Psychopharmacology of Persistent Violence and Aggression

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KEYWORDS

• Aggression • Violence • Impulsivity • Pharmacology

KEY POINTS

- Impulsive behavior is the most common form of persistent aggression among psychiatric inpatients. Psychotic and impulsive violence are amenable to pharmacotherapy. Predatory behavior demands forensic/behavioral approaches.
- For schizophrenia patients, D_2 antagonism with plasma-level monitoring is the initial strategy. Clozapine has strong evidence for treating psychotic aggression in refractory patients and for impulsive violence. The evidence for adjunctive strategies to antipsychotics is weak for psychotic and impulsive violence.
- The traumatic brain injury (TBI) literature contains only a small number of good-quality randomized clinical trials (RCTs) that demonstrate efficacy in persistent aggression: centrally acting β-blockers, divalproex, or carbamazepine and possibly dopaminergic agonists. There is no literature to support the use of antipsychotics.
- Evidence-based pharmacotherapy for persistently aggressive dementia patients includes use of acetylcholinesterase inhibitors (AChEIs) for mild–moderate stage patients and selective serotonin reuptake inhibitors (SSRIs). Antipsychotics carry dose-dependent mortality risks. The data for valproate also show increased risk for mortality risk and poor tolerability.

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INTRODUCTION

Violence and aggression are major societal concerns and often intersect with psychiatric providers in both acute and subacute settings.[1] Although the terms, *aggression* and *violence*, are often used synonymously, there are distinct differences in their meanings. Aggression represents acts that may lead to harm (toward self or others), whereas violence is a subcategory of aggressive acts that causes harm to others.[2] The presentation of aggression in unmedicated or inadequately treated psychiatric patients is often dramatic and associated with agitation, yet these patients often respond robustly in the short term to standard pharmacologic interventions, including antipsychotics alone or with benzodiazepines.[1,3–5] (For a comprehensive review, see Newman.[2]) The more vexing clinical issue is the management of persistent aggression toward others encountered in psychiatric inpatient and forensic settings.[6] Although the diagnostic mix in these environments weighs heavily toward schizophrenia spectrum diagnoses, intellectual disability, and cognitive disorders, clinicians must accurately classify the nature of aggressive events before embarking on any pharmacologic course of action. Such categorization is critical to the determination of appropriate management strategies that are necessarily based on the interplay between underlying psychiatric diagnosis and the nature of the violent episodes.[7]

The purpose of this review is to provide a rational therapeutic approach to the problem of persistent aggression and violence seen in long-term psychiatric inpatient settings and focus on how the categorization of violent acts informs medication strategies within the most common diagnostic groups: schizophrenia spectrum disorders, TBI, and dementia. Self-injurious behavior and other aggressive acts toward self, as well as the acute management of agitation in minimally treated patients, are not discussed to focus attention on the more intractably aggressive patient. The treatment of behavioral disturbance in nonpsychotic patients with intellectual disabilities is typically confined to specialized facilities designed to meet the unique needs of this population. Readers are referred to several excellent reviews for discussions about the appropriateness and nature of pharmacotherapy for aggressive patients with intellectual disabilities.[8–11]

Although pharmacologic approaches may be useful, and necessary, for certain types of violence, it must be noted that environmental variables, staffing ratios and expertise, and psychosocial stressors play an important role in aggressive behavior. These areas must also be addressed to obtain the maximum benefit from medication options.[6]

Classification of Aggression

Although persistent violence has long been recognized among chronic psychiatric inpatients, only in the past decade has there emerged a clinically useful and empirically derived categorization scheme. Investigators within the New York State Hospital system videotaped a series of assaults and then supplemented the videos with assailant and victim interviews to determine the motivation for each violent act.[12] These detailed assessments led the investigators to conclude that 3 categories could be used to define these aggressive acts: psychotic, impulsive, and predatory (also called organized or instrumental). Despite that a majority of patients had schizophrenia spectrum diagnoses, the investigators were intentionally agnostic regarding the underlying psychopathology, thereby acknowledging that a patient with schizophrenia might engage in violence for psychotic reasons (due to delusions and hallucinations), as an impulsive overreaction to a perceived threat, or for purely manipulative purposes. This research also clarified that impulsive violence is the most common form seen among chronic