International Journal of Medical Science and Clinical Invention 10(3): 6622-6634, 2023
DOI:10.18535/ijmsci/v10i3.06
https://valleyinternational.net/index.php/ijmsci

Research Article,

Non-Pharmacological Interventions for the Disinhibition in Patients with Dementia. A Cross-Over Randomized Controlled Trial

Dimitriou Tatiana-Danai[1], Papatriantafyllou John[2], Konsta Anastasia[3], Kazis Dimitrios[4], Athanasiadis Loukas[5], Ioannidis Panagiotis[6], Koutsouraki Efrosini[7], Tegos Thomas[8], Tsolaki Magda[9]

[1]Department of Neurology, Aristotle University of Thessaloniki, Greece
[2]Neurology Department University of Athens, 'Attikon' Hospital
[3,5]Department of Psychiatry, "Papageorgiou" General Hospital of Thessaloniki, Aristotle University of Thessaloniki, Greece
[4]Neurology Department, "G.Papanicolaou" General Hospital of Thessaloniki, Aristotle University of Thessaloniki, Greece
[6,7,8,9]Department of Neurology, AHEPA, General Hospital of Thessaloniki, Aristotle University of Thessaloniki, Makedonia, Greece
Email Address: **tt.kirxof@gmail.com**

Abstract:

Objectives: Behavioral and Psychological Symptoms of Dementia (BPSD) are very frequent, and they affect approximately 90% of the patients with dementia (PwD). Disinhibition refers to inappropriate behavior, and involves impulsivity, social difficulties, and poor risk assessments. Disinhibition can lead to reduced social acceptance, early institutionalization, poor prognosis, and affects the quality of life of both patient and his/her caregiver.
Methods / Design: A cross-over randomized controlled trial with 60 patients with PwD and disinhibition symptoms was conducted in Greece. The patients were randomly assigned to 6 different groups of ten participants each and received three non-pharmacological interventions: a) Aromatherapy and Massage b) Body Exercise (BE) and c) Psycho-educational program of caregivers. The interventions lasted for 5 days and there was two days off, as a wash-out period. There was no drop-out rate. The measurements which were used are MMSE, ACE-R, GDS, FRSSD, NPI questionnaires at baseline and NPI after each intervention.
Results: No effective combination of non-pharmacological interventions was found for the patients. For the caregivers' burden the most effective combination for the reduction of their distress was: Psycho-educational program (p=0.014), followed by BE (p=0.018), followed by aromatherapy and massage (p=0.027).
Conclusions: An effective combination of non-pharmacological interventions that can reduce caregivers' burden because of the disinhibition symptoms of their patients is Psycho-educational program, followed by BE, followed by aromatherapy and massage.

Key words: dementia, Alzheimer's disease, BPSD, non-pharmacological interventions, Disinhibition, cross-over randomized controlled trial.

1. Introduction:

Dementia means cognitive impairment mainly due to neurodegenerative mechanisms. It affects all the cognitive abilities to such an extent that the patient with dementia (PwD) finally cannot function normally in his/ her daily life and activities[1]. It also affects the emotions and the personality of the patient. Every 3 seconds someone in the world develops dementia[2]. In 2020 there are over 55 million of dementia patients, globally [(2)]. According to the World Health Organization [(2)] this number will almost double

the next 20 years. In Greece, according to a valid study[3], the estimated annual incidence rate for all the types of dementia was 57/1.000 persons (aged >70 years old). Specifically, for the Alzheimer's disease 39.9/1.000, for the vascular dementia (13.9/1.000) and for the other types of dementia 3.5/1.000[(3)]. The prevalence of all the dementia types increased with age and was higher in females. AD was the most common type of dementia, and this study was in accordance with other similar European studies[(3)]. Furthermore, another recent Greek study[4] refers that the incidence rate of dementia was 19 cases per 1.000 persons, for patients older than 65 years old, of which the 16.3/ 1.000 suffered from AD. Each additional year of age increased dementia risk (by 19.3%), but each additional year of education decreased the risk (by 12.1%). This recent study is also in accordance with other European and North American studies.

Behavioral and psychological symptoms of dementia (BPSD) are very frequent, and they affect approximately the 90% of the PwD[5]. The BPSD are associated with worse prognosis, misuse of medication, increased healthcare costs, decreased quality of life for both the PwD and their caregivers, and fostering the institutionalization[6]. Neuropsychiatric Inventory (NPI) includes questions for 12 BPSD[7]: delusions, hallucinations, agitation/ aggressive behaviour, depression, anxiety, euphoria, apathy, disinhibition, irritability, wandering, sleeping problems, and eating disorders.

When a PwD suffers from disinhibition he/ she may be expressed in inappropriate manners, saying things that are not supposed to be told in public or acting impulsively without thinking[8]. The patient may hurt the feelings of others without doing anything like that on purpose. Furthermore, the PwD may say crude things or make inappropriate sexual remarks, talks openly about private things publicly, touches and hugs strangers[9]. Disinhibition refers to inappropriate behavior, and involves impulsivity, social difficulties, and poor risk assessments[10]. Patients who suffer from disinhibition they cannot control their behavior and they may act inappropriately in public situations [(10)]. Therefore, disinhibition can lead to reduced social acceptance [(10)]. According to the literature[11], the right inferior frontal cortex plays a major role in disinhibition. Damages to the right inferior frontal cortex affect performance in executive tasks [(11)]. The left prefrontal cortex and anterior cingulate cortex are also involved [(11)]. Disinhibition is also associated with reduced gray matter in the right middle frontal, precentral gyri and bilateral cingulate[12].

Behavioral disinhibition is a complex phenomenon. There is no universally accepted conception of the term "behavioral disinhibition". Some definitions refer to socially inappropriate behavior, or loss of manners and impulsivity. Inappropriate sexual behavior is defined by Johnson as "a disruptive behaviour characterized by a verbal or physical act of an explicit or perceived sexual nature, which is unacceptable within the social context in which it is carried out"[13]. Inappropriate sexual behaviour includes sex talks, sexual acts (touching, grabbing, etc), and implied sexual acts which can occur in private or public areas[14]. The concept of appropriateness varies among different cultures and religious, however public sexual acts are inappropriate in most developed countries. The prevalence of PwD with inappropriate sexual behaviours range from 7-25%, with a higher prevalence in patients with severe dementia [(14)]. The neurobiology of inappropriate sexual behaviour includes four different brain regions: the hypothalamus, the frontal lobes, the cortico-striatal circuits, and the temporo-limbic network[15].

Disinhibition, sexual and behavioral, is more common in patients with frontotemporal dementia (FTD)[16]. FTD is a term that describes a group of neurodegenerative diseases that affect executive functions, behavior, and language[17]. It is the third most common disease that causes dementia, following Alzheimer's disease (AD) and Lewy Body Dementia (LBD) [(17)]. It is a cluster of syndromes that result from deficits of the frontal and temporal lobes [(17)].

The current pharmacological treatments for disinhibition include antidepressants (SSRIs), antipsychotics, benzodiazepines and cholinesterase inhibitors[18]. SSRIs are widely used in the management of disinhibition due to lower side effects. The antipsychotics should be used very carefully[19]. The Food and Drug Administration has not approved any antipsychotic drug to treat BPSD[20]. In Europe risperidone is approved in some countries for treating agitation in AD patients [(20)]. Antipsychotics have been showed to cause stroke, hallucinations, extrapyramidal symptoms, and

mortality [14]. Benzodiazepines in some cases increase hypersexual behaviors and tend to be poorly tolerated due to severe side effects [14]. The use of cholinesterase inhibitors may help the PwD with disinhibition symptoms, but more research is needed to determine the benefits of their use[21]. Sexual disinhibition arises some ethical issues too. Chemical castration, such as estrogen therapies can be considered as a human rights violation [14]. Most non-pharmacological interventions recommend "distraction or ignorance" of PwD who suffer from disinhibition [14]. Reminding patients of where they are, what they do, and why this behavior is inappropriate may help orient individuals to time and place[22]. Ignorance of the disinhibition symptoms is a strategy to avoid conflict and agitation [18]. The aim of this study is to find a combination of non-pharmacological interventions that can effectively reduce disinhibition in PwD and reduce caregivers' distress due to the disinhibition symptoms of their patients.

2. Methods:

2.1 Subjects

In this study, sixty patients (N=60) with different stages and types of non-reversible types of dementia, with symptoms of disinhibition were included. Their caregivers were also included. The sample was recruited from the Neurological Departments of the General Hospitals of Thessaloniki and Athens. The caregivers have been informed about the whole process and they have given consent. There was no dropout rate. The sample suffered from the following different types of dementia; Alzheimer's disease (AD), Parkinson's dementia (PDD), Frontotemporal dementia (FTD) and Mild Cognitive Impairment (MCI). Table 1 shows the baseline characteristics of the sample. Thirty-two (32) of the participants were females (52.7%). The average years of age was 71.4 years (SD 9.4) and the average score of the education years was 8.9 (SD 4.21).

2.2 Procedure

This is a cross-over randomized controlled trial. The Neuropsychiatric Inventory (NPI) inventory (the sub-questions about disinhibition) was applied to the family caregivers at the beginning of the process. The results were recorded and then the patients were randomly assigned into 6 different groups of 10 participants each. Every group received the same non-pharmacological interventions, but on a different sequence. The sequence of the interventions among groups is shown on table 2. In that way we avoided the risk of bias. Each treatment was taken place for five days, there was two days wash-out period and at the morning of the 6th day NPI questionnaire (only disinhibition questions and sub-questions) were applied again, to record the results.

2.3 Interventions

The interventions were chosen based on five factors: a) they should be easily performed by the unprofessional caregivers, b) they belong in different categories; Aromatherapy and massage are sensory interventions, BE belongs to "other interventions" and Psychoeducational program is a behavioural intervention, c) they are pleasurable, d) they have no known side-effects, and e) the interventions have been proven useful in the management of other BPSD according to literature.

A) Aromatherapy and Massage therapy

Aromatherapy in combination with massage therapy has shown promising results on the reduction of some BPSD (agitation, sleeping problems and anxiety)[23]. Nevertheless, the mechanisms of action of aromatherapy are yet unknown[24], however lavender oil, melissa- based and lemon balm oil have been reported with antioxidant actions of vitamin E. These oils improve the state of blood vessels close to the skin and that is why there are the most common used oils[25 26]. The treatment was administrated in the back and lower limbs for 20 min. every morning after breakfast. This hour was a common time that all caregivers agreed that they could apply the intervention. The study used lavender, based on its beneficial results, according to previous studies[27].

B) Body Exercise

Exercise has shown very promising results on the reduction of some BPSD[28, 29]. However, the literature mentions that the duration of the exercise remains unclear[30, 31]. Some studies claim that 30-45min. of body exercise 3 times a week can give promising results[32]. The frequency of the body exercise seems to be related to better results. Our intervention was administrated every day for 30 min. every morning after breakfast for 5 days. Again, this time was chosen because it was the most convenient for the caregivers. All the family caregivers chose walking, as the easiest physical

activity for their patients. The intervention was taken place every morning after breakfast.

C) Psycho-educational Program for the Caregivers:

The psycho-educational program of Aristotle University of Thessaloniki in collaboration with EU ("ASPAD" program) was a program that aimed to inform the dementia caregivers about dementia and its progress, the BPSD, the non-pharmacological management and how to deal with daily challenges. The program took place in face to face and skype meetings. The seminars started 3 months before the trial onset. The duration of the program was 12 weeks and included 24 seminars. Every seminar lasted approximately for two hours. One private personal counseling session (60min.) was also included. The clinician gave strict guidelines. At any time, the caregivers could communicate with the clinician. The psycho-educational program was well structured, and the guidelines of the clinician were clear and strict. Specifically, for the current BPSD, the guideline that the program gave to the caregivers was to "do nothing at all and completely ignore the disinhibition symptoms of the patient". According to the literature[33], disinhibition may increase because the caregivers react badly (yelling, crying etc.) and hence the patients feel agitated or anxious, and continue the unwanted behavior. Therefore, this intervention aims to decrease the symptoms if the caregivers ignore the behavior completely.

2.4 Measures

Mini Mental State Examination (MMSE) [34, 35]: MMSE is a 30-point questionnaire that is used to evaluate the cognitive status. It is used to estimate the severity of cognitive decline. The questionnaire examines registration, attention, recall, language, and orientation. Higher scores indicate better cognitive performance and lower scores severe cognitive decline.

Addenbrooke's Cognitive Examination Revised (ACE-R) [36, 37]: ACE is a 100-point questionnaire that is used to evaluate the cognitive impairment. It includes MMSE. It is highly sensitive and can be used for the diagnosis of dementia. It includes questions about orientation, registration, attention, concentration, recall, verbal fluency, memory, language, spatial abilities, perceptual abilities, and recognition. Higher scores indicate better cognitive performance.

Geriatric Scale of Depression (GDS) [38, 39]: This scale is a questionnaire of 30 questions that examines if the patient has depression. The patient answers with a YES / NO. Higher score indicates higher level of depression.

Functional Rating Scale for Symptoms in Dementia (FRSSD)[40, 41]: It is a scale to access the Activities of Daily Living. The scale is a questionnaire to the caregiver and includes 14 different daily activities, such as eating, dressing**,** incontinent, speaking, sleeping, faces' recognition, personal hygiene, name memory, fact memory, alertness, agitation, space orientation, emotional status, socializing. The scale is scored from 0-3 (whereas 0= fully independence and 3= fully dependence).

Neuropsychiatric Inventory (NPI) [42, 43]: The questionnaire is administrated to the caregiver. The questionnaire evaluates the frequency and severity of the symptom as long as the impact that each behaviour has on the caregiver. Frequency is scored from 0-4 (0= rarely happens, 4= happens every day), severity from 1-3 (1=mild severity, 3=severe) and the distress is scored from 0-5 (0= not at all, 5= extremely). The domain total score is the product of a) frequency X severity score and b) the total score of caregivers' distress. A total score is obtained by summing all the domain total scores. The questions for the disinhibition symptoms are:

- Does the resident act impulsively without thinking of the consequences?
- Does the resident talk to total strangers as if he/she knows them?
- Does the resident say things to people that are insensitive or hurt their feelings?
- Does the resident say crude things or make inappropriate sexual remarks?
- Does the resident talk openly about very personal or private matters not usually discussed in public?
- Does the resident fondle, touch or hug others in a way that is inappropriate?
- Does the resident show any other signs of loss of control of his/her impulses?

2.5 Data Analysis

Categorical variables were presented as percentages while continuous variables were presented as Mean value and Standard Deviation (SD). Because the distribution of the differences

between the samples cannot be assumed to be normally distributed Wilcoxon signed-rank test was used. To find the differences in gender in the 6 groups the Chi-square test was used. Finally, to find the type of dementia in each group the z value score was also used. P values less than 0.05 were considered statistically significant. For the statistical analysis the SPSS 25.0 (IBM Inc., Armonk, NY) was used.

3. Result:

The Mean scores of all the patients at baseline were; MMSE 17.7 (SD 4.59), ACE-R 53.7 (SD 19.26), GDS 7.3 (SD 4.81), FRSSD 17.2 (SD 8.49), NPI Result 7.1 (SD 1.48) -only for disinhibition- and NPI Distress 3.7 (SD 0.92). The sample of the study was 60 participants (N=60) of whom; the 61% suffered from AD, the 13.2% from MCI, the 9.9% from PDD and the 14.8% of FTD (table 3). Table 4 shows the results of the 6 combinations of the non-pharmacological interventions. No effective combination was found for the reduction of disinhibition in PwD. Nevertheless, for caregivers' distress a combination that can reduce their burden was found. Group 6 had statistically significant results. Specifically, psychoeducational program (p=0.014) followed by body exercise (p=0.018), followed by aromatherapy/ massage (p=0.027) can reduce caregivers' burden.

4. Discussion:

The literature lacks evidence of management for the disinhibition symptoms in dementia. The current study did not find an effective combination that can reduce the behavior, but it found a combination that can reduce caregivers' burden. Considering that the caregivers usually are called "the second patients" it is important to find non-pharmacological treatments that can reduce their distress[44]. Specifically, more than 90% of PwD live in their homes in Greece and other countries, therefore the caregivers are their spouses and/ or adult children[45]. According to the literature there is a lack of formal support systems for the dementia caregivers[46]. This has an impact on their mental and physical health [(44)]. Studies have shown that dementia caregivers suffer from depression, anxiety, emotional difficulties, and economic problems (such as loss of income and lack of employment opportunities)[47 , 48]. The family caregivers experience a numerous of negative feelings and sometimes they lack knowledge and experience of how to deal with some unwanted behaviors, such as disinhibition[49]. Therefore, the psycho-educational program can be helpful.

Our results seem to be in accordance with the literature so far[50]. Online psycho-educational programs have proven very useful, educational, low cost and convenient to the dementia caregivers[51]. According to the literature, STAR training in Netherlands and United Kingdom pointed positive impact on the caregivers[52]. One hundred forty-two (142) people participated in the study (N=85 in Netherlands and N=57 in the United Kingdom). The participants could choose the number of modules they wanted to follow. There was also a control group. The experimental group was following the modules that consisted of text, videos, test, and exercises. The themes that have been covered were; what is dementia, living with dementia, diagnosis, practical daily difficulties, behavioral problems, strategies, effective communication and emotional impact and looking after yourself. After two to four months all participants received a link to the post-test measurements. The results of the STAR study were positive.

Moreover, beneficial effects from Internet-based interventions mention other trials, as well[53, 54, 55, 56, 57]. The general health of the caregivers has been improved. The psycho-educational programs are powerful, and they can improve the quality of life of the PwD and therefore the caregivers' quality of life, too[58]. Furthermore, another interesting result is that the programs can delay the institutionalization[59].

Another large trial that conducted in Estonia, England, Finland, France, Germany, the Netherlands, Spain, and Sweden, used a mapping system in 2010-2011 to gather information about utilization, availability from professional and informal caregivers[60]. According to the results, countries with care systems and national guidelines for dementia were more aware of the importance of knowledge about dementia. The understAID platform is an online e-learning application that aimed to help the dementia caregivers and it was evaluated in Denmark, Spain, and Poland[61]. The evaluation was done in a randomized controlled trial that lasted 3 months (N=61). There was also a control group that did not have access to the learning platform. The database was organized in 5 modules with 15

different topics. The platform used text, videos, images, and references to other websites. The modules included information on several topics, such as; cognitive decline, daily tasks, behavioral changes, social activities and caregivers. The study found positive results of the educational platform. It is a matter of fact that the caregivers realized their doubts and feelings and were encouraged to be informed and reduce their emotional burden. Furthermore, another study assessed the effectiveness of the Internet-based interventions. The study used the name "Mastery over Dementia", and it was a RCT that conducted in the Netherlands with 251 caregivers[62]. The participants were randomly assigned to two groups (experimental group N=149 and control group that received a minimal intervention N=96). The participants were spouses or children. The study found that "Mastery over Dementia" was an effective treatment for the dementia caregivers as it reduced the depression and anxiety symptoms. The program consisted of 8 lessons and a booster session that happened a month later. Each lesson had the same structure and consisted of information (text and videos), homework and exercises. The elements were; behavioral problems, relaxation, and communication with others. After every lesson, the participants sent their homework to a coach. The coach sent electronic feedback. The study pointed positive results on the reduction of the caregivers' burden.

NYUCI-AC is a single-blinded randomized controlled trial with 107 participants (experimental group N=54, control group N=53)[63]. The participants completed assessments at baseline and at 4-month intervals during the first year and every 6 months after. There were three components; counseling, group participation and ad hoc counseling. The trial found positive effects of the program in terms of reduction the caregivers' burden.

DE-REACH is another randomized controlled trial with 92 caregivers[64]. The intervention comprised 12 individual 2 weekly sessions (9 at home and 3 via telephone). The trial had 5 modules; security, social support, challenging behaviors, emotional well-being and self-care. The study pointed reduction of the caregivers' burden. eHM-DP study conducted in Germany and used a participatory design (N=42)[65]. This pilot study used face-to-face interviews. During the demonstration, questions from the participants were allowed. The demonstration lasted 60-70min. The interviews included information about the caregivers' needs, medical decision aid, recommendations, and socio-demographic data. Each interview lasted approximately 45min. The study also underlines the effectiveness of the internet-based interventions. Likewise, another program that conducted in Iran[66] included 5 weekly sessions and question and answer table. The duration of the sessions was 90min. There was a supervision of the first researcher. CDs of all sessions were provided to caregivers, as well. The study also pointed significant reductions of the caregivers' burden after following the program.

An important advantage of the psycho-educational programs is that they are of low cost. This is a factor that should not be underestimated. In the UK the care provided by the dementia caregivers in 2008 was valued to be £23 billion, including social and informal care and health care[67]. The 37% of the dementia patients live in long term care institutions, that cost £9 billion per year in social care[(67)]. Another trial has come to the conclusion that total annual costs amounted to an average of 77.832 and 75.201 euros per care dyad (PwD and caregiver)[68]. The results are in accordance with some systematic reviews[69, 70]. Another vital advantage is that internet-based interventions have the benefit of bringing the intervention into the home and therefore they can reduce the social isolation that several dementia caregivers experience[71].

Furthermore, face-to-face meetings seem to be more helpful when important decisions should be made. Internet resources are used as a method of preparation for discussions[72]. Nevertheless, there is a need for further research because promising results of the internet-based interventions have been shown even in elderly studies[73, 74]. A recent review points that there are significant reductions in caregivers' stress, strain, depression, anxiety symptoms and additionally increases in self-efficacy[75]. Future studies should focus on how to make the interventions more personalized. If the needs of the caregivers are not met, they feel frustrated and disappointed. Moreover, it is also crucial not to forget the elderly caregivers. Adults over 70 years old experience difficulties using the Internet in some countries. We have to try ti find out how we can help them.

The literature so far lacks trials that could prove the effectiveness of Aromatherapy and Massage and Body Exercise on the reduction of the disinhibition. The current study used a cross-over randomized controlled trial in order to avoid risk of bias. Apart from the heterogeneity of the sample, it seems that our results affect both genders, different types, and stages of dementia. NPI is an effective, valid, and reliable tool that evaluates the frequency and the severity of the behaviors. It is a tool that can assess a wide range of psychopathology across different ethnic groups[76].

Limitations

The limitations of the current study are that the interventions lasted for a short period of time and there was no follow-up. However, the caregivers needed direct and rapid solutions to their problems and therefore the short length of the interventions can be justified. Moreover, the interventions were administrated by the caregivers, however the guidelines were clear, and the caregivers could anytime be in contact with the clinician. Future studies should focus on findings of non-pharmacological interventions that can effectively manage the disinhibition symptoms of PwD. The psycho-educational programs seem to be very promising, but some elderly caregivers may not have access to them. We should find ways in order to educate the caregivers and support them emotionally.

Conclusions:

In conclusion, the current study did not find any effective combination of non-pharmacological interventions for the management of disinhibition in PwD, but it found significant benefits of the psycho-educational program in terms of reducing the caregivers' burden. The effective combination that can reduce caregivers' burden is psychoeducational program, followed by exercise, followed by aromatherapy/ massage. This is an essential finding. It is important not to forget the dementia caregivers. They experience an increased risk of stress, strain, depression and have higher mortality compared to other caregivers who caring other older persons without dementia. Caring a PwD can affect the health, quality of life, economic status, career, and social networks[77]. Therefore, the psycho-educational programs can be helpful.

Conflict of interest

The authors declare that they have no conflict of interest.

Funding

None

Author Contributions

T.D.: write, editing, investigation, software J.P.: supervision, resources A.K.: supervision, D.K.: supervision, L.A.: supervision, P.I.: supervision, E.K.: supervision, T.T.: supervision M.T.: supervision, conceptualization, resources, methodology

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study

Abbreviations:

ACE-R: Addenbrooke's cognitive examination
AD: Alzheimer's disease
CNS: Central Nervous System
DA: Dopamine agonist
FRSSD: Functional Rating Scale for Symptoms in Dementia
FTD: Frontotemporal dementia
GDS: Geriatric depression Scale
LBD: Lewy Body dementia
MCI: Mild cognitive impairment
MMSE: Mini Mental State Examination
MT: Music Therapy
NPI: Neuropsychiatric Inventory
PDD: Parkinson's Disease Dementia
PwD: Patients with Dementia
RCT: Randomized Controlled Trial
RT: Reminiscence Therapy
VaD: Vascular Dementia
VT: Validation Therapy

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