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A NARRATIVE REVIEW OF THE MANAGEMENT OF BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA

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ABSTRACT Dementia is a chronic or progressive neurodegenerative condition which is organic in origin. There will be impairment of thinking, memory orientation, comprehension, language, calculation, and judgement. Alzheimer's disease facts and figures in 2021 according to Alzheimer's association shows Alzheimer's disease accounts for 60% to 80% of the total cases. Behavioural and psychological symptoms of dementia also known as neuropsychiatric symptoms are a group of symptoms with behavioural and psychological manifestations. Disturbances include behavioural symptoms like wandering, hoarding, physical aggression, sexually disinhibition, culturally inappropriate behaviour, agitation and psychological symptoms like apathy, depression, anxiety, delusions, and hallucinations, sundowning, elation. Scales like the Neuropsychiatric Inventory, the Behavioural Pathology in Alzheimer Disease rating scale, the Consortium to Establish a Registry for Alzheimer Disease Behaviour Rating Scale for Dementia, Dementia Behaviour Disturbance scale, and the Neurobehavioral Rating Scale can be utilized to recognise BPSD.Neuropsychological assessment also have an important role. Non-pharmacological methodologies contain different sorts of treatment: tactile stimulation, pressure point massage, fragrant healing, light treatment, garden exercises, music therapy, dance therapy, and Snoezelen multisensory therapy, psychological strategies of multicomponent treatment strategies. Broadly focussing on sensory stimulation, social activities, structural activities, behavioural activities, environmental activities, and training programmes. Pharmacological treatment includes antipsychotics, mood stabilizers and antidepressants in treating BPSD, and cholinesterase inhibitors and memantine for the situation of Alzheimer's dementia sedative/hypnotics for sleep issues. Treatment can be further categorized based on individual NPS like agitation, psychosis, apathy, depression, sleep problems and other symptoms. Future treatment which has less evidence as of now includes rTMS, TDCS and Photo biomodulation therapy.

KEYWORDS : Alzheimer's, Behavioural, Dementia, Psychological

INTRODUCTION AND BACKGROUND

Dementia is an organic brain disorder which is chronic or progressive and primarily neurodegenerative in nature. There will be impairment of thinking, memory orientation, comprehension, language, calculation, and judgement. Agitation, aggressiveness, apathy, and psychotic disturbances are often reported behavioural disturbances in dementia. It will be difficult for caregivers to oversee and manage these symptoms. Alzheimer's disease facts and figures in 2021 according to Alzheimer's association shows Alzheimer's disease accounts for 60% to 80% of the total cases. Around 6.2 million Americans aged 65 and older have Alzheimer's dementia in 2021. 72% are aged 75 or older. One in nine people over the age 65 has Alzheimer's dementia.[1] In 2016, the overall prevalence of dementia was around 43.8 million, addressing a 117% expansion from 1990 and 28.8 million incapacity changed life years, and it was the world's fifth driving reason for mortality. Nearly 10.5 million people in Asia live with dementia, with the number expected to increase to 13.4 million of each 2030. Most patients with dementia experience behavioural and psychological symptoms of dementia (BPSD) eventually, up to 97% are affected by any one manifestation during a lifetime of presentation. Clinical manifestation increases with time, and it is associated with more hospital admission [2].

BPSD may not be a major feature during the beginning phases of Alzheimer's dementia, however these symptoms are likewise present in dementia disorder other than Alzheimer's dementia, for example, dementia with Lewy bodies or frontotemporal lobar degeneration where they may show up additionally in the beginning phases. Various patients with dementia with comorbidities, for instance, cardiovascular conditions, diabetes, epilepsy. Etc Opiates, anti-epileptic drugs and antipsychotics can worsen cognition in people with dementia. Additionally, treatment with antipsychotics have an extended threat of cardiovascular accidents and mortality. Several studies in literature reviews have been done to rate the effectiveness of non-pharmacological treatment for behavioural and psychological symptoms of dementia (BPSD).[3] Current pharmacological therapy with limited efficacy for dealing with neuropsychiatric symptoms requires a multidisciplinary approach including professionals like clinical psychologists, physiotherapists, and occupational therapists to give comprehensive care and case based intensive management. Nonpharmacological treatment can improve quality of life, functional independence, and cognitive functions in dementia with BPSD.It focusses on different interventions with emphasis to reduce patients' symptoms, decrease the care giver stress and environmental modifications. [4-6] These range from basic individual treatment to complex approaches with involvement of virtual media and automation of home. They help to improve involvement with the society and as the disease progresses can decrease disability and thereby improve both subject and care givers quality of life. [7,8]

REVIEW

Definition and symptoms of Behavioural and psychological symptoms of dementia

Behavioural and psychological symptoms of dementia also known as neuropsychiatric symptoms are a group of symptoms with behavioural and psychological manifestations.

Disturbances include behavioural symptoms like wandering, hoarding, physical aggression, sexually disinhibition, culturally inappropriate behaviour, agitation and psychological symptoms like apathy, depression, anxiety, delusions, and hallucinations, sundowning, elation. Symptom clusters in BPSD with the overlapping of symptom presentation is given in figure 1.

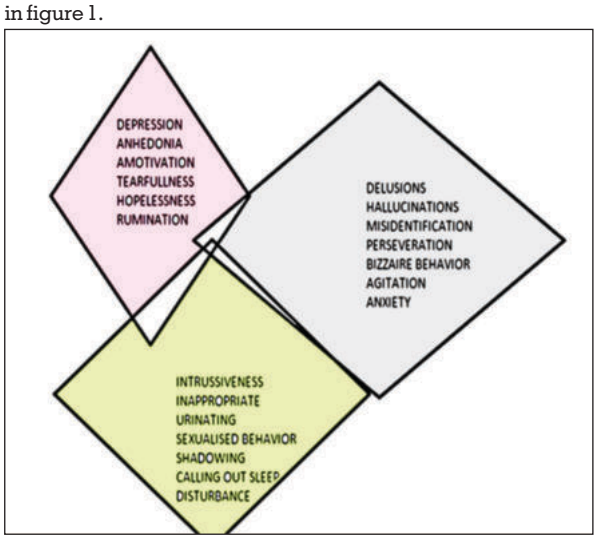


Figure 1-symptom Clusters In BPSD

Even though BPSD is seen over all stages of dementia disease, side effects of drugs and cognitive symptoms worsening the behavioural and psychological symptoms happen in moderate to severe stages of dementia. Clinical picture differs in different kinds of dementia. For example, psychosis and visual hallucinations are more common highlights of Lewy body dementia. Moreover, disinhibition, apathy, and social disinhibition are regularly seen in frontotemporal dementia. Although memory impairment is the sign of dementia, BPSD can make the life difficult for patients and their care givers. Care giver mismanagement can lead to faster disease progression and expanded bleakness and mortality. Behavioural aggravations need nursing home treatment and hospitalization, bringing about expanded care for the patient. BPSD with additional care giver stress and depression can result in decreased caregiver unemployment. About 33% dementia care costs are credited to management of BPSD, identified with expanded help use, care expenses, and care giver time. [9]. Table 1 shows the basic classification of BPSD into behavioural and psychological symptoms. There are numerous other ways for classifying behavioural and psychological symptoms. Cohens Mansfield inventory, neuropsychiatric inventory and BEHAVE AD are some of them to classify and rate behavioural and psychological symptoms of dementia. [10,11]

Table 1. Bpsd Can Be Broadly Classified Into Behavioural And Psychological Symptoms.

BEHAVIORAL SYMPTOMS	*PSYCHOLOGICAL SYMPTOMS*
Wandering	*Apathy*
Hoarding	*Depression*
Physical aggression	*Anxiety*
Sexually disinhibition	*Delusions and hallucinations*
Culturally inappropriate behaviour	*Sundowning*
Agitation	*Elation*

Neurobiology of BPSD

There is persuading proof that the origin of BPSD in Alzheimer's dementia due to anatomical and biochemical abnormalities. Given the wide exhibit of psychopathologic manifestations in Alzheimer's dementia, it is far-fetched that brain structure and changes relate to a particular BPSD.Neuroanatomical abnormalities showed hippocampus, prefrontal cortex and amygdala are the main regions involved. Volume reduction can impact serotonergic and BDNF symptoms.[12] Genetic studies show that chromosomal abnormalities are a risk factor for the prognosis of BPSD. [13] For instance, a connection between presenilin 1 and psychosis has been demonstrated. An association has additionally been appeared between polymorphism of serotonin receptors qualities (5HT2A 102-T/C and 5HT2C Cys23Ser) and visual and auditory hallucinations, with the two polymorphisms additively affecting visual hallucination. Polymorphism of the dopamine receptors qualities is likewise included in AD, homozygous for DRD1 allele B1 and homozygous for DRD3 allele were both related with psychosis. A genetic polymorphism of the serotonin carrier advertiser district (L/L genotype) has been shown in aggressive behaviour in patients with AD. [13]A similar genotype is by all accounts partner with a particular aggregate portrayed by psychosis and behavioural manifestations. The common pathologic lesions of AD, neurofibrillary tangles (NFT), show a trademark appropriation design that relates to dementia stage. In the previous stages, there is an evidence from the entorhinal cortex to the hippocampus, while in further developed stages there additionally is an involvement of the neo-cortex.[8,12,13] While "negative" symptoms (like apathy) can be obvious even before an analysis of AD is made, "positive" manifestations show up for the most part at later phases of dementia, after the presence of intellectual decline and probably when the neo-cortex contains NFT. Neuritic plaques and neurofibrillary tangles in the frontal and temporal cortices are associated with BPSD It has been shown that individuals with Alzheimer's dementia who has psychosis have a 2.3-overlap more prominent thickness of NFT in the neo-cortex (middle frontal, anterior third of the superior temporal, inferior parietal) contrasted with dementia patients who does not have psychosis Neurofunctional imaging considers have shown that psychosis in dementia is related with a decrease in prefrontal, left front, and metabolism in right parietal region.

Delusional misidentification, (for example, the conviction that a nearby relative has been supplanted by some other individual having a similar appearance) have been discovered to relate to lower neurone include in the CA1 space of the hippocampus; in a similar report a lower neurone include in the dorsal raphe was related with delusions and hallucinations[12]Higher NFT focus has been accounted for in the orbitofrontal region of Alzheimer's patients with agitation, while single-photon emanation CT exhibited hypoperfusion of the left anterior temporal cortex in Alzheimer's patients showing aggression. Likewise, in non-AD dementia, there is a relationship between area of pathological lesions and social behaviour. In Lewy's disease, for example, it has been shown that there is a solid relationship between the thickness of Lewy's bodies in the amygdala and parahyppocampal cortex and the presence of serious visual hallucination.[5]. High premorbid levels of neurotic feature are associated with depressive symptoms, apathy, and anxiety. Presence of APOE4 allele is associated with earlier age of onset of cognitive symptoms,APOE2 allele is associated with depressive symptoms, homozygotes for APOE4 allele is associated with disorientation,agitation,aggression and motor disorders,APE3 allele is associated with anxiety and sleep disorders, serotonin 2A receptor polymorphism is associated with visual and auditory hallucinations,hyperphagia,and aggression; dopamine receptor polymorphisms are associated with aggression and psychosis.[12] Frontal, parietal, and temporal cortical dysfunction are associated with psychotic symptoms. Greater EEG delta-power over the right hemisphere is associated with delusional misidentification syndrome. Damage to cholinergic neurons in the frontal and temporal cortices and adrenergic and serotonergic system in prefrontal and anterior cingulate and dopaminergic system in the substantia nigra and lower levels of serotonin in the

presubiculum are associated with psychotic symptoms [6,12-14]

Assessment

Assessment incorporates comparable data from caregivers as well as relatives. Collateral data helps in deciding the beginning, the course, and the differential diagnosis of BPSD. Physical, ecological, and psychosocial stressors might be triggers for the beginning of BPSD symptoms. Basic ailments, including pain disorder, urinary infection, and dehydration can bring about intensification of symptoms. [10].

Scales like the Neuropsychiatric Inventory, the Behavioural Pathology in Alzheimer Disease rating scale, the Consortium to Establish a Registry for Alzheimer Disease Behaviour Rating Scale for Dementia, Dementia Behaviour Disturbance scale, Manchester and Oxford Universities Scale for the Psychopathological Assessment of Dementia for overall BPSD; and the Neurobehavioral Rating Scale can be utilized to recognise BPSD.[47,48]Neuropsychological assessment also have an important role. These instruments help recognize symptoms and rate their severity. They can likewise help with rating progression and in observing treatment effect.[9] Comprehensive history often takes as collateral and from multiple family caregivers, cognitive assessment premorbid function assessment, psychiatric and medical history must be taken. Serum markers like vit B12, Vit d3, folate, homocysteine, T3 are to be looked for. Neuroimaging with MRI with Magnetic resonance spectroscopy, PET and SPECT findings can confirm the diagnosis of dementia and the region responsible for BPSD symptoms. [15]

Non-pharmacological Strategies

Various non-pharmacological methods are utilized explicitly in the initial stages of dementia with BPSD, many are first line options for treating neuropsychiatric symptoms as they have less side effects [11,16]Literature on non-pharmacological mediations have higher detailing quality and almost our insight on the part of non-pharmacological treatment will be consistently improved as more investigations are performed .Non-pharmacological methodologies contain different sorts of treatment: tactile stimulation ,pressure point massage, fragrant healing, contact treatment, light treatment, garden exercises, music therapy, dance therapy, and Snoezelen multisensory therapy, psychological strategies of multicomponent treatment strategies.[16,17]Nonpharmacological methodologies were even to be more superior than pharmacological medicines and appear to have less unfavourable impacts than pharmacotherapy with antipsychotics. As Nonpharmacological treatment upholds standard treatment in reducing manifestations and improving the personal improvement of patients and considered as parts of a more extensive idea of individual focused consideration and thereby supporting the person-centred approach which helps in understanding their experience, endeavours to help them and their family in arriving at the most ideal personal satisfaction. [18] The prognosis of a patient with dementia can be accomplished. through understanding the individual requirements and history of each patient. NPS can stem either from neurocognitive impairment related with dementia or from the neglected necessities of the patient. In instances of dementia where intellectual capacities are impeded, patients lose their capacity to impart through language. In such cases, they would be able to show their requirements, like agony, hunger, weariness, uncertainty, or nervousness, through their conduct. Nonetheless, such conduct might be affected by their intellectual impedance, which influences the way they see, decipher, and respond to the environment: patients may have issues with express memory, acknowledgment of visual movement or on the other hand spatial direction, and geographical confusion. Non-pharmacological treatment can be divided into direct ones focused on patients and backhanded ones focused on their environment. Studies propose that a mix of both immediate and aberrant non-pharmacological mediations might be fundamental to decrease BPSD. Besides, a new report of health-related quality of life (HRQOL) for individuals with dementia found antipsychotic stopping to detrimentally affect HRQL. [19,20] This negative effect was, in any case, moderated by friendly cooperations. For treatment to be fruitful, it ought to think about the significance of a mindful environment, i.e., the physical, constructed. one, and the social climate, just as care ability advancement and support, and taking an individualized way to deal with every persistent. Table 2 shows the non-pharmacological methods in management of BPSD. Broadly they can divide based on those focussing on sensory stimulation, social activities, structural activities, behavioural activities, environmental activities, and training programmes. There is lack of substantive evidence of any one nonpharmacological method superior to others. The combined effort of two or more nonpharmacological methods showed good improvement in early stages of neuropsychiatric symptoms. [21-23] Activities of daily living (ADL) of people with dementia of any severity, exercise therapy and light therapy were beneficial in improving ADL. Music therapy was effective in reducing the overall BPSD with a medium effect size in two meta-analyses. [23,47]

Nonpharmacological management of BPSD		
Sensory stimulation	Social activities	Structural activities
• Massage and touch, warmed blankets • Individualized music and music therapy • White noise • Controlled multisensory stimulation (Snoezelen) • Art therapy • Aroma therapy • Gardening • Cooking	• Individualised social contact • Reminiscing • Pet therapy • 1:1 social interaction • Simulated interaction/family videos, skype, phone calls, letters from family.	• Recreational activities • Outdoor walks • Physical activities • Exercise • Meaningful activities e.g.- folding laundry, delivering newspaper
• Behavioural activities	• Environmental activities	• Training programmes
• Differential reinforcement • Stimulus control • Cognitive stimulation	• Safe environments to walk. • Reduced stimulation. • Light therapy • Easy access to outdoors	• Staff education and support • Training programs for family caregivers

Nonpharmacological methods given via caregivers can diminish the recurrence of manifestations and can lessen burden of caregivers, with effect sizes like those related with pharmacotherapy. Successful treatments included roughly 9 to 12 individual meeting sessions intended to address the issues of the patient and their guardians and were conveyed in the patient's home utilizing various parts more than 3 to 6 month with occasional development. There are measurably huge outcomes for nonpharmacological mediations on at any rate one symptom of BPSD.These interventions included staff preparing in social administration procedures, emotional wellness and treatment arranging, work out, sporting exercises, and music treatment or different types of tactile or other sensory stimulation. [9] In any case, there were methodological bias that recommend a potential risk of predisposition. Additionally, for a significant number of the interventions, generous resources from outside administrations were required alongside extensive time requirement from the nursing staff for the execution of these procedures. [4,9,11,24]

Pharmacological Treatments

As of now, non-pharmacological and pharmacological treatment alternatives exist for treating NPSs. Pharmacological mediations have numerous limits in old patients with dementia and social indications. Neuropsychiatric manifestations, on the other hand, happen in most of kinds of dementia, not simply Alzheimer's dementia. SSRI antidepressants citalopram and sertraline has shown improvement in these symptoms, with a rate of adverse effects similar to placebo, although trazodone was found not effective. When treating mild to moderate BPSD with SSRIs it's always good to follow 'start low, go slow, but go as high as you need to go' because too-rapid titration can worsen agitation.[24] Most studies centres around the usefulness of antipsychotics, mood stabilizers and antidepressants in treating BPSD, and cholinesterase inhibitors and memantine for the situation of Alzheimer's dementia. Just couple of medications are shown for treating BPSD in dementia. [25,26] Tiapride is suggested in cases with dementia in Poland, and pimavanserin for psychosis related with Parkinson's disease in the USA. The starting and target dose is the same (34 mg). Like other antipsychotics, it prolongs the QT interval and carries a black box warning about the increased risk of death in dementia Likewise, risperidone is suggested for treating aggression in moderate to-extreme cases of Alzheimer's dementia not responding to non-pharmacological mediations and when there is a danger to the patient. Also, the combination of dextromethorphan and quinidine, which has approval in the U.S. and Europe for pseudobulbar affect. Even though endorsing psychotropic prescriptions to a patient with dementia gives off an impression of being clinically supported, it stays an off-name request in many nations. [25,26]The fundamental technique for pharmacological treatment of BPSD depends on antipsychotics. Antipsychotics are excessively frequently utilized in more population for different signs, not just psychosis. Many doctors accept that antipsychotics are multipotential: they may likewise be successful in other clinical conditions, and their essential action does not concern psychoses. If an antipsychotic not beneficial, an alternative antipsychotic can be tried using a cross-titration, but olanzapine is avoided due to its anticholinergic effects and lower benefit overall. Prazosin or dextromethorphan-quinidine are potential therapies tried with moderate results in BPSD.[27]Regardless of whether recommending a neuroleptic to an individual with dementia seems, by all accounts, to be clinically supported, it stays an off-mark request in many nations .Antipsychotics have been reliably connected with genuine side effects and expanded mortality in patients with dementia .Antipsychotic treatment can bring about cerebrovascular occasions (e.g., stroke), cardiovascular impacts (e.g., orthostatic hypotension, heart arrhythmias, and QTc prolongation), metabolic impacts, extrapyramidal indications, and falls, just as pneumonia .The developing assemblage of proof regarding the expanded danger identified with antipsychotic use among patients with dementia brought about backbox warnings being given by the FDA . A study showed the risk of death was more among people who were treated with atypical antipsychotics.[28] Another study tracked down those customary antipsychotic prescriptions were related with an essentially higher danger of death than were atypical antipsychotic medications. The danger of cerebrovascular events was 1.3 to multiple times higher with usual treatment contrasted with placebo treatment; the danger of death was about 1.2 to 1.6 times higher.[29] The risk is comparable for typical and atypical antipsychotic specialists. A higher-than-average dose of a medication, more the age, vascular dementia, and comorbid atrial fibrillation have been noted as risk factors for cerebrovascular events. Elderly, male sex, severe dementia is related with higher risk of death. [30,31] Table 3 shows the list of drugs used in behavioural and neurological symptoms of dementia also given the mechanism of action, dosage, and adverse effects.

TABLE 3 Pharmacotherapeutic therapeutic agents for behavioural and psychological symptoms of dementia

Medication	Daily dose	Adverse effects	Mechanism of action
Cholinesterase inhibitors			
Donepezil	5 to 10 mg	Bradycardia, confusion, GI symptoms, sedation	Selective reversible non-competitive inhibitor of AChE
Galantamine	4 to 24 mg	Nausea, vomiting, hallucination, depression, syncope	Reversible inhibitor of AChE, presynaptic modulator of nicotinic AChE
Rivastigmine	1.5 to 12 mg or 4.6 to 9.5 mg patch	Anorexia, dizziness, nausea, vomiting, diarrhoea	Pseudo-irreversible inhibitor of AChE and BChE
Memantine	7 to 28 mg	Drug hypersensitivity, somnolence, dizziness	NMDA antagonist
Mood stabilizers			
Carbamazepine	100 to 400 mg	Confusion, falls, hyperammonaemia, liver dysfunction, steven Johnson syndrome	Sodium channel blocker
Valproic acid	125 to 1000 mg	Liver dysfunction, sedation, thrombocytopenia, pancreatitis, oedema	Inhibits GABA transaminase

Antidepressants			
Citalopram	5- 20 mg	Dry mouth, falls, headache, GI symptoms, sedation, sexual dysfunction	Inhibit reabsorption of serotonin in presynaptic end
Paroxetine	5-40mg		
Sertraline	25 -100mg		
Trazodone	25-300mg	Nausea, falls, sedation, postural hypotension, priapism	Alpha 1 adrenergic, weak 5HT2A antagonism, blocking uptake of 5HT
Venlafaxine	75-225mg	Nausea, headache, sexual dysfunction, insomnia, constipation	SERT and NE inhibition
Mirtazapine	15-45 mg	Nausea, dizziness, sexual dysfunction, constipation	Blockade of alpha 2,5HT2A,5HT2C,5HT3
Antipsychotics			
Aripiprazole	2.5mg – 10 mg	Akathisia, hypothyroidism	Partial agonist at dopamine D2, D3,5HT1A receptors, antagonist at 5HT 2A
Risperidone	2.5mg – 10 mg	Cerebrovascular events, death, extrapyramidal symptoms, falls, metabolic syndrome, neuroleptic malignant syndrome prolongation, sedation, sexual dysfunction	D2 and 5 HT2 blockade
Olanzapine	0.25mg – 2mg		D2 and 5 HT2 blockade
Quetiapine	25mg- 200mg		D2 and 5 HT2 blockade
Pimavanserin	17 -34mg	Peripheral oedema, nausea, and confusional state. Hallucinations, constipation, and gait disturbances	5HT2A antagonist/inverse agonist

Management of major symptoms in BPSD

Agitation

Agitation is a serious issue in patients with Alzheimer-type dementia. Non-pharmacological medicines as first-line alternatives must be considered first. Although different classes of psychotropic medications are utilized for treatment of agitation in dementia, it is associated with risk benefit ratio. These include typical (promazine) and atypical antipsychotics, antidepressants, anticonvulsants, antihistaminergic drugs (hydroxyzine), and natural drugs.

The greater part of these are off-label psychotropic prescriptions because there is lacking or no information for their usefulness and wellbeing in patients with dementia, and their solution depends on custom and genuine beliefs of doctors. [5,10] For instance, a new Cochrane metanalysis recommends that valproate, which are generally utilized for behavioural disturbance and epilepsy in treating individuals with dementia. A meta-analysis reported that the citalopram and sertraline were more successful in diminishing side effects contrasted with placebo in two studies. SSRIs and trazodone were additionally found to be very much tolerated when contrasted with typical and atypical antipsychotics. [31,32,44,46] Likewise, no distinctions were noticed among antidepressants and typical and atypical antipsychotics regarding effectiveness.

A new methodical survey and meta-analysis of RCTs performed to decide the most effective and worthy treatment of BPSD in dementia found that haloperidol shown little adequacy contrasted with placebo treatment. Likewise, dextromethorphan/ quinidine and risperidone were altogether more effective than placebo treatment, as were SSRIs when considered as a class, however not at the point when broke down exclusively. [32] In addition, randomized controlled trials (RCTs) on treating agitation in dementia of Alzheimer-type with new drugs. Considering the accessible information on drug efficacy, antagonistic impacts, accessibility, and novel medication enlistment methods, it appears to be that citalopram might be the most reasonable alternative for some doctors in controlling agitation in dementia.[34] The studies suggest beginning treatment with risperidone, at that point aripiprazole or quetiapine, carbamazepine and afterward citalopram. Because of citalopram, it is significant to know about the increased danger of QTc prolongation, which can be hazardous in geriatric patients. [33,34]

An alternative method of treating agitation in dementia is by electroconvulsive therapy (ECT). A recent review of paper investigating the use of ECT for treating agitation in dementia found promising results in decreasing agitation in patients with dementia; however, the studies have many methodological limitations regarding the type of study, us of psychotropic medications, choice of scales, lack of control group and number of patients, among others.[35]

Psychosis

Most psychotic symptoms that happen in dementia are delusions and hallucinations, and numerous patients require antipsychotic treatment to manage of such troubling mental manifestations. This is particularly obvious when a patient follows up on the hallucinations, encounters danger, or if their security is compromised. Antipsychotics are still generally recommended, even in instances of dementia without psychosis. [36]

In 2016, the American Psychiatric Association distributed a Practice Guidelines on the utilization of antipsychotics to treat psychosis in dementia .The rules involve 15 proclamations on antipsychotic use in dementia, assembled into five segments: evaluation of social/ mental indications of dementia; improvement of an exhaustive treatment plan; evaluation of advantages and dangers of antipsychotic treatment for the patient; dosing, span, and checking of antipsychotic treatment; and utilization of explicit antipsychotic prescriptions relying upon clinical setting. [35,36] The antipsychotic olanzapine, quetiapine, and risperidone in treating dementia were analysed in the CATIE-AD study. Other second-age antipsychotics, for example, aripiprazole and ziprasidone, have too shown security and efficacy in treating AD. [37-39]

Apathy

Apathy is a non-psychological manifestation and quite

possibly the most pervasive social and mental manifestations of dementia, which can be noticed even at the prodromal stage. It is difficult to distinguish apathy from depressive symptom. Lack of emotionality is said as a feature of dementia. It tends to be portrayed as lessened inspiration or indeed, even absence of inspiration and loss of activity. It is an enduring state that is related with increased mortality and a significantly more noteworthy risk for caregiver's apathy, anxiety, and depression which causes care giver burnout. [39,40]A higher level of burnout was identified with hostility, delusions, and hallucination.

Various nonpharmacological treatment have been utilized: music-based, normal individualized one-on-one individual contact, social and ecological modification, combined workmanship treatment, the utilization of restorative functions and Snoezelen-based therapy .Be that as it may, a survey of existing proof demonstrates it to be an underexplored field.[40,46]Cholinesterase inhibitors, memantine, antidepressants, antipsychotics, psychostimulants, and drugs with different mechanism of action have exhibited blended outcomes.

Agomelatine was associated with a huge decrease of apathy in FTD, while bupropion was insufficient in the treatment of apathy in Huntington's illness Parkinson's dementia, and dementia with Lewy bodies, essentially influencing the course of on account of the last mentioned.[41] Be that as it may, no efficacious treatment presently is known to exist. Prevalence of apathy aggravates with time and correlates with disease severity. Over the course of dementia has clinical relevance of apathy is significant.

Depression

Depression is inseparably connected to cognitive impairment and dementia. Throughout the long term, there has been a conversation about the connection among depression and dementia. On the other hand, depression has been demonstrated to be a normal in beginning of dementia or MCI and is in certainty part of the clinical image of dementia. [39,41] In most of patient's pharmacological treatment is the first line treatment. A question emerges whether there is adequate proof for suggesting the utilization of pharmacotherapy in treating depression in patients with dementia. A meta-analysis found pretty much nothing support for the adequacy of antidepressants for treating depression in dementia.

Similarly, as with all BPSD, the administration of clinical depression should begin with the improvement of dementia treatment. [42,46] However, while acetylcholinesterase inhibitors and memantine are powerful in treatment of AD, current proof proposes that they have restricted adequacy for the treatment of depressive manifestations in dementia. [42-44] Moreover, non-pharmacological treatment which are a favoured starting approach for all BPSDs, have restricted proof for depressive manifestations. Modifiable elements causing depression for patients living in long term care services can be managed with non-pharmacological treatment.

Sleep Problems

Sleep problems in patients with dementia are regular, influencing somewhere in the range of 25 and 80% of patients; these figures are higher than those related old age can be due neurodegenerative changes in the brain. The results of difficulty in sleep cause increased risk of intellectual disability and dementia, yet in patients with dementia, outcomes depend on comorbidity, risk of falling, poor quality of life, and increased mental issues in the caregiver. At last, they frequently disturb the course of dementia through fatigue and lassitude during the day, in this way weakening intellectual execution, driving, and social exercises [41-43] Alzheimer's illness is described by a diminished mood, sundowning and obstructive rest apnoea. Parkinson's dementia is described by REM sleep disorder, sleep deprivation, hypersomnia, a propensity to fidget while Dementia with Lewy body patients exhibit REM sleep behavioural, hypersomnia, occasional and unpredictable sleep wake rhythms. [12-14] FTDs have sleep deprivation, unreasonable daytime sleepiness furthermore, less continuous a propensity to fidget. It is troublesome, or even unthinkable, to propose a general technique for treating sleep problems in dementia because of this critical variety in clinical picture and neuropathology.

Mainstream drugs for sleep disturbances in dementia such as melatonin, trazodone, benzodiazepines, Z-drugs (zolpidem, zopiclone, and zaleplon), and as of latest ramelteon. At this point, it is important to review that old benzodiazepine turned out to be more delicate to compared to other drugs. Paradoxical reactions (increased tension, intense fear and hyperactivity) can be seen at times.[44] In addition, the Z-drugs have reported evening confusion and falls.Other treatment modalities include antihistaminergic drugs, natural preparations, or antidepressants like mianserine and mirtazapine. [39-41]

Other Symptoms

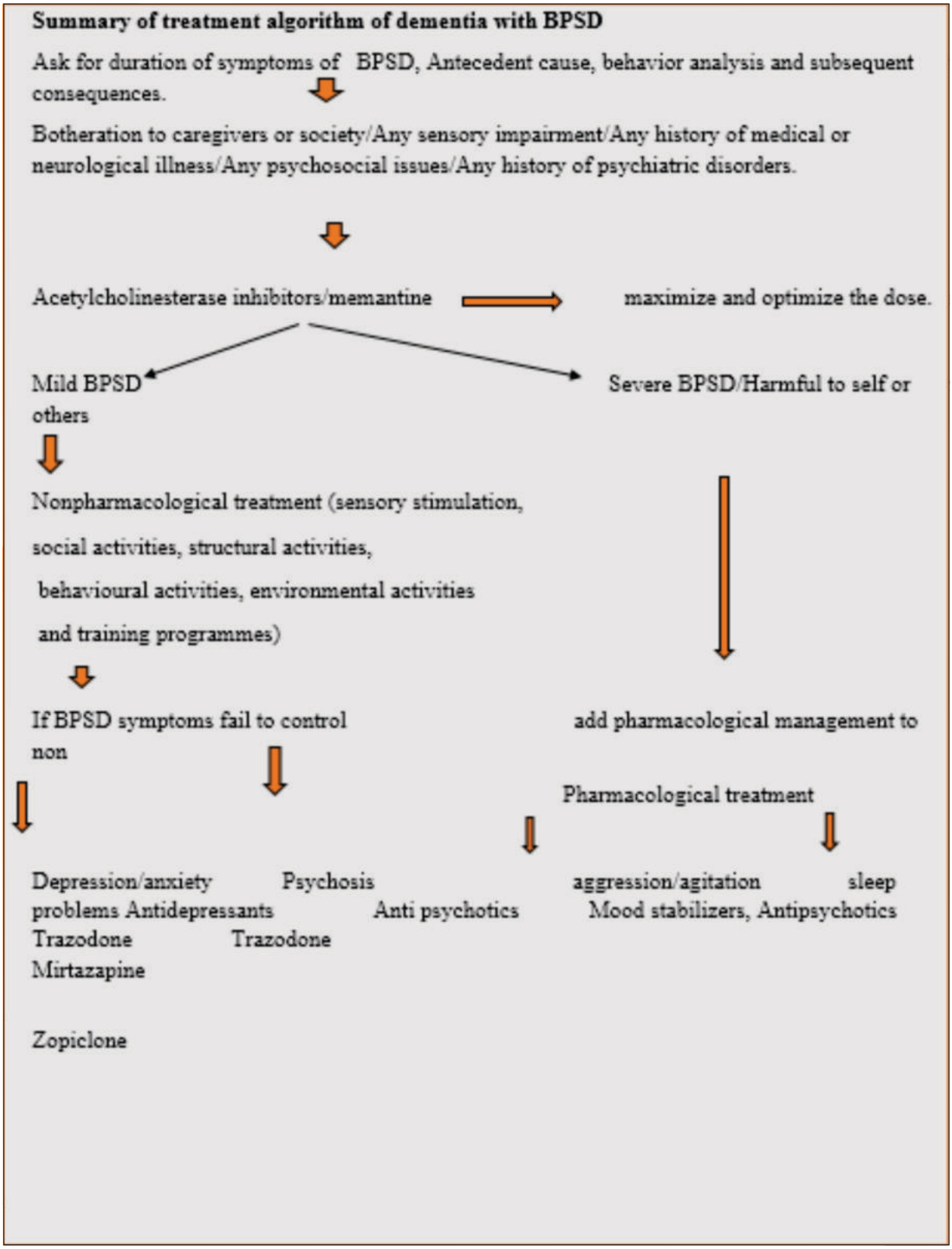
Assessment of behaviour such as wandering is subjective, according to the observer's approving/ disapproving attitudes, rather than the behaviour per se. Wandering is one of the most troublesome symptoms reported by family caregivers. Caregiver education and behavioural modification has shown benefits in wandering. [39] Screening tools can help differentiate between different types of wandering and help develop an individualised person-centred intervention. Identifying and modifying the potential dangers near home, creating the list of places person wanders and get the help of police and dementia wandering service are the options. [39,40]

Sexuality is expressed very differently across different cultures and societies, and it is therefore difficult to define what constitutes an appropriate behaviour. Sexual disinhibition can be extremely disturbing to the caregivers, with reports of anxiety, feeling of unease among the caregivers and may result in legal actions. [44,45] Also, clinicians ought to consider that sexual desire and libido is still present well into the old age and the inappropriate behaviour may surface due to a lack of willing sexual partner or privacy especially among the institutionalized elderly. [45,46]. Limiting the medications which cause sexual disinhibition has shown good results.[46]

Sundowning is restlessness, increasing confusion or changed behaviours in a patient with dementia that can occur late in the afternoon or early evening. There are different patterns of wandering behaviour and different management issues and levels of risk based on predominant psychopathology. It is almost always associated with hallucinatory behaviour. [42,44-47]

Hoarding behaviour is the manifestation of personality traits, and it is more severe as the dementia stage is advances. It has got the worst prognosis compared to other behavioural symptoms. Senile squalor syndrome is a behaviour of hoarding which is common in western culture with socially isolated old age couples with cognitive impairment amounting to dementia. Behaviour modification therapy and cognitive stimulation therapies has been tried with poor outcome [16,48,49].

A summary of the management of BPSD is given step wise in the following algorithm.



Future therapeutic options of BPSD

Masupirdine is a pure 5-HT_6 receptor antagonist under clinical development for the management of behavioural and psychological symptoms of dementia and has shown efficacy in agitation/aggression and psychotic symptoms with positive effect on cognition.[50] Although gingko biloba has shown consistent benefit for BPSD but has got low evidence in RCT's. Yokukansan is a traditional Japanese Kampo medicine has gained recent attention among the complementary and alternative medicine in treating hallucinations, apathy low mood, impulsivity, and anxiety.[51] As current systems for the treatment of BPSD frequently need effectiveness, there is a need to recognize other treatment alternatives. Most studies centre around pharmacological mediations, some include strategies known for their adequacy in another clinical field. Non-invasive cerebral stimulation strategies, for example, repetitive transcranial magnetic stimulation, (rTMS) and transcranial direct current incitement (tDCS) have been tried

in apathy, schizophrenia, chemical disturbance, and psychological symptoms in dementia.[52] Recent studies showed rTMS to exhibit adequacy yet not tDCS, nonetheless, both were found to show efficacy and superiority in the studied sample. TDCS for management of agitation in AD and repetitive transcranial magnetic stimulation (rTMS) for depression in Alzheimer's dementia. [12] Light therapy with melatonin at bedtime may be useful to treat sleep or circadian rhythm disorders, 'sundowning' and day sleepiness. Photo biomodulation therapy is new entity for potential treatment for neuropsychiatric symptoms in neurocognitive disorders. [53,54]

CONCLUSION

Nonpharmacological treatment remains the gold standard and mainstay of treatment of dementia with behavioural and psychological symptoms.Pharmacological treatment can be considered in failed cases of first line treatment after assessing the risk benefit ratio. Neurostimulation therapies like ECT which has got good evidence and upcoming rTMS, TDCS is being used widely now a days. Traditional light therapy and newest therapy of photo biomodulation is still under research phase and needed evidence from randomised controlled trials. The future of dementia management with its due importance in management of BPSD is given in the ongoing dementia trials.

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