

Treatment of Dementia Symptoms: Scoping Review of Complementary and Alternative Medicine Approaches

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Abstract

Aim: This article presents an overview of complementary and alternative medicine approaches (CAM) to treat symptoms of dementia.

Method: Retrieving of studies from several bibliographic databases (January 1998 to March 2020) applying pre-specified selection criteria and methodological quality assessment.

Results: CAM approaches reduce symptoms of dementia, slow down the progression, and create relief for patients, while not intending to prevent and cure dementia. Psychological interventions are helpful for families to establish more and better interactions with patients. Traditional Chinese medicine (acupuncture and Chinese herbal medicine) is promising strategies to treat memory loss. Homeopathy might be effective in treating symptoms of dementia. Light therapy reduces sleep deprivation, depression and agitation. Aroma & music therapy improve quality of life and recalling thoughts and feelings. Nutrition shows variant effects on dementia symptoms and development of AD, such as with folate-rich foods, low-fat dairy products, and intake of fish or omega-3 fats. Red grapes show a protective effect on AD and VaD. Exercises enhance memory. Controlled Multisensory Therapy (Snoezel therapy) shows short-term effects on mood and behaviour.

Conclusion: CAM is an alternative for conventional treatments, like medicines to relieve symptoms, however good CAM trials are lacking. Analysed studies were of low quality, having no control groups, small samples, and only case and animal studies. Research on a combination of conventional and CAM is needed to show the additional effects on conventional treatments.

Keywords: Dementia; Complementary and Alternative Medicine (CAM); Psychological interventions; Traditional Chinese medicines; Homeopathy; Light Therapy; Aromatherapy; Music Therapy; Nutrition; Exercise; Snoezel therapy

Introduction

In 2017, 50 million people worldwide were diagnosed with dementia, a statistic that is increasing annually due to aging populations [1]. The ICD-10 definition of dementia stresses that dementia is a syndrome due to disease of the brain, usually of a chronic and progressive nature, in which there is deterioration in cognitive function beyond what might be expected from normal aging. It affects memory, thinking, orientation, comprehension, calculation, learning capacity, language, judgement and sleeping. Impairment of cognitive function is commonly accompanied and occasionally preceded by deterioration in emotional control, social behaviour or motivation, and influences a person's entire daily life by a severe reduction of daily activities [2-4].

The disease itself is not discussed by paying a lot attention to the pathophysiology, epidemiology, several types of dementia and conventional treatment, because that is already published elsewhere [5]. The main aim of this scoping review is to describe the application of Complementary and Alternative Medicine (CAM) approaches to symptoms of dementia.

CAM

CAM refers to a group of diverse medical and healthcare systems and practices that are not considered to be part of the conventional treatments [6,7]. CAM consists of five different categories and combinations of them: alternative medical systems (homeopathy and traditional Chinese medicine), mind-body interventions (music therapy, meditation and hypnotherapy), biologically based therapies (vitamins and herbs), manipulative & body-based methods (massages) and energy-oriented therapies (therapeutic touch, Reiki) [7,8].

Some complementary psychological interventions part of CAM also exists, often applied to people with dementia and their family members. There has been a growing interest in the use of CAM therapies, because the conventional treatments are often perceived as ineffective [7].

Methods

Search and scoping

The databases PubMed, Scopus, Google Scholar, and Cochrane Library were searched for documents dated between January 1998 and March 2020 and restricted to papers and reviews written in English. In January 2019, we selected the first 15 articles from the databases and a second search was done in March 2020 to update the references. Additional papers were identified by searching the reference lists from the retrieved studies and reviews. Five independent reviewers (the first five listed authors) screened the publications that were relevant and trustworthy according to the abstracts. Quality was assessed based on the relevance to the topic, the type of study, the number of participants in the study, the presence of a control group, and the date of publication.

Many articles were excluded for a variety of reasons; they had not been conducted on dementia patients or dementia models, they were descriptive and anecdotic articles, they were not relevant to the therapies discussed, they contained unclear interventions, or they used a small number of patients. The terms of the search strategy were: dementia, CAM, psychological interventions, cognitive behavioural therapy, depression, interpersonal psychodynamic therapy, counselling, anxiety, acupuncture, Chinese herbal medicine, huperzine A, Alzheimer's disease, homeopathy, lycopodiumclavatum, ignatiaamara, light therapy, aromatherapy, lavender, rosemary, music therapy, cognition, nutrition, snoezelen, physical activity and exercises.

These were also used in multiple combinations with each other, using terms both with and without 'and'.

Studies found

Table 1 shows the number of studies found and included in our scoping review. The following symptoms were mentioned: anxiety, depression, inadequate behaviour, social relationships, spatial learning, memory, cognitive functioning, quality of sleep, night-time awakening, agitated behaviour, relaxation, emotional wellbeing, apathy, loss of decorum, happiness, focussed, and spontaneous talking. The number of found studies are mainly (>300) applying psychological interventions, traditional Chinese medicine, music therapy, nutrition, and exercises.

Results

Psychological Interventions

Psychological interventions may help to lower anxiety and depression. As complementary interventions, they are currently not incorporated into conventional treatments of dementia and can be applied as alternatives for drugs, like Cognitive Behavioural Therapy (CBT), Interpersonal Psychodynamic Therapy (IPT) and counselling, aiming to change the thoughts and behaviour of patients by conversation, although the focus is different in each kind of therapy [9].

Type of therapies	Studies found	Studies used
Psychological interventions	51.000 about counselling	1
	11.500 about interpersonal psychodynamic therapy	2
	167.000 about cognitive behavioural therapy	4
Traditional Chinese medicine	6.030 about huperzine A	3
	232 about acupuncture	6
Homeopathy	46 about lycopodiumclavatum	2
	21 about ignatiaamara	1
Light therapy	871	10
Aromatherapy	28	3
Music therapy	669 on music therapy in general and 254 about cognition	4
Nutrition	3955 about nutrition and dementia	4
	79 about dairy and dementia	2
Exercises	3148	3
Snoezel therapy	54	9

Table 1: The number of studies found and included in the review.

Cognitive Behavioural Therapy (CBT): The core of CBT is that negative thoughts and feelings can keep patients in a vicious cycle. The aim is to get them out of this circle by talking about their feelings so that patients can note how negativity influences their lives [10]. The main goal is to change thinking and behaviour patterns to deal with

emotional burdens due to dementia [11]. CBT is an effective and practical method to reduce anxiety and depression in patients with mild to moderate dementia, alongside their usual treatment [12]. The same effects on the depression of patients and this effect were maintained in the follow-up measure [13]. A pilot study conducted by

Stanley et al. found a decrease in anxiety and an increase in the quality of life in dementia patients after receiving 3 months of CBT [14]. However, significance was lost at 6 months. This was probably due to the pilot nature of the trial. Therefore, we conclude that CBT can be considered as a complementary approach to the current treatment policy of depression and anxiety in patients with Alzheimer's Disease (AD).

Interpersonal Psychodynamic Therapy (IPT): In IPT, the focus is on the patient's problems with other people and feelings linked to problems in the past [15]. There is no evidence to introduce IPT as a general treatment for emotional problems in dementia. However, the treatment may improve the coping of caregivers with the symptoms of AD [16].

Therapeutic counselling: Therapeutic counselling consists of clarifying problems, describing the future and changing behaviour after counseling. Unlike CBT and IPT, this kind of therapy is focused on the future [17]. In a meta-analysis, it was found that counselling may benefit people with dementia by reducing symptoms of depression and anxiety, which improves their psychological well-being [9].

To conclude, psychological interventions help patients and caregivers with any form of dementia to reduce and cope with depression and anxiety, thus improving their quality of life. More research is needed to optimize psychological interventions.

Traditional Chinese Medicine

Acupuncture and Chinese herbal medicine are part of traditional Chinese medicine, based on common concepts, like the harmony between two opposing forces, yin and yang. Imbalance may result in diseases [18].

Acupuncture: Acupuncture intends to treat Vascular Dementia (VaD), based on two theories. One theory is that biomolecules can be released by inserting a needle into an acupoint [19]. Another theory is that the imbalance of electrical properties at the acupoint is restored with acupuncture [20].

Ye et al. found studies (in mouse models) on anti-oxidizing, anti-apoptotic and anti-inflammatory effects, applying multiple acupoints [21]. The most selected one was acupoint GV20, also known as Baihui, located on top of the head. This acupoint reduces the oxidative stress, apoptosis, neuroinflammation, regulates glucose metabolism, modulates neurotransmitters, and improves synaptic plasticity as well as blood vessel functions. The effects depend on the acupoints used, since some can lead to either enhanced or reduced expression of proteins [21]. A meta-analysis on the effectiveness of acupuncture on humans compared to conventional medication treatments such as donepezil [22]. Acupuncture caused a significant increase of effectiveness based on the efficacy rate, Mini-Mental State Examination, Activities of Daily Living (ADL) Scale and Alzheimer's disease Assessment Scale-Cognition. However, due to the poor quality of the studies, the results should be used with caution. Furthermore, acupuncture has yet to be compared to control groups who received either placebo or no treatment [22].

More research is needed on the long-term effects, because acupuncture is a promising strategy, but the quality of current research on humans is poor compared to mice studies.

Chinese herbal medicine: Chinese herbal medicine is used for plants as well as minerals and animal products. Currently, most studies are

done on the separated herbs. By combining herbs, synergic interactions can occur [18].

Huperzine A (HupA), an alkaloid found in the club moss *Huperziasserrata*, is a reversible inhibitor of Acetylcholinesterase (AChE). HupA can reduce neuronal cell death caused by excess glutamate and improves cognitive functions and quality of life in patients with AD [18]. Of the patients treated with HupA, 58% showed significant improvement in memory over baseline tests, in comparison with placebo, only 36% showed improvement over baseline tests [23,24]. HupA showed improvement in cognitive and memory functions for people with AD or VaD [25].

Based on the studies found, HupA is an important candidate for potential treatment for AD and VaD. More research is needed to implement HupA in standard therapy.

Homeopathy

Homeopathy is a solution of a compound diluted by up to 1060 that stimulates self-healing abilities of the body; however, the mechanism has not been identified. *Lycopodiumclavatum* (Lyc) was found to have an increase in the cerebral blood flow (CBF) [26,27]. Increase in CBF and ACh levels due to Lyc 200c may result in an improvement in learning and memory [27]. Homeopathic mother tincture of *Gelsemium* (1 mg/kg) may help to improve learning, memory deficit and brain oxidative damage by inhibiting AChE and BACE1, and up regulating of endogenous antioxidant (GSH) defence in mice models [28]. *Ignatiaamara* used at 200c dilution, can block the glycine receptor, relieving anxiety and depression symptoms associated with dementia [29,30]. Other homeopathic treatments include *Nux Vomica* for treatment of paranoia or *Mercurius* for impaired memory, but most are not yet tested in dementia patients [31].

So, symptoms of dementia can be alleviated using homeopathy, but so far only found in animal models. Homeopathy cannot be recommended as a complementary treatment, because there is not enough evidence of effectiveness in humans.

Light therapy

Light therapy is used to treat sleep, mood and behaviour disturbances. The applied types of light depend on the moment of the day [32]. Patients can be exposed to bright light in the morning and blue light in the evening, reducing nocturnal sleep disturbance [33]. Light therapy may work by affecting the suprachiasmatic nucleus (SCN), in which the biological clock is located, which regulates the sleep/wake-cycle. In AD, the SCN is damaged. By stimulating it with light at specific times during the day, it can be activated, resulting in less sleepiness and more wakefulness [34].

Bright light therapy: Forbes et al. reviewed several studies of bright light therapy. They only found an effect on the quality of sleep, probably induced by a significant reduction in night-time awakenings, an effect that was enhanced in studies with morning-therapy [32]. The frequency and duration of treatment differed quite a lot between the studies (2,500 to 10,000 lux for 0.5 to 2 hours). Hence, more research on the frequency, time of day and duration of bright light therapy is needed [32].

A positive effect on depression too, not only on sleep quality [35]. Patients were exposed to bluish-white lights (300-400 lux), incorporated into their rooms for four weeks. A positive effect on global sleep scores was found. Furthermore, they showed a decrease in

depression and agitated behaviour. A tailored lighting intervention in an RCT, which showed the same positive effects on patients with moderate to late-stage AD and related dementias [36].

Bright light therapy was equally effective for mild or moderate and severe dementia, while the sleep quality of patients with severe dementia showed more improvement than in mild or moderate dementia [37]. However, light therapy only has a positive effect on patients with mild or moderate AD [37,38]. The nocturnal sleep of patients with dementia with Lewy bodies and VaD was not improved. They suggested that bright light therapy is effective for patients with AD in the early stages. This study, however, was conducted without the inclusion of a control group, using a small number of patients.

There seems to be discordance about the effects of bright light, but it is trending to a positive effect [39]. More research is needed with both larger patient groups and control groups, as Mitolo et al. also concluded after their systematic review [39].

Flashing light therapy: Flashing light therapy aims to change the oscillations in the brain, important for the reduction of gamma waves in AD. Thomson studied effects of flashing light on optogenetics, showing that flashing light alters the gene expression, leading to removal of amyloid- β (an important characteristic of AD) by activated microglia. However, only the plaques were measured and not the effect on the cognitive abilities. In addition, they noticed a reduction of amyloid- β plaques in the visual cortex, while the hippocampus is mostly affected in AD [40]. More research is needed to investigate the effectiveness of flashing light therapy.

In general, it is shown that light therapies may have positive effects on quality of sleep, lowering depression and unrest in dementia patients. Flashing light therapy can have a stimulating effect on the reduction of amyloid- β plaques. However, the frequency and optimal time of day for both therapies are unclear. Missotten et al. recommend a light intensity peak with a minimum threshold of 2,000 lux, based on their systematic review [41]. Neither is it clear for which type of dementia light therapy is useful. More research is needed on both types of light therapy.

Aromatherapy

In aromatherapy, patients are exposed to specific odours and oils often function by coupling to personal memories causing different responses between people to the same odour. Furthermore, administrations differ between aromatherapies from using diffusers to massaging [42,43]. Hence, it is difficult to show which aromatherapy is most effective for treating dementia.

Jimbo et al. showed improvements of ability to form abstract ideas, cognitive functioning, and conceptual understanding, when rosemary and lemon essential oils were applied in the morning, and lavender and orange oils in the evening [42].

Rosemary inhalation (4 and 8 $\mu\text{L/L}$) improved cognitive function, memory and learning abilities in mice model [44]. Participants wearing a cloth patch for 2h with 2 drops of lavender and lemon oils showed a reduction in agitation, irritability and non-aggressive behaviours [45]. This by a decrease in aggression and agitation in patients after diffuser administration of lavender odour [46].

Although the mechanism of action of aromatherapy remains unknown and every person has a unique response to different aromatherapies, lavender and citrus aromas showed promising results. The effectiveness of these therapies varied between different studies,

due to different responses to the same odours. Anderson et al. suggested that the improvement could also be due to touch and interaction [47].

Music therapy

Music as a therapeutic tool is used passively by listening to music or actively by singing songs and playing instruments, to improve memory, orientation and attention and to reduce anxiety [48,49]. It is currently used in all phases and kinds of dementia, but in particular in early phase AD patients.

The exact mechanism of action is currently unknown, although some studies have tried to determine four theories [48]. Firstly, music therapy improves neuroplasticity of the brain, the ability to form new connections within the brain. Secondly, music adjusts steroid hormone levels by lowering stress levels; steroids regulate the neurogenesis, regeneration and repair of neurons [48,49]. Thirdly, music therapy influences hormone levels, neurotransmitters and neuropeptides. Fourth, music therapy influences emotions, influencing cognitive functions [48]. Solé et al. engaged participants in music, measuring the quality of life, with results showing that the quality of life decreased slightly [49]. However, it cannot be concluded whether the changes are due to the therapy or the progression of the disease itself. The emotional well-being did increase, but the quality of interpersonal relations decreased, perhaps caused by the progression of dementia itself [50].

Music does not always affect people positively. The preferred music by patients can be songs that do not influence a person positively, because they are listening to sad music and hearing music that triggers emotions. Garrido et al. investigated whether cognitive decline, depression, anxiety and apathy influenced the mood of people [51]. People who have apathy and dementia showed the most enjoyment when listening to music which can re-engage them with others, especially when the music is familiar. Music may therefore help people, but it can also harm them. The psychological history should always be kept in mind, since it can influence someone's response to certain songs [51].

Based on this, a pilot RCT study was conducted in 2018 to assess the feasibility and effect of personalized music interventions which showed that it can be implemented in nursing homes to improve well-being, agitation and sleep quality, but a larger sample size is needed to confirm these results [52].

Music can be used as a therapy since people retain their response to music even when their mind deteriorates. Active and passive music therapies have been developed to increase the quality of life, while the improvement due to music therapy depends on the stage of dementia [50]. Passive music therapy should be assessed carefully. The preferred music by patients is currently used, but the mental state of patients can affect the response to that type of music [51].

Nutrition

VaD is generated by multiple infarcts in the brain. Diet rich in salt, red meat, liquorice (tea), and a lack of exercise may cause hypertension. This will subsequently increase the risk of cardiovascular diseases, such as infarcts in the brain and VaD [53].

Effects of vitamin B12 and folate: A possible cause of dementia could be lack of vitamin B12 and folate. Dementia caused by a vitamin B12 deficiency is very different compared to AD and can be reversed

by treatment with vitamin B12 supplements [54]. Low vitamin levels are related to high homocysteine levels in the blood, and in combination with low folate levels they account for a greater cognitive decline [55]. So, the ingestion of folate-rich foods such as beans and nuts may prevent AD [56].

Dairy products: Oleamide and dehydroergosterol are molecules produced during fermentation and can prevent cognitive decline by reducing microglial inflammatory responses and neurotoxicity. The latter is developed due to toxic cytokines produced by overactive microglia, which causes inflammation in the brain, which may have a correlation with the development and progression of AD [57]. Crichton et al. showed that people consuming low-fat dairy products had a higher cognitive function compared to those who did not [58].

Docosahexaenoic acid: Research of post-mortem AD brain samples has shown lower levels of docosahexanoic acid (DHA) than in people without AD. Therefore, it has been suggested that regular intake of fish or omega-3 fatty acids can reduce the risks of developing AD in animals, but this has not yet been confirmed in humans RCT [59].

Red grapes: Red grapes contain the polyphenol resveratrol, which has a neuroprotective effect on AD as well as on VaD [60].

Exercises

Studies on the effects of exercise on the progression of dementia showed different effects. One group of researchers found that exercise may help to ameliorate the memory function of patients with mild cognitive impairment [61]. Another line of research has shown that a moderate-intensity aerobic dance routine did improve the cognitive function in cognitively-impaired patients [62]. A study by Maltais et al. on the effects of a 6-month exercise intervention on pain, neuropsychiatric symptoms and medication intake in older people with dementia, showed that there were no differences in these parameters between the exercise intervention and the social intervention (the control group) [63]. It can be concluded that exercise may enhance memory, but the physical movements itself do not influence the progression of dementia.

Snoezel therapy

“Snoezelen” (Dutch) is a form of multisensory stimulation, applied for four purposes: (a) to reduce maladaptive behaviours (e.g. avoiding certain situations) and to increase positive behaviours, (b) to promote positive mood and affect, (c) to facilitate interaction and communication, and (d) to promote the relationship with the caregivers and to reduce the stress of caregiving [64]. Snoezel therapy can be used to stimulate contact of the patients with the outside world. This therapy is not only helpful for patients, but also for family caregivers, to increase the contact with them [65].

The effects of Snoezel therapy on mood and behaviour, which was integrated into the 24-hour care, and led to a significant decrease in apathetic, depressive, rebellious and aggressive behaviour, and less loss of decorum [66]. In addition, an increase in positive feelings and the ability to adapt were seen when Snoezel therapy was applied in the morning care. There was only a small difference in restlessness and verbal anger found between the treatment and control group. In contrast to Van Weert et al., and Bauer et al. demonstrated a significant reduction in restlessness and wandering during their study [64,67].

Maseda et al. compared the effects of two-weekly snoezel sessions and music therapy on mood and behaviour of patients with severe

dementia [68]. It was shown that the patients were positively influenced by both therapies; they were happier, talked more spontaneously, reacted better to other people, were able to focus more and felt more relaxed. The last observation was strengthened by the fact that the heart rate was decreased and the oxygen saturation increased after the sessions, showing a short-term positive effect of snoezelen [68]. This was confirmed by Hope, finding a positive effect on the different moods after the snoezel sessions. Snoezel therapy may also decrease agitation behaviour, however the effect found by Berkheimer et al. was not significant [69,70].

Sleep quality can also be influenced by Snoezel therapy, resulting in a higher quality of life. However, this effect was only observed in the first week of the intervention and not in the second week. More research with a larger sample size is needed to demonstrate the long-term effects of Snoezel therapy on sleep [71]. Only short-term effects of snoezelen have been proven and there is a need for more research on the long-term effects. Conclusive evidence is still lacking [72]. However, Snoezel therapy seems to have positive effects on the patient's mood, behaviour and interaction with other people. It might also have positive effects on the symptoms of dementia [64]. Snoezelen can probably also result in a small reduction of agitation and may have a positive influence on the quality of sleep [69,70].

Discussion

We have presented an overview of different Complementary and Alternative Medicine (CAM) approaches to treat symptoms of dementia. Studies were retrieved from several bibliographic databases. The scoping review shows in general that CAM approaches may reduce symptoms of dementia and slow down the progression of the disease, but none of the CAM therapies are intended to prevent or cure dementia.

It may be concluded that only some CAM treatments have shown reduction of the symptoms of dementia, and providing relief for the patients. Overall, this scoping review shows that there are not enough clinical trials on CAM treatments to determine their effectiveness in treating dementia symptoms. Another point of criticism is that many of the studies used were of low quality, either lacking control groups or a sufficient number of participants, or there were problems with the type of study. Furthermore, not all kind of CAM treatments are included in this scoping review for several reasons (e.g. massage, feet reflex therapy and therapeutic touch). Included were the most used and accepted therapies.

Practices implications

Even if the effectiveness of CAM treatments options were to be proven, we would recommend using them only as complementary treatments to conventional treatments. Some CAM treatments may only slow down the progression of dementia and not cure it. However, the CAM treatments can be a good alternative for conventional treatments that relieve the symptoms of dementia, such as the use of sleeping pills. More research on the combination of conventional and CAM treatments in humans is needed to elucidate whether CAM treatments can have beneficial effects in addition in addition to conventional treatments.

Conclusion

Current conventional treatments are able to slow down the progression of dementia or to diminish the symptoms. However, none

of the studied CAM therapies were able to cure, although some may prevent dementia and lessen the symptoms. There is also the possibility, in some cases, to slow down the progression of the disease. Psychological interventions as complementary therapies may be helpful for the family of the patients by increasing the interaction with the patients. Acupuncture and HupA used in Chinese herbal medicine are promising strategies to treat memory loss caused by dementia. Homeopathy might be effective in treating symptoms of dementia, but to date it has only been tested in mice models. Light therapy especially had effect on symptoms such as sleep deprivation, depression and agitation. Meanwhile, flashing light therapy could be of greater significance due to the stimulating effect on removing amyloid- β plaques, but further research needs to be done. The effectiveness of music therapy concerns the improvement of the quality of life. It may also help in remembering specific events, because certain memories are coupled to music. This situation is similar for aromatherapy. Some foods can lower the risk of developing dementia and might even prevent dementia. Exercise can enhance memory, but it does not influence dementia itself. In addition, Snoezel therapy has some short-term effects on mood and behaviour, only targeting some of the symptoms.

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