Chemical Restraint

Updated: Nov 21, 2016
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OVERVIEW

Overview

Many physicians and healthcare workers will be or have been threatened by an agitated patient. Workplace violence is increasing. Between 1993 and 1999, 1.7 million episodes of workplace-related violence were reported annually in the United States; in 12% of these episodes, the victim was a healthcare or mental health worker. [1]

Such threats are often underreported in the emergency department (ED). In 2004, Gates et al reported that most of the emergency care workers in 5 midwestern hospitals had experienced verbal abuse and that 51% of physicians and 67% of nurses had been physically assaulted at least once in the preceding 6 months. [2] In addition, up to one fourth of staff feel unsafe in the ED, and 20% of EDs reported that guns or knives were brought to the ED on a daily or weekly basis. [1] Furthermore, a survey of psychiatry residents showed that 73% had been threatened and 36% had been physically assaulted during residency. [3]

Agitation in the violent patient that manifests in an acute care setting likely has many contributing causes. Agitation is generally multifactorial and can be the result of long wait times, confusion, substance intoxication and withdrawal, significant illness, and mental health crisis. The possible physical causes of agitation (e.g., hypoxia, dementia) must be assessed. Behavioral emergencies are frequently complex and dangerous and require prompt control to prevent injury to the patient, staff, and others present in the department.

Ultimately, a patient who poses a threat to himself or others requires some form of restraint. Physical and chemical restraints can be used as a last resort to help control a violent situation. The 3 main classes of medications used to chemically restrain a patient are benzodiazepines, typical or classic antipsychotics, and atypical antipsychotics.

Route of Administration

Many options exist regarding how and when to use a medication to control agitation. The ideal chemical restraint has a rapid time to onset, regardless of route of administration, and causes few adverse effects.

After interviewing the patient, carefully consider the difference between a patient who is obviously agitated and poses an immediate threat and one who is only mildly agitated. Patients who do not present an immediate threat can often be calmed using verbal techniques and open communication. However, patients who are uncooperative, severely agitated, or showing signs of immediate violence often require immediate restraint.

If the patient is willing to cooperate with treatment, oral medications (PO) should be the first option. Oral medications have been shown to have similar onset of action compared to intramuscular (IM) administration, are less invasive, and are more widely accepted by patients. [4] Offering an oral medication to the patient first can help build trust and suggests an internal rather than an external locus of control. [5] Furthermore, a study conducted by Currier et al showed that an oral dose of risperidone or lorazepam was tolerable and comparable to the traditional dosing of IM haloperidol and lorazepam. [6]

However, speed of onset is crucial in emergencies. Therefore, many experts suggest oral liquid concentrates, orally dissolving formulations, and IM formulations over oral tablets because of the slower onset of action of tablets and the possibility of the patient hiding tablets in his mouth (known as cheeking). In addition, many studies have shown a slight time advantage for IM medications as opposed to oral concentrates. [7] Intravenous (IV)
medications have the fastest onset times, but the acutely agitated patient often does not have IV access, and gaining access is often difficult.

In conclusion, if no immediate threat is displayed and the patient is cooperative, oral medications should be considered as first-line therapy, followed by either IM or IV administration, depending on the medication choice and ease of access.

Drug Classifications

After determining whether the patient poses an immediate threat, a potential threat, or no threat (mild agitation), the correct medication to best calm or help the patient must be determined. If the agitation has a medical cause (eg, drug intoxication, delirium, psychiatric disturbance), it needs to be identified. Classically, this treatment consists of a benzodiazepine, an antipsychotic, or a combination of the two. Recently, several studies have shown increased safety and agitation control from atypical antipsychotics, especially in persons with a known psychotic disorder.

Benzodiazepines

Multiple studies have shown the efficacy of benzodiazepines for acute agitation and sedation. In addition, some evidence indicates that patients with unknown causes of agitation or causes secondary to alcohol intoxication or withdrawal have better results and fewer adverse effects using benzodiazepines alone compared with benzodiazepines in combination with antipsychotics or antipsychotics alone. [8]

The 2 main benzodiazepines used to control agitation are lorazepam and midazolam. Both can be administered orally (PO), intravenously (IV), or intramuscularly (IM); IV administration has the fastest onset (2-3 min for IV midazolam and 1-5 min for IV lorazepam). Multiple studies have compared benzodiazepines with typical antipsychotics and have shown similar effectiveness in reducing aggression and time to sedation. For example, Knott et al showed in a double-blinded randomized trial that midazolam was just as effective as droperidol in achieving sedation. [9] Others have shown a more rapid sedation with midazolam than with haloperidol or lorazepam. [10]

The main adverse effect of benzodiazepines is respiratory depression. Therefore, patients should be monitored appropriately. Other adverse effects include hypotension and extreme somnolence.

Despite the adverse effects, benzodiazepines remain a highly useful medication to control agitation and provide sedation. They are especially effective in patients with alcohol withdrawal syndrome, agitated patients who have a seizure disorder or are at risk for seizures, and patients at high risk of extrapyramidal effects with antipsychotics. Midazolam should be considered if rapid immediate sedation is required.

Classic or typical antipsychotics

Classic or typical antipsychotics include the butyrophenones and phenothiazines. The main 2 drugs used for acute agitation and violence are haloperidol and droperidol. Haloperidol has been used for years, either PO or IM, to control violence and acute psychosis. Clinton et al showed that disruptive behavior was alleviated using haloperidol within 30 minutes in 113 of 136 patients who presented to the ED with acute agitation from various causes. [11] In addition, droperidol and haloperidol have been found to have similar time of onset in both IV and IM forms; in IM form, droperidol has a faster onset than haloperidol. [12] The onset of haloperidol IM is about 30-45 minutes and may take up to 60 minutes in some patients. The onset of droperidol IM is 3-10 minutes, and peak action may take up to 30 minutes.

The major drawback to the typical antipsychotics are their adverse effects. Droperidol was given a black box warning by the US Food and Drug Administration (FDA) because of the risk of QT prolongation, and haloperidol received a warning from the FDA in 2008 regarding its use in treatment of elderly patients with dementia-related psychosis. [13, 14] QT prolongation can result in torsade de pointes and other cardiac dysrhythmias. In addition, typical antipsychotics are known for causing extrapyramidal adverse effects. Extrapyramidal symptoms (EPS) are the various movement disorders such as tardive dyskinesia, dystonia, akathisia, torticollis, and drug-induced parkinsonism.
In conclusion, administration of typical antipsychotics remains a highly effective method for sedation and controlling acute agitation, but they must be used with caution, especially in patients at risk of QT prolongation.

A study by Gomez and Dopheide found that among patients in a psychiatric ED who were administered an antipsychotic for acute agitation, mean length of ED stay varied according to the drug used. The study, which looked at 388 cases, found a 29.7-hour mean length of stay in cases of intramuscular haloperidol administration, compared with 30.3 hours for other intramuscular antipsychotics and 22.6 hours for cases in which oral second-generation antipsychotics (SGAs) were used. The investigators also found that of the 122 cases (31%) in which repeat medication was employed, mean time to repeat use did not significantly differ between the different agents. However, while cases requiring repeat doses of intramuscular antipsychotics were associated with a significantly longer ED stay than were cases without repeat doses, this was not true for patients given oral SGAs. [15]

**Combination therapy**

A few randomized trials have indicated that the combination of a benzodiazepine with a traditional or classic antipsychotic results in a more rapid onset of sedation with a similar adverse effect profile. [16, 17] In addition, more extrapyramidal adverse effects were exhibited in the haloperidol only group than in the combination group. [17]

Therefore, combination therapy such as lorazepam and haloperidol can be reasonably considered to control violence and agitation in an acute setting.

Isbister et al compared intramuscular use of droperidol, midazolam, or the combination of these drugs for sedation in violent and acute behavioral disturbances in the emergency department. [18] The duration of the disturbances was similar following either droperidol or midazolam or the combination, although the midazolam group was more likely to require additional sedation. A higher incidence of adverse effects was observed in the midazolam group because of oversedation.

**Atypical antipsychotics**

Atypical antipsychotics such as risperidone, olanzapine, and ziprasidone have become available relatively recently. Classic antipsychotics block the D2 dopamine receptor, whereas atypical antipsychotics block the 5-HT2 serotonin receptor with low D2 receptor blockade. This mechanism is thought to lower the adverse effect profile of EPS in atypical antipsychotics.

Several studies have shown equal effectiveness or improved effectiveness of atypical antipsychotics as compared to typical. Brooks et al showed that IM ziprasidone was superior in reducing symptoms of acute psychosis and had fewer adverse effects than haloperidol. [19] In another 6-week randomized trial, ziprasidone was shown to have better efficacy and tolerability than haloperidol. [20]

Olanzapine has also been compared with typical antipsychotics and benzodiazepines. For example, in a double-blind comparison of olanzapine versus lorazepam in controlling acute psychosis, olanzapine was found to be equally effective and better tolerated than lorazepam. [21] One double-blind, multicenter, placebo-controlled study showed that IM olanzapine (10 mg) reduced agitation significantly more than IM haloperidol (7.5 mg) in agitated patients with schizophrenia, schizophreniform disorder, or schizoaffective disorder. [22] In addition, acute dystonia occurred in 7% of the patients treated with haloperidol but in none of those treated with olanzapine. [22]

Risperidone has also been shown to be as efficacious in treating psychosis as haloperidol, with significantly less adverse effects. [23] Currier and Simpson found that "oral treatment with risperidone and lorazepam appears to be a tolerable and comparable alternative to intramuscular haloperidol and lorazepam for short-term treatment of agitated psychosis in patients who accept oral medications." [23] However, risperidone has mostly been studied in schizophrenia, and its use in acute agitation from other causes is limited.

Overall, patients may benefit from atypical antipsychotics, especially if the patient has a known psychiatric disorder such as schizophrenia or bipolar disorder. Olanzapine is generally given as a 10-mg IM dose, and ziprasidone has been used in both 10-mg and 20-mg IM doses. In conclusion, atypical antipsychotics show a promising improvement over classical antipsychotics with fewer adverse effects.
Special Considerations

Pregnancy

Few recommendations are available regarding the treatment of agitation and psychosis during pregnancy. Dangers to physical restraint exist, especially in the second and third trimesters, given a reduction in venous return caused by being placed in a supine position. Therefore, chemical restraints are preferred. Although the data on the development of children following in-utero exposure to psychiatric drugs are limited, no clear evidence of long-term adverse effects on the development of children exposed to most psychotropic medications is available. A retrospective chart review of 16 women who used an atypical antipsychotic during pregnancy found 1 major malformation, but confounding potential causes are unknown.

Although benzodiazepines are not contraindicated in pregnancy, prescribers should use with extreme caution in pregnancy, as increased risk of congenital and developmental abnormalities is possible. Adverse effects have been suggested to occur in early gestation, during organogenesis and brain development, and/or in late gestation, resulting in neonatal flaccidity and respiratory problems. In pregnancy, benzodiazepines should be used at low, divided doses and for the shortest duration possible.

Given the limited information on treatment adverse effects, minimal doses should be used and for a limited duration to help prevent any unnecessary birth defects. Some have recommended 2 mg of oral risperidone with oral lorazepam, or 5-10 mg of oral olanzapine, as the best options.

Pediatrics

Haloperidol and lorazepam are the preferred agents for undifferentiated agitation in the pediatric population. The dosing of haloperidol and lorazepam is the same for PO, IM, or IV administration. For children aged 6-12 years, haloperidol is dosed at 0.025-0.075 mg/kg with a maximum of 2.5 mg/dose. For the same group, lorazepam at 0.05 mg/kg with a maximum of 4 mg/dose may be used.

Legal considerations

Any time the decision is made to restrain a patient, either physically or chemically, legal considerations must be taken into account. A 1982 Supreme Court Decision Youngberg v. Romero stated that "restraints are justified to protect others or self in the judgment of the health professional." In addition, one must consider the competency of the patient, which is defined as "the capacity or ability to understand the nature and effects of one's actions or decisions." Furthermore, although being in the ED does legally imply consent to treatment, a patient does have the right to refuse a treatment course, unless the patient is deemed incompetent or a threat to himself or others.

If a patient imposes no threat to himself or others and has the capacity to make reasonable decisions, then he cannot be confined or restrained without his permission. If held against his will, a patient has the right to charge the health professional with false imprisonment or battery. Note that each state, though covered by federal law, has its own set of laws governing the rights of patients and the restriction of those rights by healthcare workers. Physicians must make themselves aware of these laws.

Medicolegal Pitfalls

See the list below:

- Failure to recognize a medical cause for agitation or assumed psychosis
- Inadequate monitoring of vital signs after sedation
- Failure to recognize potential lethal cardiac adverse effects from medications given
- Failure to comply with state laws regarding patient competency and confinement