, which makes the diagnosis difficult. Therefore, once a diagnosis of epilepsy is confirmed and the risk of seizure recurrence is high, it is necessary to start antiepileptic drug with monotherapy in a small dose at first and then upwardly titrating slowly [7]. Since carbamazepine has many drug interactions and adverse effects including cardiac conduction disorder, hyponatremia, and over-sedation, it should be used with caution in older patients. Benzodiazepines, primidone, and phenobarbital are not recommended because they worsen cognitive function. Sodium valproate has little effect on cognitive function, and it is effective for convulsive seizures in older patients and for behavioral and psychological symptoms of dementia such as irritability, aggression and mood disorders.

New antiepileptic drugs (lamotrigine, levetiracetam, gabapentin, topiramate) are effective for seizures in older patients and cause few adverse events. Among them, lamotrigine and levetiracetam are effective for epilepsy in patients with amnestic mild cognitive impairment or early Alzheimer's disease [5]. In Japan, monotherapy of these drug is also indicated for the treatment of epilepsy. Rowan et al. [8] recommend lamotrigine and gabapentin as antiepileptic drugs for older people with dementia, because they have less adverse effects compared with carbamazepine. Levetiracetam has been shown to be effective and safe also in post-stroke epilepsy patients, and have less effect on cognitive function than carbamazepine [9].

In general, since older people often have lower serum albumin and liver and kidney dysfunctions, serum levels of antiepileptic drugs can be readily elevated. Therefore, monotherapy of antiepileptic drugs starting with a low dose is highly recommended. In addition, careful attention should be paid for drug interactions in older patients with dementia, because they are usually taking multiple drugs.

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Search formula

PubMed search: July 5, 2015 (Sunday)
#1 ("Dementia" [Mesh] OR dementia OR "Cognition Disorders" [Mesh] OR cognition disorder* OR cognitive disorder*) AND ("Seizures/therapy" [Mesh] OR (seizure* AND (therapy OR therapeutic OR treatment OR prophylaxis OR prevention)) OR ("Seizures" [Mesh] AND "Anticonvulsants/therapeutic use" [Mesh]) OR (anticonvulsant* AND (therapy OR therapeutic OR treatment OR prophylaxis OR prevention)))

Ichushi search: June 23, 2015 (Tuesday)
#1 (Dementia/TH OR Dementia/TI OR Cognitive impairment/TH OR Cognitive impairment/TI OR Cognitive function impairment/TI) AND (Epilepsy/TH OR Epilepsy/TI OR Epilepsy/TI) AND ((SH = Therapeutic use, treatment, drug treatment, surgical treatment, transplantation, dietary treatment, psychiatric treatment, radiologic treatment) OR Treatment/TH OR Treatment/TI OR Therapy/TI OR Preventive/TI OR Anti-convulsive agent/TH OR Anti-convulsive agent/TI OR Anti-epileptic drug/TI OR Anti-convulsive agent/TI OR Anti-epileptic drug/TI OR Anti-convulsive drug/TI OR Anti-epileptic agent/TI OR Anti-convulsive drug/TI OR Anti-epileptic agent/TI)

CQ 3C-3

What are the interventions for dysphagia (including prevention of aspiration pneumonia)?

Recommendation

To prevent the onset of aspiration pneumonia, angiotensin converting enzyme (ACE) inhibitor, amantadine, cilostazol (not covered by insurance), capsaicin, oral care, swallowing rehabilitation, chin down maneuver, maintaining sitting position for 1 hour after eating, and influenza and pneumococcal vaccination are effective.

There is no data showing the usefulness of percutaneous endoscopic gastrostomy (PEG) in preventing aspiration pneumonia or improving activities of daily living (ADL) and survival in patients with advanced stage dementia.

2D

Comments and evidence

In frontotemporal lobar degeneration and Alzheimer's disease dementia, abnormalities in eating behavior such as overeating occur due to functional impairment of the limbic system and frontal lobe, and are particularly marked in the former. Vascular dementia and dementia caused by parkinsonism often manifest impaired swallowing reflex, and aspiration pneumonia is often caused by occult aspiration at night. On the other hand, in Alzheimer's disease dementia, the swallowing reflex is preserved until the late stage of the disease, and is often maintained even in a bed confined state.

Activation of the dopamine–substance P system is important for the prevention of aspiration pneumonia. Sensory stimulation of the oral cavity through oral care increases substance P, increases the sensitivity of the cough reflex, and consequently improves the swallowing reflex [1, 2]. Administration of ACE inhibitors that suppress substance P degradation is also useful [3]. In addition, cilostazol [4] and amantadine with dopamine release effect [5] have been reported to be effective in the prevention of aspiration pneumonia. Furthermore, rivastigmine [6] and the Kampo herbal medicine "*banxia houpo tang*" [7] have been reported to improve swallowing function. Conversely, since cholinergic and dopaminergic systems act to maintain the swallowing function, drugs with anticholinergic action and dopamine antagonistic action increase the risk of aspiration pneumonia [8].

In the advanced stage of dementia, use of PEG does not show benefit regarding survival duration, improvement of quality of life (QOL), or reduction of aspiration pneumonia [9]. Systematic reviews that evaluate the effect of PEG in dementia patients with dysphagia have not found a survival-extending effect [10, 11].

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Search formula

PubMed search: July 15, 2015 (Wednesday)

#1 ("Dementia" [Mesh] OR dementia OR Alzheimer* OR "Cognition Disorders" [Mesh] OR cognition disorder* OR cognitive disorder*) AND ("Deglutition Disorders/therapy" [Mesh] OR ((deglutition disorder* OR swallowing disorder* OR dysphagia) AND (therapy OR therapeutic OR treatment OR prophylaxis OR prevention)) OR "Pneumonia, Aspiration/therapy" [Mesh] OR (aspiration pneumonia* AND (therapy OR therapeutic OR treatment OR prophylaxis OR prevention)))

Ichushi search: July 15, 2015 (Wednesday)

#1 (Dementia/TH OR Dementia/TI OR Cognitive impairment/TH OR Cognitive impairment/TI OR Cognitive function impairment/TI) AND (dysphagia/TH or dysphagia/TI OR Pneumonia-aspiration/TH or aspiration pneumonia/TI) AND ((SH = Therapeutic use, treatment, drug treatment, surgical treatment, transplantation, dietary treatment, psychiatric treatment, radiologic treatment, rehabilitation, prevention) OR Treatment/TH OR Therapeutic use/TH OR Treatment/TI OR Therapy/TI OR Prevention/TI)

CQ 3C-4

What are the interventions for eating disorder and undernutrition?

Recommendation

In Alzheimer's disease, eating difficulties may be caused by changes in eating behavior, loss of appetite, dysphagia, and autonomic disturbance. It is important to take history of the changes in body weight and quantity of food eaten; implement nutritional assessment, prevention of aspiration, and review of medications; and examine the merits and demerits of oral intake and tube feeding. 2C

Comments and evidence

Many people with dementia are affected by eating disorders, weight loss, and undernutrition.

Among people with mild Alzheimer's disease, over 30% experience some changes in eating behavior, and 16% have loss of appetite [1]. Riviere et al. [2] studied 224 people with moderate Alzheimer's disease, and observed that 26% had eating behavior disorders such as "getting up while eating" and "eating by hand". In patients with severe dementia, 80% showed weight loss, dysphagia, eating refusal, reduced food intake, and dehydration [2].

To investigate why people with Alzheimer's disease lose appetite, Ismail et al. [3] observed reduced blood flow in various regions including the anterior cingulate gyrus on blood flow SPECT, and speculated that these changes were related to appetite loss.

The adverse effects of cholinesterase inhibitors used as a treatment for Alzheimer's disease include gastrointestinal symptoms, although the symptoms are generally transient. There is a report suggesting that long-term administration of these agents may prevent weight loss [4].

In 2014, Goldberg et al. [5] conducted a systematic review on the usefulness of percutaneous endoscopic gastrostomy (PEG) for severe dementia with dysphagia (publications from 1995 to 2012), and reported no evidence that PEG prolongs survival long-term [5].

According to a review by Affoo et al. [6], while evidence suggests a possibility that dysphagia and autonomic nervous system dysfunction may occur together in Alzheimer's disease, the relationship between the two has not been clarified.

■ References

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2) Riviere S, Gillette-Guyonnet S, Andrieu S, et al. Cognitive function and caregiver burden: predictive factors for eating behaviour disorders in Alzheimer's disease. Int J Geriatr Psychiatry. 2002; 17(10): 950-955.
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■ Search formula

PubMed search: June 8, 2015 (Monday)

#1 ("Dementia" [Mesh] OR dementia) AND ("Deglutition Disorders/therapy" [Mesh] OR (dysphagia AND (therapy OR therapeutic OR treatment))) AND ("percutaneous endoscopic gastrostomy" OR PEG OR ("Endoscopy" [Mesh] AND "Gastrostomy" [Mesh] AND "percutaneous") OR "Enteral Nutrition" [Mesh] OR "tube feeding")

Ichushi search: June 8, 2015 (Monday)

#1 (Dementia/TH or Dementia/TI) AND (Eating dysfunction/TH or Eating disorder/TI) AND (Gastrostomy construction/TH OR PEG/TI OR Gastrostomy/TH OR Gastrostomy/TI OR Enteral nutrition/TH or Tube feeding/TI)

CQ 3C-5

What are the interventions for sarcopenia and frailty?

Answer

Dementia tend to coexist with sarcopenia and frailty. Resistance training may be useful in improving sarcopenia and frailty associated with dementia. C

Comments and evidence

Sarcopenia is a common pathological condition seen in old age. Sarcopenia is defined as "a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse outcomes such as physical disability, poor quality of life and death" [1]. The causes of sarcopenia include aging, reduced activity, poor nutrition, and disease [1]. Frailty is the decline of various physiological functions with ageing, and is a risk factor that leads to undesirable outcomes such as falls, hospitalization, and death.

Sarcopenia and frailty tend to occur more frequently in older people with dementia than in older adults with normal cognitive function. In recent years, the relationship between frailty and cognitive impairment has attracted attention [2].

Persons with Alzheimer's disease in a nursing home who received the dual-task intervention of walking and conversation showed less decline in physical function compared with persons given either conversation or walking intervention alone [3]. When frail persons with Alzheimer's disease living at home participated in a home-based exercise program (aerobics, strength training, and balance exercise) guided by the caregiver for 12 weeks, their hand function and lower extremity strength significantly improved compared with the control group [4]. A three-month resistance training program designed specifically for older dementia persons significantly improved muscle strength and physical function compared with the control group [5]. A cohort study of frail older adults with dementia also found that 4 weeks of resistance exercise improved muscle strength and physical functions [6]. The above evidence shows that sarcopenia and frailty may be improved in people with dementia through exercise customized for each individual.

Although there is no interventional study of nutrition therapy focused on people with dementia, nutritional supplementation for sarcopenia generally improves muscle mass and muscle strength of older people [7]. Hence, together with exercise, nutritional supplementation is important.

References

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6) Cadore EL, Moneo AB, Mensat MM, et al. Positive effects of resistance training in frailty elderly patients with dementia after long-term physical restraint. Age (Dordr). 2014; 36(2): 801-811.
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Search formula

PubMed search: June 8, 2015 (Monday)
#1 ("Dementia" [Mesh] OR dementia) AND ("Sarcopenia/therapy" [Mesh] OR(sarcopenia AND "Muscular Atrophy" [Mesh]) OR (sarcopenia AND (therapy OR therapeutic OR treatment)) OR (frailty AND (therapy OR therapeutic OR treatment)))

Ichushi search: June 8, 2015 (Monday)
#1 (Dementia/TH OR Dementia/TI) AND (sarcopenia/TI OR Sarcopenia/TH OR frailty/AL)

CQ 3C-6

What are the interventions and preventive measures for falls and fractures?

Answer

People with dementia have approximately 8 times higher risk for falls and approximately 3 times higher risk for fracture compared with people without dementia. To prevent falls, use multi-faceted interventions including treatment of underlying diseases, adjustment of drugs, exercise, walking and balance training, training wearing aids, environmental modification, and training to adjust to home environment. Also consider treatment for osteoporosis. B

Comment and evidence

In older people, fracture caused by falling is one of the main causes of confining to bed, and falls lower the ability of activities of daily living (ADL) and motivation, and also induce delirium.

People with dementia have approximately 8 times higher risk for falls and approximately 3 times higher risk for fractures compared with people without dementia [1]. Dementia patients with orthostatic hypotension have a higher frequency of falls compared to patients without orthostatic hypotension, with a hazard ratio of 2.13. For the incidence of falls, Parkinson's disease with dementia (PDD) was the highest, followed by dementia with Lewy bodies (DLB), vascular dementia, and Alzheimer's disease (AD). For PDD and DLB, the high incidence may be related to orthostatic hypotension and autonomic nervous system dysfunction [1].

A retrospective study conducted from 1988 to 2007 in the UK showed that the incidence of hip fracture was 17.4 per 1,000 people with dementia and 6.6 per 1,000 people without dementia, and the risk was 3.2 times higher in patients with dementia [2].

The guidelines for fall prevention prepared by the Orthopedic Surgery Committee of American Geriatric Society/ British Geriatric Society[3] recommends multifactorial interventions including minimization of medications, customized exercise program, treatment of vision impairment, management of orthostatic hypotension, management of arrhythmia, vitamin D supplementation, management of foot and footwear problems, modification of the home environment, and providing education and information. However, there is insufficient evidence for supporting any single or multifactorial intervention to reduce fall risk in older people with cognitive impairment. Subsequently, a meta-analysis of exercise interventions (7 randomized controlled trials) was conducted, and found that exercise interventions reduce falls in people with dementia (odds ratio, 0.68) [4].

Although people with dementia are prone to osteoporosis-derived fractures, they are often not treated with drugs for osteoporosis. Consider appropriate assessment, treatment and guidance for osteoporosis [5]. The risk of femoral neck fracture is increased in older patients with Alzheimer's disease who have vitamin K and vitamin D deficiency [6].

References

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6) Sato Y, Honda Y, Umeno K, et al. The prevention of hip fracture with menatetrenone and risedronate plus calcium supplementation in elderly patients with Alzheimer disease: a randomized controlled trial. Kurume Med J. 2011; 57(4): 117-124.

Search formula

PubMed search: June 9, 2015 (Tuesday)
#1 ("Dementia" [Mesh] OR dementia) AND ("Accidental Falls/prevention and control" [Mesh] OR (accident* AND (falls OR fall) AND (prevention OR preventing)))

Ichushi search: June 9, 2015 (Tuesday)
#1 (Dementia/TH OR Dementia/TI) AND (Falls/TI OR Falls/TH) AND (Accident prevention/TH OR (SH = Prevention) OR Prevention/TI OR Prevention/TI)

CQ 3C-7

What are the interventions for pressure ulcers?

Answer

Currently, there is no clear evidence for the therapeutic or preventive effects of supplements, tube feeding, and parenteral nutrition for pressure ulcers, and there is a lack of high-level evidence for comprehensive management. For local treatment, refer to the "Evidence-based Guidelines for Local Treatment of Pressure Ulcers" published by the Japanese Society of Pressure Ulcers. 2C

Comment and evidence

Pressure ulcers are necrosis of ischemic cutaneous or subcutaneous tissues caused by blood circulation failure due to continuous pressure on localized skin area. Pressure sores are formed frequently in sites with bone protrusion and little subcutaneous fat tissue, and are strongly affected by ageing, undernutrition, motor paralysis, joint contracture, and urinary and fecal incontinence. Pressure ulcers tend to occur when activities of daily living (ADL) decrease accompanying progression of dementia.

Although it has been reported that an increase in number of pressure ulcers is related to higher risk of death in people with advanced dementia [1], there is currently no clear evidence for the therapeutic or preventive effects of supplements, tube feeding, and parenteral nutrition for pressure ulcers [2].

A meta-analysis has indicated that the presence of increasing pain is more useful than purulent exudate, heat, and redness for the diagnosis of pressure ulcer infection [3].

■ References

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■ Search formula

PubMed search: June 9, 2015 (Tuesday)
#1 ("Dementia" [Mesh] OR dementia) AND ("Pressure Ulcer" [Mesh] OR "bed sore" OR bedsore OR "decubitus position" OR "decubitus ulcer" OR "pressure sore" OR "pressure ulcer")

Ichushi search: June 9, 2015 (Tuesday)
#1 (Dementia/TH OR Dementia/TI) AND (Pressure ulcer/TI OR decubitus ulcer/TH)

CQ 3C-8

What are the approaches to treat acute physical illness?

Answer

In people with dementia, acute physical illness is difficult to detect because typical symptoms are frequently absent and the patients cannot complain. In Alzheimer's disease, as dementia becomes severe, the number of hospital admissions increases and mortality also increases. C

Comment and evidence

There is still no evidence for acute physical illness in people with dementia.

According to the 2014 data of the Fire and Disaster Management Agency of Japan [1], 61.6% (2.03 million) of the patients transported to emergency department were elderly, which doubled the percentage of 28.8% in 1993. Among these cases, cerebrovascular system, heart disease, and respiratory system accounted for 11% each. For people with dementia transported to emergency department, the major causes are pneumonia, stroke, fractures of lower limbs, bruise or sprain, ileus, and gastrointestinal bleeding [2, 3]. In addition, more than 70% of 107 cases of suffocation are secondary to neurological disorders including dementia, cerebral infarction, schizophrenia, and Parkinson's disease [4]. Therefore, neurological disorders including dementia can be considered to be risk factor of suffocation. People with Alzheimer's disease have more hospital admissions than the general elderly population, and people with severe Alzheimer's disease are hospitalized 2.3 times more than the general elderly population [5]. Moreover, people with dementia who require emergency admission have high death rate [6].

When a person with dementia is admitted to the hospital, make sure that the patient is placed in a room that is within watching distance from the nurses, and avoid rooms near the entrance and exit of the ward. Ensure safety by using measures such as a bed exit sensor and a protective cover to prevent needle removal. Provide care with consideration to monitor changes in patient's symptoms or conditions. People with dementia are prone to develop delirium due to anxiety and fear as a result of change in environment and physical distress. As a measure for delirium, provide care with special considerations for patients with dementia: ask family members to accompany the patient, have the same nurse in charge of the patient, explain the nurse call and location of the toilet in simple language, tell patient the status repeatedly, resolve pain / anxiety / insomnia, and do not restrain actions. Consider medication as necessary.

When dementia is advanced, detection of urinary tract infection is difficult because typical symptoms are frequently absent, and the patients cannot complain[7].

References

1) Homepage of Fire and Disaster Management Agency. Status of emergency actions. http://www.fdma.go.jp/neuter/topics/eldList9_3.html (In Japanese)
2) Kimbara, Y, Yamada H, Kitagawa Y, et al. A survey of clinical characteristics of medical and psychiatric comorbidity patients at Emergency Medical Center, Nagoya Ekisaikai Hospital. Journal of Japanese Society for Emergency Medicine (Nihon Rinsho Kyukyu Igaku Gakkaishi) 2014; 17(5): 675-679. (In Japanese)
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7) D'Agata E, Loeb MB, Mitchell SL. Challenges in assessing nursing home residents with advanced dementia for suspected urinary tract infections. J Am Geriatr Soc. 2013; 61(1); 62-66.

Search formula

PubMed search: June 10, 2015 (Wednesday)
#1 ("Dementia" [Mesh] OR dementia) AND ("Pneumonia/therapy" [Mesh] OR (pneumonia AND (therapy OR therapeutic OR treatment)) OR "Acute Disease/therapy" [Mesh] OR "Emergency Medicine" [Mesh])

Ichushi search: June 10, 2015 (Wednesday)
#1 (Dementia/TH OR Dementia/TI) AND (Pneumonia/TH OR Pneumonia/TI OR Acute illness/TH OR Acute illness/TI OR Emergency medicine/TH)

CQ 3C-9

How should decisions be made regarding invasive examinations and treatments including dialysis and dental treatment?

Answer

When a person with dementia requires dialysis, refer to the "Proposal for the shared decision-making process regarding initiation and continuation of maintenance hemodialysis" published by the Japanese Society for Dialysis Therapy. Dental treatment and oral care are essential for people with dementia, and providing preventive and continuous oral hygiene management is recommended. D

Comments and evidence

As of the end of 2010, 9.9% of the total dialysis population had dementia (23,000 of 234,000 of all dialysis patients, excluding those unknown and undocumented). For dialysis patients aged 90 years or above, 25-35% also have dementia and require support [1]. As the number of people with dementia who require dialysis increase, there is also an increase in number of patients who stand up or become restless during dialysis, impeding safe execution of dialysis. There are limits to sedation and caregiver attendance.

The "Proposal for the shared decision-making process regarding initiation and continuation of maintenance hemodialysis" in Japan are recommendations on providing appropriate information to patients, giving support to patients when making their own decisions, and obtaining written informed consent [2]. Among the situations that require review of whether to suspend dialysis, "extracorporeal circulation cannot be performed safely without restrain and sedation using medications" and "oral intake not possible" and included, and these situations may arise in people with dementia.

As dementia emerges, self-cleaning behavior is impaired, and the state of oral hygiene worsens. People with dementia have more caries and periodontal diseases than healthy people [4]. Evidently oral care is important for the prevention of aspiration pneumonia. In the clinical setting, patients with dementia often discontinue dental treatment because they do not understand the meaning of the treatment. As a result, some patients require treatment under general anesthesia since the inflammation cannot be controlled. Before dementia deteriorates to the above states, providing continuous preventive oral hygiene management to people with dementia is recommended.

References

1) Japanese Society for Dialysis Therapy. Data in Japan compiled by the Statistical Study Committee. http://docs.jsdt.or.jp/overview/index2011.html (In Japanese)
2) Watanabe Y, Hirakata H, Okada, et al. Proposal for the shared decision-making process regarding initiation and continuation of maintenance hemodialysis. Ther Apher Dial 2015; 19Suppl 1: 108-117.
3) Wu B, Plassman BL, Crout RJ, et al. Cognitive function and oral health among community-dwelling older adults. J Gerontol A Biol Sci Med Sci. 2008; 63(5): 495-500.

Search formula

Trauma

PubMed search: June 10, 2015 (Wednesday)

#1 ("Dementia" [Mesh] OR dementia) AND ("Wounds and Injuries/therapy" [Mesh] OR ((fracture OR fractures OR trauma OR traumas) AND (therapy OR therapeutic OR treatment))

Ichushi search: June 10, 2015 (Wednesday)

#1 (Dementia/MTH OR Dementia/TI) AND (Wound and injury/MTH OR Fracture/TI OR Trauma/TI)

Invasive examinations

PubMed search: June 12, 2015 (Friday)

#1 ("Dementia/diagnosis" [Mesh] OR (dementia AND (diagnosis OR diagnostic))) AND ("Endoscopy" [Mesh] OR "Endoscopes" [Mesh] OR endoscopy OR endoscopic OR endoscope* OR "invasive examination")

Ichushi search: June 12, 2015 (Friday)
#1 (Dementia/TH OR Dementia/TI) AND (Endoscopy/TH OR ((Endoscope/TH OR Endoscope/AL) AND (Diagnosis OR Examination)) OR (Invasive examination/AL NOT (Non-invasive examination /AL OR Non-invasive examination/AL)))

Surgery or dialysis
PubMed search: June 12, 2015 (Friday)
#1 ("Dementia" [Mesh] OR dementia) AND ("surgical indication" OR operability OR "Renal Dialysis" [Mesh] OR dialysis OR hemodialysis OR dialyses OR hemodialyses) OR "Dementia/complications" [Mesh] AND ("Surgical Procedures, Operative" [Majr] OR "surgery" [Subheading]) AND "Risk" [Mesh]

Ichushi search: June 12, 2015 (Friday)
#1 (Dementia/TH OR Dementia/TI) AND (Surgical indication/AL OR ((Surgery/MTH OR(SH = Surgical therapy) OR hemodialysis/TH OR Dialysis/TI) AND Risk/TH))

CQ 3C-10

What are the interventions for edema?

Answer

In addition to interventions for immobility due to long-term bed confinement and undernutrition, provide treatments for underlying diseases as well as for concomitant diseases such as skin infections and pressure ulcers. Pay attention to the possibility of edema induced by drugs such as *Yokukansan* and antipsychotics, and consider discontinuation or dose reduction of the causative drugs as appropriate. C

Comments and evidence

Diseases that cause edema commonly seen in older people include: (1) causes of systemic edema; congestive heart failure, renal disease, hepatic disease, and hypothyroidism, and (2) causes of localized edema; cerebrovascular disroder, deep vein thrombosis, knee osteoarthritis, and malignant tumors. Edema becomes more common with ageing, due to variability of capillary pressure, changes in interstitial components and reduced tissue pressure, lowered plasma osmotic pressure due to decreased serum albumin, and increased capillary permeability.

In people with dementia, it is necessary to consider the possibility of edema induced by drugs including antipsychotic drugs [1] and *Yokukansan* [2], and to consider discontinuation or dose reduction of the causative drug as appropriate [2]. According to an observational study that examined the safety and efficacy of long-term use of *Yokukansan* in 163 patients who had been prescribed *Yokukansan* for more than 6 months, edema appeared in 10.8% of the patients and many recovered by discontinuing *Yokukansan* with no need for treatment [2].

Treatment of edema involves the treatment of underlying diseases identified by diagnosis of the cause as well as treatment of coexisting illnesses such as skin infections and pressure ulcers. Especially in older people, extreme salt restriction and water restriction to reduce edema may cause rapid intravascular dehydration, because of the low water and sodium retention ability in older people. When using diuretics, monitor body weight to ensure that fluid is removed gradually. In addition, since diuretics tend to disrupt electrolyte balance and cause hypotension, hypernatremia or hyponatremia, and hypokalemia, close monitoring of blood electrolyte levels and urinary electrolyte excretion is necessary.

■ References

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2) Okahara K, Ishida Y. Safety and efficacy evaluation of long-term treatment with a traditional Japanese medicine, Yokukansan, on behavioral and psychological symptoms of dementia. Dementia Japan. 2012; 26: 196-205. (In Japanese)

■ Search formula

PubMed search: June 12, 2015 (Friday)
#1 ("Dementia" [Mesh] OR dementia) AND ("Edema" [Mesh] OR edema)

Ichushi search: June 12, 2015 (Friday)
#1 (Dementia/TH OR Dementia/TI) AND (Edema/AL OR Edema/TH)

CQ 3C-11

What are the interventions for urinary disorder?

Answer

Many people with dementia have functional urinary incontinence and urge urinary incontinence. Behavioral therapy can be expected to be effective for urinary disorder, after ruling out underlying urological disorder. On the other hand, there is no sufficient evidence for pharmacotherapy in people with dementia. C

Comments and evidence

Carefully investigate the presence or absence of organic diseases causing urinary disorder, and rule out a diagnosis of such diseases. In people with dementia, functional urinary incontinence and urge urinary incontinence are common. Treat these conditions by referring to guidelines (https://minds.jcqhc.or.jp/) [1-3].

1. Behavioral therapy [4-6]

The following interventions are recommended: (1) toileting assistance: [1] toileting at fixed time, [2] toileting according to an established voiding pattern, and [3] reeducating toileting habit; (2) bladder training; and (3) pelvic floor muscle rehabilitation for stress urinary incontinence.

2. Pharmacotherapy for urinary disorder

For urge urinary incontinence in women, use anticholinergic drugs (propiverine and tolterodine). For prostatic hypertrophy in overflow urinary incontinence, use the sympathetic selective α1 inhibitors (tamsulosin and naftopidil). For neurogenic bladder, use cholinergic agonists (muscarinic receptor agonists; bethanechol). Attention should be paid to aggravation of constipation and cognitive decline caused by anticholinergic drugs [7], and orthostatic hypotension caused by α1 inhibitors.

For overactive bladder with major symptoms of urinary urgency, urge incontinence, and frequent urination, use selective muscarinic receptor antagonists (anticholinergic drugs) including fesoterodine, tolterodine, solifenacin, imidafenacin, and oxybutynin; and the β_3 receptor agonist mirabegron [3]. Oxybutynin is highly fat-soluble and crosses the blood-brain barrier, and the possibility of this drug of causing cognitive impairment has been suggested [8]. In addition, combined use of cholinesterase inhibitor and anti-cholinergic drug causes significant decline in activities of daily living compared with cholinesterase inhibitor monotherapy [9].

3. Other treatment methods [1]

The following interventions have been recommended: (1) modify the environment depending on cognitive function and physical function; (2) modify clothes; (3) use urinary catheter, suprapubic catheter, external urine receptacle, or urine absorbent product; (4) use of bladder support device has been proposed; and (5) if urinary incontinence is detected, wipe the genital area promptly to maintain cleanliness.

4. Drug-induced urinary disorder

Tricyclic antidepressants should be avoided as much as possible in male patients with urinary disorder [10]. Among the drugs for Parkinson's disease, levodopa is recommended, whereas trihexyphenidyl and biperiden may cause urinary disorder.

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Search formula

PubMed search: June 12, 2015 (Friday), July 18, 2015 (Saturday)
#1 ("Dementia" [Mesh] OR dementia OR alzheimer* [TI]) AND ("Urinary Incontinence/therapy" [Mesh] OR "Urinary disorders/therapy" [Mesh] OR "Urinary Bladder Diseases/therapy" [Mesh] OR "Dysuria/therapy" [Mesh] OR (("urinary incontinence" OR urinary disorder* [TI] OR urinary incontinence* [TI] OR urinary bladder disease* [TI] OR bladder dysfunction* [TI] OR neurogenic bladder* [TI] OR dysuria [TI]) AND (therapy OR therapeutic OR treatment OR management OR care OR training OR intervention)))

Ichushi search: June 12, 2015 (Friday), July 18, 2015 (Saturday)
#1 (Dementia/TH OR Dementia/TI) AND (urinary disorder/TH OR urinary disorder/TI OR Urinary incontinence/TI OR Bladder disease/TH OR Bladder disease/TI OR Micturition pain/TH OR Micturition pain/TI OR Neurogenic bladder/TI OR Overactive bladder/TI)

CQ 3C-12

What are the interventions for constipation?

Answer

Constipation is a common disease among people with dementia, and may impair quality of life (QOL) and cause delirium. Differentiate constipation from organic diseases, and use laxatives when diet (high fiber foods) and exercise do not improve the constipation. C

Comments and evidence

Constipation impairs QOL of people with dementia, causes irritability, decreases appetite, and may even result in delirium. The rates of constipation by subtype of dementia are 43% in dementia with Parkinson's disease, 28% in Lewy body disease, and 26% in vascular dementia, and were all higher than the rate of 2% in controls; whereas the rate is 3% in Alzheimer's disease and not significantly different from controls [1].

Constipation becomes more common with aging, due to weakness of the pelvic floor muscles, autonomic disturbances, and abnormalities in the colon wall. Constipation is classified into functional (atonic, convulsive, rectal), organic, symptomatic (such as diabetes and cerebrovascular disorder), and drug-induced. Atonic constipation is the most common, and is classified as functional constipation. Organic constipation is caused by colon cancer or scarring. Medications associated with constipation include anticholinergic drugs, antidepressants, antipsychotic drugs, antiparkinsonian drugs, antihistamines, diuretics, and opioids [2]. Symptoms of nausea/vomiting, abdominal distension, and retention of feces and gas suggest ileus. Change in stool caliber, occult blood in stool, bloody stool, iron deficiency anemia, and weight loss are signs of suspected organic constipation [2].

After ruling out the above conditions, use non-pharmacological interventions such as lifestyle modification and diet therapy. Recommend patients to (1) eat a fiber-rich diet, (2) keep regular eating and defecation habits, and (3) do walking exercise. For convulsive constipation, it is important to remove stress. For atonic constipation, advice patients to drink sufficient water to prevent hard stool, and to take water-soluble vitamins such as vitamins B_1 and B_2, as well as to increase bifidobacteria in the bowel. If there is no improvement despite the above interventions, prescribe pharmacotherapy. Laxatives include osmotic laxatives (magnesium oxide), colonic stimulants (such as senna, sennoside, *Daio*, and sodium picosulfate), chloride channel activator (lubiprostone) that promotes water secretion in the intestinal tract, *Daikenchuto* suppository, and enemas. Select medications according to the number of defecations and the nature of the stool.

Although enema is widely used, the rates of complications such as perforation, hyperphosphatemia, and sepsis are particularly high in older patients, and should be used with caution [3].

References

1) Allan L, McKeith I, Ballard C, et al. The prevalence of autonomic symptoms in dementia and their association with physical activity, activities of daily living and quality of life. Dement Geriatr Cogn Disord. 2006; 22: 230-233.
2) Lindberg G, Hamid SS, Malfertheiner P, et al. World Gastroenterology Organisation global guideline: Constipation- a global perspective. J Clin Gastroenterol. 2011; 45(6): 483-487.
3) Niv G, Grinberg T, Dickman R, et al. Perforation and mortality after cleansing enema for acute constipation are not rare but are preventable. Int J Gen Med. 2013; 6: 323-328.

Search formula

PubMed search: June 12, 2015 (Friday), July 18, 2015 (Saturday)
#1 ("Dementia" [Mesh] OR dementia OR alzheimer* [TI]) AND ("Constipation/therapy" [Mesh] OR "Colonic Diseases, Functional/therapy" [Mesh] OR ((constipation [TI] OR bowel dysfunction* [TI] OR colonic disease* [TI] OR neurogenic bowel*[TI]) AND (therapy OR therapeutic OR treatment OR management OR care OR training OR intervention)))

Ichushi search: June 12, 2015 (Friday), July 18, 2015 (Saturday)
#1 (Dementia/TH OR Dementia/TI) AND (Constipation/TH OR Constipation/TI OR Defecation disorder/TH OR Defecation disorder/TI OR Colonic disease-functional/ TH OR Functional colonic disease/TI OR Neurogenic bowel/TI OR irritable colon/TI)

CQ 3C-13

How should diabetes, hypertension and other lifestyle-related diseases be managed?

Recommendation

Individualized approach to diabetes control is recommended, with consideration of the severity of dementia and physical dysfunction, coexisting diseases, frailty, and other factors. Although there is little evidence regarding the effects of antihypertensive treatment for hypertensive patients with dementia, treatment that does not excessively reduce blood pressure should be considered. 2C

Comments and evidence

It has been pointed out that lifestyle-related diseases (or vascular risk factors) such as hypertension, diabetes, dyslipidemia, and obesity that coexist with dementia may potentially modify the progression of cognitive dysfunction. Proper treatment of vascular risk factors accompanying Alzheimer's disease dementia has been shown to mitigate the deterioration of Mini Mental State Examination (MMSE) score [1].

For glycemic control in older diabetic patients who have developed dementia, set the treatment target considering the activities of daily living (ADL), coexisting diseases, and risk of severe hypoglycemia. Hypoglycemia, falls and fractures increase when HbA1c is less than 7.0%; and cognitive decline, frailty, and geriatric syndrome increase gradually when HbA1c exceeds 8.0%. In older people with diabetes, setting HbA1c target for individual patient is recommended, taking into consideration not only the presence or absence and severity of dementia, but also the coexisting diseases, basic ADL (BADL) and instrumental ADL (IADL), frailty, and risk of severe hypoglycemia [2]. Current recommendation is HbA1c 7.0% to below 7.5% for older people with normal cognitive and physical functions, below 8.0% for mild to moderate dementia, and below 8.5% for moderate to severe dementia or severely impaired physical function. Furthermore, according to the proposal of the Joint Committee in Japan, lower limits of the targets have been set to avoid hypoglycemia in patients using drugs for which severe hypoglycemia is a concern (such as insulin, sulphonylureas, and glinides).

There is little evidence for the effect of antihypertensive agents in hypertensive patients with dementia. An observational study finds that antihypertensive therapy prevents the progression of mild cognitive impairment to Alzheimer's disease dementia [3]. Antihypertensive treatment should be considered [4]. However, although there are no descriptions for the recommended blood pressure targets for older people with frailty or dementia, care should be taken not to excessively lower blood pressure in older people with dementia receiving antihypertensive treatment [5].

■ References

1) Deschaintre Y, Richard F, Leys D, et al. Treatment of vascular risk factors is associated with slower decline in Alzheimer disease. Neurology. 2009; 73(9): 674-680.
2) The Japan Diabetes Society / Japan Geriatrics Society Joint Committee on Improving Care for Elderly Patients with Diabetes. Glycemic targets for elderly patients with diabetes. 2016. (In Japanese)
3) Li J, Wang YJ, Zhang M, et al. Vascular risk factors promote conversion from mild cognitive impairment to Alzheimer disease. Neurology. 2011; 76(17): 1485-1491.
4) Japan Society for Hypertension Committee for Guidelines for the Management of Hypertension. Guidelines for the Management of Hypertension 2014 (JSH 2014). Tokyo: LifeScience Shuppan; 2014. (In Japanese)
5) Mossello E, Pieraccioli M, Nesti N, et al. Effects of low blood pressure in cognitively impaired elderly patients treated with antihypertensive drugs. JAMA Intern Med. 2015; 175(4): 578-585.

■ Search formula

PubMed search: July 3, 2015 (Friday)
#1 ("Dementia/prevention and control" [Majr] OR (dementia [TI] AND (prevent* OR control*)) OR "Cognition Disorders/prevention and control" [Majr] OR ((cognition disorder* [TI] OR "cognitive dysfunction" [TI]) AND (prevent* OR control*))) AND ("Diabetes Mellitus" [Mesh] OR "Hypertension" [Mesh] OR (("diabetes mellitus" [TI] OR hypertension [TI])) OR "Life Style" [Majr] OR lifestyle related disease* [TI] OR lifestyle disease* [TI])

Ichushi search: July 3, 2015 (Friday)
#1 (Dementia/MTH OR Dementia/TI OR Cognitive impairment/MTH OR Cognitive impairment/TI) AND ((SH = Therapeutic use, treatment, drug treatment, surgical treatment, transplantation, dietary treatment, psychiatric treatment, radiotherapy, rehabilitation, prevention)OR Pharmacotherapy/TH OR Pharmacological effect/TH OR Treatment/TI OR Therapy/TI OR Control/TI OR Prevention/TI) AND (Lifestyle related disease /TH OR Lifestyle related disease /TI OR Diabetes/TH OR Diabetes/ TI OR Hypertension/TH OR Hypertension/TI)