Psychopharmacology in the Emergency Room

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The emergency room is in many ways a unique setting in the practice of psychiatry. The combination of high acuity, behavioral dyscontrol, and diagnostic uncertainty that characterizes only the most difficult cases in other settings drives the routines of emergency care. The setting calls for rapid resolution of acute symptoms even as the process of evaluation remains incomplete. Yet even in this setting, attention to the long-term treatment of the patient and to the ongoing or anticipated patient-physician relationship remain significant issues.

Treatment Principles

Several principles need to be kept in mind throughout all aspects of emergency care. First, patient and staff safety are the highest priorities for care. The decision to make a pharmacologic intervention will often be driven by this concern, and the selection of treatment must always take this into account. Most legal jurisdictions recognize this priority and grant physicians certain leeway in providing care even to uncooperative and nonconsenting patients.

Second, pharmacologic interventions in the emergency room are limited to specific situations and target symptoms. Because evaluation, treatment, and follow-up options are limited, treatments should be focused on acute symptoms that require immediate intervention to maintain safety, address emergent medical problems, or provide short-term relief of intolerable symptoms. The treatment of nonemergent issues will typically be deferred to other venues. However, it is important to be aware that medication selection in this setting has implications for long-term treatment, as these medications may be continued in subsequent settings.

Third, not all target symptoms are likely to respond to pharmacologic intervention. Acute agitation (including psychotic agitation), severe anxiety, and acute dystonic reactions are appropriate for emergent medication and will be discussed further (though appropriate for emergency treatment, alcohol withdrawal is beyond the scope of this article and will not be addressed). In contrast, suicidality, major depression, and other drug withdrawal are unlikely to benefit from urgent medical treatment and are best handled by other emergency room interventions and referral to a more appropriate setting to establish and maintain treatment.

Finally, drug selection should be based on target symptoms, underlying pathology, and preferred route of administration. In the absence of appropriate target symptoms, treatment in the emergency room setting is rarely justified. An assessment of underlying pathology, though necessarily preliminary, will assist the emergency room psychiatrist in making treatment choices that enhance rather than interfere with long-term therapeutic goals. Psychotropic medications are available in standard tablets or capsules, disintegrating tablets, liquid concentrate, IM injectable, IV injectable, and IM depot forms. Specific situations may make one of these more desirable than others. Because not every medicine is available in every formulation, the selection of a route of administration may drive medication selection.

Acute Agitation

Agitation is an acute state of anxiety, heightened arousal, and increased motor activity, most often occurring in the context of drug or alcohol intoxication, alcohol or sedative withdrawal, personality disorders, mood disorders, psychotic disorders, delirium, or other cognitive impairments. The agitated patient is often uncooperative, hostile, aggressive, and desperate to flee. Rapid control of agitation is essential to ensure the safety of the patient and others.

Psychotic agitation due to bipolar mania or schizophrenia may be worsened by the disturbing content of hallucinations or delusions, thought disorganization, perceived intrusion of law enforcement or mental health workers, or akathisia from ongoing antipsychotic treatment. The ideal treatment will relieve the immediate symptoms and address the underlying psychopathology.

The 2 basic medication treatments for agitation are antipsychotics and benzodiazepines, each of which is available in oral and injectable forms. Although debate continues regarding the relative efficacy of these classes of medication, at least 1 study has reported that the combination of the 2 is more effective than either one alone.[1]

Oral administration of medications has the advantages that it enhances patient cooperation, is easy to administer, avoids potential health threats from needle sticks, and maintains patient dignity and autonomy. The onset of action of oral and injectable medications is comparable in acute agitation.[2] When given the choice between oral and injectable medications, most patients, even when psychotic and agitated, agree to the oral form.

Among oral medications, rapidly disintegrating tablets have the advantage of easy administration even in minimally cooperative patients and provide assurance to staff that the medication was in fact swallowed. Three antipsychotics, aripiprazole,[3] olanzapine,[4] and risperidone,[5] are available in rapid-disintegrating formulations. Olanzapine is given in 5- or 10-mg doses at intervals of 30 minutes to 2 hours, up to a total of 20 mg/day, with an average dose of 10 mg/day. Risperidone is given in 1- or 2-mg doses at intervals of 30 minutes to 2 hours, up to 6 mg/day, with an average dose of 4 mg/day. Aripiprazole may be administered in 5- or 10-mg doses at intervals of 2 hours up to a total of 30 mg/day. None of the drugs is absorbed transmucosally, all must be swallowed to be effective, and each has the same pharmacokinetics as standard tablets. Aripiprazole has a slightly higher risk of nausea and has the longest clearance half-time; olanzapine is slightly more sedating and anticholinergic; risperidone carries somewhat higher risk of extrapyramidal side effects (EPS).

For intramuscular administration, most conventional antipsychotics, as well as the atypical drugs aripiprazole,[6] olanzapine,[7] and ziprasidone[8] are available. Each of these drugs has been shown to be more effective than placebo and comparable to haloperidol with or without lorazepam for acute psychotic agitation in patients with schizophrenia or bipolar mania. Only conventional drugs have been approved for intravenous use. Haloperidol for IM or IV administration is typically given in 5 mg doses at intervals of 30 minutes to 2 hours, up to 20 mg/day, with an average dose of 10 mg/day. Aripiprazole IM is recommended in 9.75-mg doses as frequently as every 2 hours up to a total dose of 30 mg in 24 hours. Olanzapine IM is usually given in 10-mg doses every 30 minutes to 2 hours, with an average final dose of 20 mg/day and maximum recommended dose of 30 mg/day. Ziprasidone IM may be given in 10-, 20-, or 40-mg doses once every 4 hours, up to 40 mg/day, with an average dose of 20 mg/injection. Haloperidol is moderately sedating, but carries significant risk of EPS, including acute dystonic reactions and akathisia. Aripiprazole, olanzapine, and ziprasidone are moderately sedating and have less risk of EPS. Cardiac

problems have not been reported with any of the atypical drugs. Although no published studies showing problems are available, some expert consensus surveys recommend that olanzapine IM not be used concurrently with benzodiazepines due to a potential risk of cardiorespiratory depression, and a 1-hour lag between administration of the 2 medications has been recommended.[9]

Benzodiazepines differ in potency, route of administration, and pharmacokinetics, not in efficacy. Among benzodiazepines, only lorazepam is available for intramuscular as well as intravenous and oral administration. Although its time to peak concentration when given orally is a relatively slow 2 hours, its onset of action is rapid enough to effectively augment antipsychotic drugs when given concurrently. It has the additional advantages of producing no active metabolites and of a serum clearance time relatively unaffected by hepatic or renal impairment. The usual dose of lorazepam, irrespective of route, is 1 or 2 mg every 30 minutes to 2 hours, up to 12 mg/day, with an average dose of 2–4 mg/day.[1] The drug is highly sedating and usually well tolerated, although it may cause respiratory depression when given intravenously and can be associated with delirium and disinhibition in rare cases.

Acute Anxiety

Intense, intolerable anxiety may occur in the context of panic disorder, acute stressors, posttraumatic stress, generalized anxiety, psychosis, medical conditions, drug intoxication, or drug withdrawal. Benzodiazepines provide optimal short-term treatment for anxiety and panic symptoms irrespective of cause. Benzodiazepines may also be used as an interim treatment during titration of other medications for anxiety (e.g., antidepressants).

For oral administration, any benzodiazepine is potentially efficacious and treatment selection may be made on the basis of the patient's past experience with the medications, the physician's preference, or other factors. In some instances, such as a patient becoming acutely anxious while undergoing emergency evaluation of a possible medical problem, IV or IM administration may be advantageous, in which case lorazepam is the drug of choice.

Acute Dystonic Reaction

Dystonia is an intense cramp in a muscle or related group of muscles that may occur as a side effect of antipsychotic medication. Conventional high-potency medications, such as haloperidol, thiothixene, or fluphenazine, carry the highest risk of these reactions, but they have been reported with atypical agents as well.[10] Acute dystonic reactions are most common shortly after the drug is started or the dose is raised, but are most likely to occur at trough, rather than peak, serum levels. Among the more common patterns of muscle cramping are the extraocular muscles (oculogyric crisis), neck (torticollis), and the throat and larynx (laryngospasm). These symptoms are painful, frightening, and in the case of laryngospasm, potentially life-threatening. Patients who experience these symptoms are hesitant to resume antipsychotic medications, which poses major implications for the treatment of schizophrenia and other chronic psychotic disorders.

A standard approach to treatment employs benztropine 2 mg IM every 15–30 minutes, up to a maximum of 8 mg/day. Alternatively, diphenhydramine 50 mg IM every 15–30 minutes, up to 200 mg/day, has been reported to be effective. As second-line treatment, benzodiazepines may be administered to augment the effects of these drugs. Side effects of the drugs include other anticholinergic effects of benztropine, such as dry mouth and constipation, and sedation with diphenhydramine and benzodiazepines.

Follow-up care includes dose reduction or a change to an antipsychotic drug with lower risk for EPS, usually an atypical agent. Acute dystonic reactions tend not to be specific to any one drug, but rather to classes of medications, and are much less common after the first few days of taking a particular drug or dose. Thus, a patient who experiences acute dystonia with haloperidol may safely resume the drug at a lower dose without greater long-term risk of recurrence than would be experienced with fluphenazine or thiothixene. Similarly, the patient need not be counseled to avoid that specific drug in the future. Although in some cases a change in antipsychotic medication in the emergency room may be appropriate, the outpatient treating psychiatrist should be consulted if possible beforehand. Care must be taken not to undermine the patient's relationship with the treating psychiatrist or to discourage the patient from continuing an antipsychotic medication.

Conclusion

A focused approach to emergency room pharmacology, with careful selection of target symptoms and clear, short-term goals that do not interfere with longer-range objectives leads to optimal emergency treatment. Although systematic data on this population are limited, current evidence provides at least initial support for the treatment recommendations presented here. Of particular importance is the coordination of emergency treatment with other aspects of care, to enhance rather than detract from continuing treatment.

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Dr. Jibson is on the speakers bureaus of (in order of compensation received in the last 24 months) AstraZeneca, Janssen Pharmaceutica, and Bristol-Myers Squibb.

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