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The causes of agitation in patients with advanced dementia

Przyczyny pobudzenia u chorych z zaawansowanym otępieniem

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Abstract

Agitation is one of the most frequent symptoms of the advanced dementia and can manifest itself in different forms, such as disruptive, resistive or repetitive behaviour, hallucinations or hypersexuality. The complexity of agitation and its causes may hinder an accurate diagnosis and affect the patient's quality of life. This article distinguishes the health-related and non-health-related causes of agitation in order to simplify the diagnostic and the choice of treatment. Health-related agents include not fulfilled physiological needs, accompanying illnesses, pain and agitation-inducing drugs. Whereas non-health-related agents may be associated with the environmental effect and patient's caregiver. The authors suggest possible solutions which may minimize agitation in patients with advanced dementia. *Geriatria 2020; 14: 166-175.*

Keywords: agitation, advanced dementia, elderly patients, treatment of agitation, dementia symptoms, dementia care

Streszczenie

Pobudzenie jest jednym z częstszych objawów zaawansowanego otępienia i może objawiać się w różnych formach, jak destrukcyjne, oporne i powtarzalne zachowania, halucynacje czy hiperseksualność. Złożoność problemu pobudzenia i jego przyczyn może utrudniać postawienie trafnego rozpoznania oraz wpłynąć na jakość życia pacjenta. W artykule rozróżniono zdrowotne i pozazdrowotne przyczyny pobudzenia w celu uproszczenia procesu diagnostyki i wyboru leczenia. Do zdrowotnych czynników zaliczono niespełnione potrzeby fizjologiczne, choroby towarzyszące, ból oraz leki pobudzające. Natomiast pozazdrowotne czynniki podzielono na wynikające ze środowiska pacjenta oraz na wynikające z jego relacji z opiekunem. Autorzy proponują możliwe rozwiązania, które pomogą zminimalizować pobudzenie u pacjentów z zaawansowaną demencją. *Geriatria 2020; 14: 166-175.*

Słowa kluczowe: pobudzenie, zaawansowane otępienie, starsi pacjenci, leczenie pobudzenia, objawy demencji, opieka nad osobami z demencją

Introduction

Dementia is a neurodegenerative syndrome, which results from several causes. As it develops into more advanced stages with time and is considered incurable, dementia is said to have both progressive and chronic nature. Since the mortality rate for patients with advanced dementia is high, this condition is regarded as terminal. It should be emphasized that dementia is not a part of a usual aging process, however it does concern usually elderly patients. The syndrome affects mainly the cognitive functions and functional capability [1].

The stage of the impairment of the cognitive functions, functional capabilities and social skills of a particular patient can be used to identify the phase of dementia. However those functions and skills in the condition diminish gradually over time, not in an abrupt way, which hinders the correct diagnosis. As dementia is a syndrome, not a typical disease, and can coexist with many other conditions, the prognosis is less predictable and its course is more varied. Although when a comorbidity is not present, life expectancy from the diagnosis is strictly related to age and is shorter in older patients [1].

Statistical and forecasting data concerning dementia change very dynamically. The total number of people suffering from dementia was estimated at 35.6 million in 2010 [2] and already at 50 million in 2018, of whom 63% inhabit low- and middle-income countries [3]. In 2010 this number was projected to grow up to 115.4 million by 2050 [2], but in 2018 World Health Organization estimated it to reach 152 million [3]. Data from 2010 stated that 7.7 million people were being diagnosed each year [2], now WHO evaluates it to be 9.9 cases each year [3].

The symptoms of dementia

Dementia symptoms vary greatly depending on the stage and type of dementia. If not due to acute brain injury, dementia includes asymptomatic preclinical phase. Symptomatic stage starts after reaching individual threshold number of neuronal lesions [4]. Characteristic course of the disease is the prolonged and slow decline [5].

Symptoms usually begin with a mild cognitive impairment and memory problems which both worsen gradually. Patients themselves or their family can notice functional decline, objects misplacement or behavioral changes [6]. As the disease progresses, patients may lose the independence, personality or ability to talk. Most frequent symptoms of a severe stage of dementia include confusion, anxiety, apathy, agitation and recent weight loss [7].

Some of the most prevalent forms of agitation include:

- **Physical and verbal disruptive behaviour.** It consists of physical forms of aggression such as pushing, biting, hitting others or the patient themselves. Non aggressive forms include seeking exit or screaming.
- **Avoidance and resistive behaviour.** Those are the patients that resist taking their prescribed medication, food or fluids.
- **Preservative and repetitive behaviour.** Examples include persistent screaming for help, skin picking, banging on objects.
- **Disinhibition and hypersexuality.** Those behaviours include taking of their clothes in public, touching themselves or others in a sexual context, masturbating. Taking other people's objects or food may occur.
- **Hyperoral behaviour.** It consists of increased appetite and food-seeking. The patient may eat copious amounts of foods which lead to excessive food gain as well as risks of aspiration and choking. Some patients turn to consuming non-edible objects.
- **Hallucinations and delusions** [8].

Before death aspiration on swallowing, breathing difficulties, septicaemia and pneumonia become more common [7].

The staging of dementia

The dementia staging is of great importance to evaluate patient condition, determine treatment and to provide the caregivers with an overview of patient's state [9,10]. There are several tools to assess the stage of dementia, e.g. GDS (Global Deterioration Scale / Reisberg Scale / Global Deterioration Scale for Assessment of Primary Degenerative Dementia) from 1982 and FAST (Functional Assessment Staging) from 1988, both established by Dr. Barry Reisberg and associates. Used together, they provide universal and effective staging, called GDS/FAST Staging System [11].

GDS Scale describes 7 stages of primary degenerative dementia, especially Alzheimer's disease. It focuses on progression of cognitive impairment and its indicators. Stages 1-3 prelude dementia. Disease occurs

Table I. FAST procedure – Stage 7, advanced dementia

Stage		Features
7	a	Patient has speech limited to fewer than six intelligible words during an average day
	b	Patient has speech limited to one intelligible word during an average day
	c	Patient is unable to ambulate independently
	d	Patient cannot sit up independently
	e	Patient cannot smile
	f	Patient cannot hold up head independently

explicitly in further stages (4-7); since stage 5 patient requires constant assistance in daily living activities. Stages 7 include features of advanced dementia [10].

FAST Scale describes 16 stages and substages of disease [12]. It is derived from GDS Scale and compatible with this tool, which means that Stage 7 in FAST also is indicative of advanced dementia (Table 1) [11,13]. It estimates rather activities of daily living than symptoms of cognitive impairment [12]. It also provides the estimation of survival time – patients with dementia at or beyond stage 7c, which meet the additional medical criteria (e.g., aspiration pneumonia occurred in the past year), are estimated to survive less than 6 months, although it is not accurate prediction [13,14].

The role of the caregivers

As the result of the population aging, the amount of people suffering from dementia increases, and consequently so does the demand for caregivers who are crucial for providing essential assistance during daily tasks. Symptoms of dementia may be debilitating for the suffering patient as well as for the caregivers. Problematic symptoms of dementia have been described above. It is worth taking note of that agitation is very common and concerning for the caregivers as it is often followed by physical aggression [8]. The caretakers are at greater risk of experiencing burden as caring for dementia patients is reported to cause markedly higher both depressive and anxiety symptoms, when compared to caring for the non-dementia patients. Neuropsychiatric symptoms such as agitation, aggression and hallucinations are considered to be the most challenging behaviours for caretakers to maintain [15]. However, with the help of the day care centers, caregivers are able to alleviate their burden by being granted free time while the person with dementia may take part in social or physical activities which may result in the positive implications improving the bond between caregivers and care recipients [16]. The majority of caregivers are family members and the quality of provided help is culturally influenced. In developed countries, caring is often government-regulated with caregivers being granted access to respite programs and day care centers allowing them to give the needed care, while preserving individuality. In developing countries, the family values are commonly cultivated, as opposed to aforementioned individualistic approach. This results in a higher prevalence of children being the caregivers and reported a higher objective burden in undeveloped countries [17].

Causes of agitation in patients suffering from dementia

1) Health-related causes

Not fulfilled physiological needs

Agitation is one of the behavioral and psychological symptoms of dementia (BPSD). Those symptoms can be driven by increased vulnerability to stressors caused by unmet needs or goals and physiological changes [18]. It is complicated to define unmet needs, as it is a very wide category. Therefore in this part we will focus on the physiological needs as a subcategory. This subcategory consists of: fulfillment of a hunger and a thirst, breathing need, sleep need, sexual desire, maintaining of constant body temperature, excretion need and the need to survive in health and without a pain [19].

Quick review of the issue

Physiological disorders like urinary tract infections, constipation (disability to excrete comfortably), pneumonia (disability of breathing need), dehydration (also umet thirst), pain (as opposite to the need to survive in health and without a pain), sleep problems (unmet sleep need) can lead to BPSD and agitation as well [18].

Unexplored factors

In 2017 there was a cross-sectional study conducted in the Netherlands among 2074 nursing home residents with dementia. It was shown that some residents with very frequent agitation exhibit repetitive activities (several times a day – STD or several times an hour – STH) like inappropriate dressing or disrobing (STD 16.2%, STH 5,2%), eating or drinking inappropriate substances (STD 2.6%, STH 0.6%), making verbal sexual advances and making physical sexual advances or exposing genitals (STD 1.9%, STH 0.6%), hurting self or other (STD 9.7%, STH 2.6%), constant unwarranted requesting for attention or help (STD 29.2%, STH 32.5%), complaining (STD 29.9%, STH 7.8%), cursing or verbal aggression (STD 28.6%, STH 7.1%). Residents with agitation express also eating change – 33.3% of those with very frequent and 21.1% of those with less frequent agitation. Those activities are connected with physiological issues and despite statistical insignificance, future research should investigate their relation

to agitation and whether they are expressions of unmet physiological needs or not [20].

Body temperature

Significant relationship between physiologic discomfort and agitation was presented in 2018 research using secondary data analysis [21]. This issue was examined using Kang tool, which considers for instance the temperature and air circulation. Those factors influence maintaining of constant body temperature [22].

Sleep

The 2015 Australian study showed connection between night-time sleep and non-aggressive behavioral agitation in group of people with dementia. On the contrary, those without dementia, under the influence of reduced sleep time, exhibited rather verbal agitation. Change of sleep time impacts verbal agitation stronger in residents without dementia than those with dementia. The explanation can be lower cognitive functioning in people with dementia, so they are not able to express their unmet needs (in this case - a sleep need) in verbal ways [23,24].

Treatment

Treating agitation should include primarily non-pharmacologic interventions [18]. The efficacy of antipsychotics is questionable. Occurring of agitation may arise from changes in routine activities of daily living, for instance toilet hygiene, dressing, feeding. Usually suggested approach for the care providers is to ensure that a person with dementia is getting enough sleep, catering to hunger and toilet needs and to ask doctor's advice about reasons of acute medical problems [18]. Caregivers should also try feeding with smaller and more frequent food portions if food is refused. In case of hypersexuality appropriate outlets should be provided to enable showing affection and allow patient privacy. Additionally, it is helpful to assess nutritional intake, use cues to distinguish nonfood from food items, substitute unhealthy foods with healthy choices or try other forms of oral stimulation [9].

Due to review from 2015 it is essential to differentiate between solitary and interactive behaviors in dementia. The first ones include agitation and the second ones rejection of care. Both are linked to depression (as opposite to the need to survive in health and without a pain) and both require different treatment. Best intervention in agitation is to provide meaningful activities, for example group activities monitored by an activity professional [25].

Accompanying illnesses

Agitation can be also caused by other accompanying illnesses, such as the exacerbations of chronic diseases and undiagnosed disorders. Other division can be presented according to the type of the disease.

1. Mobility disorders

Patients with dementia suffer from fractures and osteoporosis more frequently than non-demented patients [26]. These conditions include malpositioned dental prostheses, jaw atrophy. They can cause frustration and pain which then lead to agitation [27].

2. Cardiovascular disorders

Congestive heart failure is a common problem among the patients suffering from dementia. It is accompanied by nocturia and frequent awakening. These disturbances of the sleep-wake cycle can manifest as agitation. Furthermore, neuroleptics, often given to the patients suffering from dementia, worsen this condition. Left-hemispheric cerebral ischemia can cause affective disturbance, emotional lability, agitation, delusions and aggressiveness [27].

3. Endocrine disorders

Thyroid conditions are associated with behavioural disturbances and neuropsychiatric symptoms, especially in hypothyroid patients [28]. Euthyroid patients with Alzheimer disease, agitation and irritability have lower TSH serum levels than demented patients without these symptoms [29]. Neuropsychiatric complaints tend to get better with the treatment of thyroid disorders [28].

Hypoglycemia, which is a sign of poorly controlled or undetected diabetes mellitus, may be accompanied by agitation, aggression, irritability and hunger. Early symptoms of hypoglycemia also include dizziness, headaches and sweating [30]. Low blood sugar levels are usually self-detectable by the diabetics. However, due to the reduced communication, dementia patients are not able to perform glycemic control themselves. They experience more frequent severe hypoglycemic episodes than non-demented patients [31].

4. Psychiatric disorders

Co-existing mood illnesses such as schizophrenia, bipolar disorder or depression are most commonly accompanied by agitation [32]. Delirium is also associated with acute agitation. It can be caused by many medical issues including infections or metabolic imbalances [33].

5. Other disorders

Trauma to the head, infections, sepsis, exposure to toxins, electrolyte abnormalities and post ictal state are some of the leading medical conditions causing agitation [33].

Pain

It has been confirmed that the patients diagnosed with dementia that are suffering from chronic or situational pain are more agitated than those who are not in pain or receiving routine analgesic treatment [34]. Examples of agitated behaviours stemming from underdiagnosis of pain are pushing, biting or repetitive exit seeking [40].

Significance of the issue

The estimates show that 40-60% of patients with dementia suffer from chronic pain of moderate or even severe nature [35-37]. The pain is often underdiagnosed and undertreated – in a study of 2 nursing homes in Wielkopolska region of Poland only 34% of participants consumed analgesics and only 25% had routine pain management medications prescribed [34]. Moreover, according to a study of nursing homes in United Kingdom as well as the previous one, those with high cognitive impairment receive lower doses of analgesics than those with lower levels of cognitive impairment [34,38].

Complexity of the issue due to patient characteristic

Underdiagnosis of pain is a complex problem stemming from the fact that patients suffering from dementia lack the capacity to report the pain or physical discomfort. The elderly patients often cannot communicate their pain due to deterioration of vocal communication. [39]. The neurological deficits are even more prevalent in late onset dementia. Moreover, the patients with decreased mobility are also unable to shift themselves in order to alleviate their pain stemming from somatic degenerative diseases, i.e. osteoporosis [40]. The caregivers face an obstacle in interpreting mixed signals and nonverbal communication. This is especially troublesome in nursing home residents as their caregivers are not family members and dismiss the behavioural signs of pain due to abundance of patients per caregiver and improper training. More education and practice in using observational pain scales is needed.

Obstacles in treatment

Instead of looking for the underlying cause of agitation, the patients are frequently and heavily medicated with neuroleptic drugs to reduce the symptoms [34]. Underlying causes of the agitation and pain should be investigated first to quickly eliminate any somatic or psychiatric diseases that may be contributing to the deterioration of patients' state. Purely symptomatic treatment often prevents physicians from investigating and treating the root cause of aggressive behaviours. Furthermore, prescribing high doses of neuroleptics in a short amount of time aggravates behavioural disorders instead of alleviating them [27].

Implementing routine pain assessment protocols in nursing homes and in home settings is an effective way of reducing and preventing agitated behaviours [40]. Self – report alone is not effective in the elderly patients [41].

Drug-induced agitation

Since dementia is usually associated with an older age, comorbidity is often present. Patients may require complex pharmacological treatment, which increases the risk of inappropriate drug prescribing and drug--drug interactions (DDIs) [42]. DDIs can both alter the effectiveness of the drugs and cause adverse drug reactions (ADRs), such as extrapyramidal symptoms and worsened or new behaviour [8]. The process of aging can also lead to pharmacokinetic and pharmacodynamic changes in the body, which affect the absorption, metabolism or effect of a drug, including an increase in sensitivity to medications [43,44]. Wherefore, patients with dementia may be more susceptible to ADRs [44]. In order to avoid DDIs and ADRs, it is recommended to introduce a medication at a small dose and closely monitor the patient's response. However, before introducing the sedating or calming medications, it should be analyzed whether the current treatment contributes to agitation. In this case, discontinuation of the activating drug or reduction of its dose should be considered [8].

Medication may lead to different kinds of agitation. Physical and verbal disruptive behaviour may be induced by activating drugs, such as dopaminergic medications, acetylcholinesterase inhibitors or stimulating antidepressants. Acetylcholinesterase inhibitors may also, as well as serotonergic drugs, contribute to reduced appetite or gastric ailments. The patients can express their reluctance to eat and their discomfort as avoidance and resistive behaviour. Mirtazapine (antidepressant), which is used to stimulate appetite and alleviate sleep disturbances, in higher doses may become stimulating and contribute to agitation. Another medications which stimulate appetite and may induce hyperoral behaviour are atypical antipsychotics, such as olanzapine and clozapine [8].

Disinhibition, a prevalent form of agitation, can result from the use of benzodiazepines and dopaminergic medications. Dopaminergic medications (pramipexole or levodopa) can be also associated with both hypersexuality and psychosis in a form of hallucinations and delusions [8]. It should be noted that, in elderly patients, delirium may be induced by most drugs, some of them used in the treatment of agitation, such as haloperidol and benzodiazepines [45]. Patients treated with memantine (NMDA antagonist) also experienced agitation as an adverse reaction [46].

The use of dopamine receptor-blocking agents includes the possible common adverse effects such as urinary tract infection and incontinence. Those untreated medical conditions may lead to agitation in patients with dementia. Discontinuation of the selective serotonin reuptake inhibitors (SSRIs) in patients with dementia may worsen agitation [46].

2) Non-health-related causes

Environmental effect

Patients suffering from dementia experience deterioration of the cognitive functions, which influences their understanding of the stimuli in the environment and increases their vulnerability to the environmental stressors [18,47]. Decreased stress threshold can be manifested as the behavioural and psychological symptoms of dementia (BPSD), one of them being agitation [18].

1. Overstimulation

Occurrence of the excessive stimuli in the environment, such as light, noise or smell, can be the cause of agitated behaviours. The patients often display the development of visual dysfunctions, such as irritation from glare of the light [48,49]. Higher noise levels result in BPSD [18,48,50], whereas maintaining the appropriate sound level may limit agitation [51]. The olfactory sense in the patients with dementia, when affected by unpleasant smells such as urine, excrement or chemicals, may contribute to agitation as well [48,52]. The other factors provoking the patient to be more agitated are excessive clutter and excessive number of people, which can lead to frustration [18,51].

2. Under-stimulation

Agitation arise not only from excessive stimuli, but also from lack of meaningful or physical activity, inducing stimulus-seeking behaviours such as wandering or anxiety [18,48,53]. Therefore, gardening may be one of the therapeutic solutions proposed to the patients with dementia, allowing them to engage in a regular activity [53]. The other research also proved that both the social and individualized stimulus reduce agitation [54].

3. Inappropriate indoor air temperature

The optimum indoor air temperature should lie between 20 and 26°C. Significant fluctuations below and above the optimum temperature are associated with increased manifestation and disruptiveness of agitation. The study also revealed that the occurrence of agitated behaviours correlated with the amount of hours the patients is exposed to inappropriate temperatures [55].

4. Lack of daily routine

Daily life of the patients with dementia should be based on the established routine, enabling them to engage in basic activities such as dressing, bathing or eating. Abandoning or changing the daily routine can become a stressor for the patient triggering or worsening the agitated behaviour [18].

5. Improper spatial configuration

Poorly designed living space for the patient may be associated with previously mentioned over- and under--stimulation. The characteristics of the surrounding which reduce agitation are privacy, personalization and comprehensibility. Hence, the environment should correspond to the individual needs of the patients, easy to operate and understand by them and can be personally decorated [66]. Design of the rooms should be kept simple, with no excessive furniture in order

to omit disorientation [49]. Adjusting the light and sound to the appropriate level may be necessary due to existing visual and hearing impairment [48]. Safety of the closest environment should also be ensured, including the removal of sharp objects and chemicals or medication [18].

Caregiver

Agitation in patients diagnosed with dementia is among one of the neuropsychiatric symptoms that are considered most difficult for caretakers to deal with [57]. The agitation may present itself in form of physical or verbal agitation with the second appearing more often [21,58-60]. Relieving agitation requires a proper training for caregivers that include learning about the most common factors that trigger agitation and the most efficient means of reducing it. Nursing interventions are crucial for evaluating and alleviating the agitation [61].

Impact of the suitable care

It is very hard for dementia patients to communicate their needs and, as a result, caretakers are often unable to properly satisfy their wishes and basic needs. One of the studies showed that among the most effective factor lessening the agitation in dementia diagnosed patients is avoiding noise that might cause disturbance. Due to the lowered stress threshold elderly patients diagnosed with dementia and presenting with agitation require very calm environment. Proper way of communicating and conveying the need to the caregiver lowered the disturbance. Assistance at satisfying basic physiological needs such as attending to the lavatory lessened the symptoms of agitation as well. Patients showed reduction in agitation when they were exposed to physical activities such as walking under supervision of caretakers. Providing patients with liquids or helping them drink them also alleviated the agitation. Therefore, caregivers who recognize the factors that trigger agitation are able to apply appropriate measures at relieving them more efficiently and incisively [62].

Benefits of the professional caregiving

Introduction of the professional help may enable the proper adjustment of the treatment and choosing the most effective one. It has been observed that, despite professional training being time- and cost-consuming, the total benefit of introducing the non-pharmacological interventions at relieving agitation will prove beneficial [62]. However, in case of the non-pharmacological methods proving ineffective a medication trial is recommended. Pharmacological interventions administered by the caregivers are endorsed when the behaviour of the patient is interfering with issuing care to the agitated person or when the risk of harm to either the patient or the caregiver is possible [63].

Obstacles in the caregiving

The relationship between a caregiver and his patient may have a problematic nature, resulting in the negative consequences in treatment. Verbally agitated behaviour such as screaming causes insomnia and might prove threatening to the caregivers. Constantly asking the same questions or repeating certain phrases is considered highly burdensome for caregivers and is one of the main causes for the family to decide to send the patient to either hospital or nursing home, thus raising the cost of care [21,64,65].

Physical agitation may occur when a person with dementia is being provided care that they reject due to not comprehending the intentions of the caretakers. It may result in patients trying to defend themselves in the event of caretaker being persistent and consequently incite defending mechanisms such as striking the caregiver [65]. Some patients will react negatively to certain caretakers without any substantial reason for it. This prejudice may induce fear in patients and result in physical agitation as a form of protection. In these cases it might prove beneficial for both sides to replace the caregiver with a new one to whom the person will react positively.

Conclusions

As symptoms of dementia develop relatively slowly in comparison to arising brain lesions, the number of people suffering from advanced dementia increases rapidly. Hence, it is crucial to understand the behaviour of patients with dementia and to know how to react to their agitation. Searching for causes of agitation, it is worth drawing attention not only to health-related issues, but also to other issues, such as patient's environment, daily activities and attitude towards caregivers. What should attract caregiver's/ professional's particular attention in the matter of health-related causes of agitation? Agitation can be triggered by unmet physiological needs. Having a recollection, that patients suffering from dementia lack the capacity

to report their needs, caregiver should control the appearance of those needs carefully and assist in their fulfillment. Undiagnosed, untreated or improperly treated accompanying diseases should also be taken into consideration. As far as possible, their symptoms ought to be relieved. High cognitive impairment often makes direct pain's expression impossible, thus implementing routine pain assessment could be useful. If pain is suspected, reducing the amount of analgesics is usually an error. It is also important to be wary about drug administration, as some adverse drug reactions and drug-drug interactions can lead to agitation. Medications should be introduced at a small dose after thorough analysis of the patient's history. Regarding non-health-related issues, it is worth to ensure patient safe, comfortable and relatively constant environment. Both overstimulation and under-stimulation may bring on agitation, therefore besides proper environment and daily routine, meaningful social and individualized activities should be provided. In most cases the non-pharmacological interventions are more beneficial than the pharmacological interventions. Finally, all those guidances need caregivers, family members, health care workers, activity professionals or nursing homes and day care centers support to work. On this account, more education in caregiving is still needed.

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Conflict of interest
None

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