Dementia, Agitation, and Aggression: The Role of Electroconvulsive Therapy

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What role might electroconvulsive therapy play for short-term treatment of agitation and aggression in patients with dementia?

Agitation and aggression are some of the most frequent and disruptive neuropsychiatric symptoms in patients with dementia. Approximately 45% to 80% of patients with dementia will exhibit agitation and aggression, depending on the clinical setting and dementia stage. Agitation and aggression have a major negative impact on disease burden, with higher incidence of functional decline and loss of independence, more frequent hospitalizations and premature institutionalization, higher rates of morbidity and mortality, and higher degree of caregiver stress and burnout.

Although agitation and aggression are among the most significant challenges in current dementia care, their treatment continues to be suboptimal. Currently there are no FDA-approved treatments for this indication.

Psychosocial treatments
Nonpharmacological methods of managing agitation and aggression are considered to be the first-line treatment approach. These interventions are aimed at preventing and/or containing the influence of underlying contributing factors, such as unmet needs; environmental overload; and interactions of individual, caregiver, and environmental factors. However, their use in everyday clinical practice is limited by multiple factors, most commonly lack of adequate training, time, and other resources. A recent 4-step approach—Describe, Investigate, Create, Evaluate (DICE)—that is based on the current nonpharmacological strategies with the strongest evidence-based efficacy has been formulated.

Describe. The clinician asks the caregiver to describe in chronological detail the concerning behavior. This should include any related social and environmental context, the patient’s perspective, and the degree of distress to both patient and caregiver.

Investigate. The clinician identifies the underlying, modifiable causes of agitation and aggression—those related to the individual (eg, comorbidities, pain, cognitive impairment, functional limitations) and the caregiver (eg, communication style, expectations, personal life stressors and events, cultural beliefs) as well as environmental causes (eg, safety, over-/under-stimulation, ease of navigation).

Create. The clinician, the treatment team, the caregiver, and the patient (as much as possible) collaborate to create and implement a treatment plan that addresses all the underlying causes of agitation and aggression. These generalized and targeted behavioral and environmental strategies consist of caregiver education, enhancing communication between the caregiver and the patient, assisting the caregiver to create meaningful activities for the patient, and helping the caregiver to simplify tasks and establish structured routines.

Evaluate. The clinician consistently assesses and modifies the treatment plan and specific strategies as needed, keeping in mind a personalized approach.

Psychopharmacological interventions
Psychotropics should be considered only in cases in which agitation and aggression pose a serious acute threat to the safety of the individual or that of others. Nonetheless, in clinical practice, off-label use of psychopharmacological agents for agitation and aggression—including antidepressants
Mrs A presents with advanced Alzheimer dementia. She is admitted to a geriatric neuropsychiatry unit of a university hospital for severe agitation and aggression. Alzheimer dementia had been diagnosed after a brain MRI showed diffuse severe cortical atrophy and bilateral hippocampal atrophy. Mrs A lives at home with her husband, who is the primary caregiver. She presents with severely impaired language skills (e.g., decrease in spontaneous and meaningful speech). She had been displaying major behavioral disturbances, with agitated and aggressive behavior toward her spouse and resistance to care, for 18 months before the admission. Mrs A has been hospitalized in the neuropsychiatric unit for nearly 3 months—with a short medical hospitalization for pneumonia. Multiple antipsychotics have been tried but discontinued because of significant adverse effects. Other trials included antidepressants, mood stabilizers, benzodiazepines, cognitive enhancers, and β-blockers. Most of these medications caused significant adverse effects and had little, if any, effect. Eventually all of the psychotropics were discontinued, except escitalopram.

Mrs A still exhibited agitation and aggression that frequently resulted in the need for physical restraints, including a geri-chair and multiple types of chemical restraints, which are rarely effective. Because of this ongoing agitation and aggression, her quality of life was greatly impaired and it was impossible for her to return home or to be placed in a nursing home or other similar facility. Approximately 2 months after the hospitalization, ECT was started. She received 8 inpatient bilateral ECT treatments that immediately (after the initial treatment) proved very effective at decreasing the severity of agitation and aggression, with continued improvement thereafter. She no longer has episodes of agitation or aggression, and she is calm and cooperative with her caregivers. The neuropsychiatric symptoms also improve. The only adverse effect is mild headache; there is no serious memory loss or cognitive adverse effect. At the end of the third month, Mrs A is discharged on a regimen of 20 mg of escitalopram daily and 5 mg of haloperidol daily as needed for...
sive agitation.

Mrs A continues to live at home with in-home services; once every 4 weeks she receives maintenance bilateral ECT. Despite the previous 10 years of dementia, since she began ECT treatment, she has remained fairly stable, with no more episodes of agitation or aggression or other behavioral disturbances. She has had little progression in functional decline and has not had a psychiatric rehospitalization; her overall quality of life has improved dramatically and she is able to participate in significant life events of her children and grandchildren.

Patients most likely to benefit from ECT
The studies of ECT cited earlier carry some important limitations, including lack of control groups and randomization, small sample size, heterogeneity of dementia diagnosis, and lack of systematic neurocognitive assessment at baseline and post-ECT. In all cases, only acute ECT for agitation and aggression was assessed as an add-on to other treatments for short periods, with no data on long-term efficacy and safety. These data do not allow proper identification of predictive factors that can be used to determine which patients could benefit from such treatment and when the treatment should be initiated.

Additional research is needed to further elucidate the role of ECT for the treatment of agitation and aggression. Specifically, blinded controlled prospective studies that compare ECT with other treatments; longitudinal studies that evaluate the role of continuation and maintenance ECT; and controlled studies of different ECT parameters that allow for a personalized ECT treatment strategy that maximizes efficacy while minimizing adverse effects are needed. Neuroimaging and other more specific studies should aim at understanding the etiology of agitation in dementia and whether ECT affects the overall natural course of dementia. These studies could allow for the identification of predictive factors to help clinicians decide which patients would receive the most benefit from ECT. Despite these limitations, these initial data are promising and indicate that acute ECT may be a safe and rapidly effective treatment for severe and treatment-refractory agitation and aggression. It must be emphasized that ECT is considered a last resort treatment option after all other recommended treatment options have been exhausted. It is also an option in cases of tolerance problems or when respective risks outweigh possible benefits. In certain cases in which the patient is experiencing severe agitation and aggression that is a serious risk to his or her safety and survival, ECT should be considered as a viable treatment option sooner rather than later given the rapid response. Current data on ECT for such an indication raise an important ethical concern regarding the possibility of ECT prolonging life and therefore the duration of the illness, with continued suffering for patients and their families. Whether the achieved improvement in quality of life outweighs these concerns and who ultimately makes such a decision continue to be a challenge.

Specific treatment strategies
An ECT-credentialed psychiatrist should perform the ECT consultation, and medical clearance should be achieved in close collaboration with the anesthesiologist and the internist. Before ECT is started, both informed consent from the patient’s authorized health care representative and general assent from the patient must be obtained. Seizure threshold is determined on the first ECT treatment with the empirical dose titration method; stimulus parameters are adjusted during the ECT course as indicated by seizure quality and treatment efficacy. Initial electrode placement generally is right unilateral, given the lesser cognitive adverse effects and the efficacy that is comparable to that of bilateral treatment with brief pulse width (0.5 to 1 millisecond) at 4 to 6 times seizure threshold. The clinician may choose bilateral electrode placement initially or transition to it later in the treatment when deemed clinically appropriate, with a brief pulse width (0.5 to 1 millisecond) at approximately 1.5 to 2.5 times seizure threshold. Indications include previous history of agitation and aggression treatment with bilateral ECT or inadequate response with right unilateral ECT. Severe symptoms that require prompt resolution, especially in court-ordered cases for which only a limited number of treatments are granted, may also indicate bilateral placement.

In general, the course of ECT consists of 3 treatments weekly, or less frequently if clinically indicated. Methohexital is used for anesthesia and succinylcholine for muscle relaxation. Etomidate can be substituted for methohexital in cases of inadequate seizure quality or duration. The risk of postictal confusion and delirium can be decreased by eliminating drugs such as lithium and bupropion as well as by using intravenous benzodiazepines or propofol. If postictal confusion is prolonged or delirium develops, the next ECT treatment should be delayed; treatment frequency can be decreased if there is reoccurrence. In either case, further investigation may be necessary in patients with preexisting medical illnesses and cerebrovascular disease.

Early introduction of ECT as a treatment option

The risk of
While ECT should not be considered a first-line treatment for agitation and aggression, its availability as an off-label treatment option should be presented early during treatment planning. Providing adequate, comprehensive, and timely information about possible risks and benefits associated with this specific ECT indication will allow the patient, family, and the authorized health care representative to achieve an optimal informed decision. Delay in communicating information about the potential benefits of ECT can reinforce the prevailing stigma about ECT. Consultation can be requested on hospital admission for an early assessment of the adequacy and feasibility of ECT. While there are no absolute contraindications for using ECT, certain cardiovascular, respiratory, or other medical illnesses can increase risks of adverse events from the general anesthesia or the ECT treatment itself. For patients at increased risk for adverse events, ECT should be done in a general medical setting where emergency intensive care can be accessed quickly.

Informed consent
Different states have different provisions in their statutes that regulate ECT treatment consent, refusal of ECT and involuntary treatment, use of ECT in different psychiatric disorders and different age-groups, and total number of treatments. Clinicians should be well informed about applicable local statutes and regulations. A possible challenge is the continued refusal on the patient's side to provide general assent despite ongoing efforts to identify and/or adequately address the reasons for refusal. In such a case, only a court order can allow ECT treatment to proceed.

Neurocognitive and neuropsychiatric assessments
Standardized assessment of cognition, agitation, aggression, and other neuropsychiatric symptoms of dementia at the time of admission in an acute psychiatric unit should be part of standard clinical care. At minimum, such assessment should be done at baseline before starting ECT, after the acute course, and during eventual continuation and maintenance ECT. A comparison of pre- and post-ECT neuropsychiatric and neurocognitive domains can be very informative when evaluating clinical efficacy and effects of ECT on cognitive functioning of patients with dementia. Such assessments can prove challenging, especially in the early stages of treatment, because frequently agitation and aggression will interfere with the patient’s ability to participate. Therefore, any previous cognitive assessment might be helpful in determining the cognitive progression of the patient during ECT.

Disclosures:
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