Violent behavior: Choosing antipsychotics and other agents

Therapeutic options depend on whether patient violence is transient or persistent

When a patient with major psychiatric illness exhibits violent behavior, consider the course of violence in relation to his or her fixed and changing symptoms and deficits. Although most patients with schizophrenia, major depression, or bipolar disorder are not violent, effectively treating those who are calls for:

- differentiating between transient and persistent violent behavior
- providing medications and nonpharmacologic interventions shown to reduce each behavior
- addressing substance abuse and violent behavior concurrently.

Is violence transient or persistent?

Violent behavior is a common reason for psychiatric admission and prolonged hospital stays and a barrier to appropriate community placement and successful community reintegration.

Transient violence is limited to an acute psychotic episode; as psychotic symptoms abate, the violence resolves. Delusions, hallucinations, and conceptual disorganization are key triggers of transient violence. Excitement, anger, and agitation are its prominent symptoms.

Treat a patient experiencing an acute violent episode with an oral first- or second-generation antipsy-
chotic. For acute agitation, intramuscular (IM) delivery provides more rapid symptom resolution (Table 1). IM ziprasidone is approved for agitation associated with schizophrenia and IM olanzapine for use in agitation associated with schizophrenia or bipolar mania. Try talking calmly to the patient and explaining the need for medication (Figure 1, page 66). If this is not possible, a show of force might induce the patient’s cooperation.7

For sedation, antipsychotic medication can be supplemented by lorazepam, the only benzodiazepine that is reliably absorbed when administered IM. Lorazepam has a relatively short half-life, and the usual dosage of 1 to 2 mg can be administered orally, sublingually, intramuscularly, or intravenously every 1 to 6 hours. Exercise caution, however, when respiratory depression is a possibility.

Persistent violence. Emotional turmoil is usually less pronounced in patients whose violence is persistent.8 Neurocognitive impairments, antisocial traits, and specific psychotic symptoms may exist singly or in combination in patients prone to persistent violence.

When a patient continues to be violent, consider poor treatment adherence or substance abuse, especially with outpatients (Figure 2, page 68).

**Clinical Point**
Emotional turmoil is usually less pronounced in patients whose violence is persistent

<table>
<thead>
<tr>
<th>Table 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medications used to treat violence on an emergency basis</strong></td>
</tr>
<tr>
<td><strong>Drug</strong></td>
</tr>
<tr>
<td>Benzodiazepines</td>
</tr>
<tr>
<td>Lorazepam</td>
</tr>
<tr>
<td>Midazolam</td>
</tr>
<tr>
<td>First-generation antipsychotic</td>
</tr>
<tr>
<td>Haloperidol</td>
</tr>
<tr>
<td>Second-generation antipsychotics</td>
</tr>
<tr>
<td>Olanzapine</td>
</tr>
<tr>
<td>Risperidone</td>
</tr>
<tr>
<td>Ziprasidone</td>
</tr>
</tbody>
</table>

* Use oral medication if patient is cooperative; otherwise use an intramuscular injection.
† Lower dosages are used for elderly patients or those with dementia.
‡ Antipsychotics are not recommended for aggressive patients without a psychotic disorder or bipolar mania diagnosis.

Neurological and neurocognitive impairments are associated with persistent violence. Fairly broad impairments in various domains are seen on a variety of tests. Patients with neurocognitive impairment often present with impulsivity and deficits in behavioral adaptability.

In general, the consequences of a behavior determine its course; assaultive behavior usually decreases rapidly when strongly discouraged. Violent behavior that persists, therefore, suggests that neurocognitive impairment is causing a failure in behavioral adaptability.

Psychopathy, antisocial traits, and antisocial personality disorder (APD) also can result in persistent violence.

Antisocial personality is defined primarily by behavioral symptoms such as irresponsibility and criminal activities. Psychopathy also includes these symptoms but adds interpersonal and affective impairments such as callousness, grandiosity, and lack of remorse.

Psychopathy was the strongest clinical predictor of violence in a large trial of outpatients with major psychiatric disorders.9 APD, on the other hand, was the most significant clinical predictor of violent recidivism among offenders with mental illness in a meta-analysis of predictive longitudinal studies from 1959-1995.10 In another study, psychopaths were about 5 times...
Adults with ADHD were 2x more likely to have been involved in 3 or more car crashes*1

The consequences may be serious.
Screen for ADHD.

Find out more at www.consequencesofadhd.com and download patient support materials, coupons, and adult screening tools.

*Data from a study comparing driving in 105 young adults with ADHD to 64 community control adults without the disorder.


Table 2: Medications used to treat persistent violence

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial dosage</th>
<th>Target dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Second-generation antipsychotics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clozapine</td>
<td>12.5 to 50 mg/d</td>
<td>300 to 450 mg/d*</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>5 to 10 mg/d</td>
<td>15 to 30 mg/d</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>50 to 100 mg/d</td>
<td>400 to 700 mg/d</td>
</tr>
<tr>
<td>Risperidone</td>
<td>1 to 3 mg/d</td>
<td>4 to 6 mg/d</td>
</tr>
<tr>
<td><strong>First-generation antipsychotic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haloperidol</td>
<td>5 to 10 mg/d</td>
<td>10 to 20 mg/d</td>
</tr>
<tr>
<td><strong>Mood stabilizers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>200 to 400 mg/d</td>
<td>1,000 to 1,400 mg/d*</td>
</tr>
<tr>
<td>Lithium</td>
<td>300 mg bid</td>
<td>300 mg tid*</td>
</tr>
<tr>
<td>Valproate</td>
<td>500 to 1,000 mg/d</td>
<td>1,000 to 1,500 mg/d*</td>
</tr>
<tr>
<td><strong>Beta blockers†</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nadolol</td>
<td>40 mg/d</td>
<td>80 to 140 mg/d</td>
</tr>
<tr>
<td>Propranolol</td>
<td>20 mg tid</td>
<td>200 mg to 600 mg (delayed onset of action)</td>
</tr>
</tbody>
</table>

* Serum levels should be obtained.
† Contraindicated for patients with cardiovascular disease, asthma, or diabetes.
harm him or outside forces are controlling his mind.

Junginger stressed that violent themes in a patient’s delusions are important predictors of violence. Delusions associated with violence are often chronic and well-circumscribed.

The role of antipsychotics
Pharmacologic intervention for violent behavior targets the underlying disorder, such as schizophrenia or bipolar disorder. Usual regimens used to treat patients with these disorders may need to be modified, however, for persistently violent patients (Table 2, page 65).

Second-generation antipsychotics (SGAs)—particularly clozapine—have superior antiaggressive properties beyond their antipsychotic or sedative effects, compared with first-generation antipsychotics. Retrospective studies have shown clozapine can significantly decrease the number of violent incidents and episodes of seclusion and restraint. Evidence for efficacy of other SGAs in reducing physical assaults is more limited:

- Risperidone had a greater effect than haloperidol on hostility in a large, multicenter comparison trial.
- Clozapine was more effective than haloperidol or risperidone in reducing hostility in a double-blind study of schizophrenia patients. This finding was independent of clozapine’s antipsychotic effect.

Clozapine also was more effective than haloperidol in reducing the number and severity of aggressive incidents. The patients in this study, however, were not selected on the basis of aggressive behavior.
One large federally funded, double-blind, randomized trial compared clozapine, olanzapine, and haloperidol in 110 assaultive patients with schizophrenia or schizoaffective disorder. Patients had documented episodes of recent physical assaults and persistent aggressive behaviors during a 2-week period. Clozapine showed greater efficacy than olanzapine—and olanzapine greater efficacy than haloperidol—in reducing aggressive behavior. This effect was independent of the drugs’ antipsychotic and sedative actions.

**Dual-diagnosis patients.** Clozapine may be beneficial for patients with concurrent substance abuse because in addition to reducing aggression, it also may prevent relapse to substance abuse. In addition to intoxication, drug and alcohol abuse has disruptive effects on prefrontal function. These impairments play an important role in substance use-related aggression.

Substance abuse also can exacerbate psychotic symptoms, both directly and indirectly through poor treatment compliance. Patients with psychopathy are much more likely to abuse drugs. The association between drug abuse and violence can then be due in part to the higher percentage of psychopaths in the group of drug abusers.

Fortunately, patients with dual diagnosis who receive extensive substance abuse treatment show greater clinical improvement and better outcomes. Several studies found that clozapine was associated with decreased substance use. In one trial, schizophrenic patients with a history of drug abuse who received clozapine were much less likely to use substances over the next year than patients taking other antipsychotic medications.

Thus, clozapine has clear antiaggressive effects, but its use as a first-choice treatment for aggression is limited by the risk of side effects, in particular agranulocytosis. With careful blood monitoring, this complication is very rare, but persistently violent patients might not cooperate fully with the required monitoring.

**Other medications**

Other agents used to treat violent patients with mental disorders include mood stabilizers, beta blockers, and antidepressants.
Mood stabilizers such as lithium, carbamazepine, or valproate might be useful as adjuncts to antipsychotic medications in managing assaultive patients with schizophrenia or other major psychiatric disorders. These medications might decrease violence by enhancing serotonergic activity.

Most evidence for mood stabilizers’ anti-aggressive effect comes from studies of patients with personality disorders. Divalproex, for example, was more effective than placebo in reducing impulsive aggression in patients with Cluster B personality disorders.24

Lithium reduces aggression and irritability in bipolar mania, while stabilizing the underlying disorder. Lithium can decrease aggression in other populations as well, including:

- the developmentally disabled
- prisoners with no apparent psychiatric diagnoses
- aggressive children and adolescents with conduct disorder
- adults with borderline personality disorder.

Beta blockers such as nadolol, pindolol, and propranolol have been reported to reduce aggression. Their usefulness is limited, however, because they are contraindicated in patients with cardiovascular disease, asthma, or diabetes.

Antidepressants. Selective serotonin reuptake inhibitors may reduce impulsive aggression in nondepressed patients with personality disorders.25

Nonpharmacologic treatments
To provide proper treatment, the clinician must understand the patient as a whole person, including his perception of his aggressive behavior. Nonpharmacologic interventions should be implemented with this in mind.

Compared with standard care, for example, intensive case management reduces the incidence of violence.26

Behavioral techniques can decrease violence by addressing specific impairments underlying the violence. For example, improving a patient’s cognitive functioning can counter impaired processing of feedback that is associated with neurological dysfunction.

Specific interventions, such as cueing to exaggerate the link between stimulus and response, could be beneficial.27 Similarly,
these patients might respond to a high degree of structure, supervision, and specific environmental modifications, such as transfer to a unit that specializes in treating violent patients.28

In cognitive-behavioral therapy, patients can learn ways they can satisfy their needs without being violent. They also can be trained in problem-solving skills and in understanding the consequences of their actions. Such therapy might be useful for diminishing antisocial traits. Interventions aimed at preventing, decreasing, or countering arousal are important in addressing acute violence.

Anger management programs can help patients respond to interpersonal provocations in a more adaptive way.29 These programs include:

- education about aggression
- self-monitoring of anger frequency, intensity, and situational triggers
- relaxation to reduce arousal and enable guided imagery training
- training in behavioral coping, communication, and assertiveness through role play
- practicing new anger-coping skills

Tailor treatments to the dominant mechanisms underlying persistent violence.

References

Disclosure
Dr. Krakowski receives research support from Eli Lilly and Company and GlaxoSmithKline.