only when nonpharmacologic measures have failed.[10] Notably, there is a black box warning recommending against the use of any antipsychotics in elderly patients with dementia-related psychosis.[1] While this is a consideration, studies suggesting an increase in mortality in this population were related to longer-term use rather than short-term use in the ED.[1] The American Psychiatric Association practice guideline recommends 1 to 2 mg haloperidol (lower doses of 0.25 to 0.5 mg in elderly) every 2 to 4 hours for delirium requiring pharmacologic treatment with higher IV doses as needed for agitation control.[9] Similarly, IV haloperidol is approved for managing agitation, delirium, and psychosis in many countries, with recommended initial doses ranging from 1 to 10 mg IV.[6]

Haloperidol has been used effectively to treat cannabinoid hyperemesis syndrome and abdominal pain.[2,3] A trial of 33 patients found 0.05 to 0.1 mg/kg haloperidol IV demonstrated superior symptom control compared with ondansetron 8 mg IV. All patients received an ECG prior to enrollment, and there were no cases of QT prolongation or torsades de pointes.[2] A trial including 107 patients with self-matched encounters found haloperidol was associated with reduced administration of morphine equivalents and lower rates of rescue therapy in patients with abdominal pain.[3] Over 87% of patients received haloperidol via the IV route.[3] A 2017 randomized, double-blind, placebo-controlled trial included patients with gastroparesis receiving haloperidol versus conventional therapy. Authors found IV haloperidol reduced pain and nausea at one hour.[11]

Based on the available evidence, IV haloperidol may be safely administered for acute agitation, psychotic disorders, cyclical vomiting, abdominal pain, and gastroparesis in the ED. The FDA warning should be updated to reflect the most recent evidence demonstrating a cumulative dose of $\leq$2 mg IV haloperidol does not require an ECG or additional monitoring.[4,6] Overall, significant QT prolongation and torsades de pointes associated with IV haloperidol use are rare events, but several precautions are recommended.[4,6] In those with multiple risk factors for torsades de pointes or currently receiving QT-prolonging medications, a baseline ECG to assess the corrected QT is recommended; a post treatment ECG is recommended at peak dose (30 to 60 minutes) if a higher dose (eg, >5 mg) of IV haloperidol is administered.[4,6] In practice, an ECG may often occur after medication administration in agitated patients. Telemetry monitoring is only recommended for those at high risk for torsades de pointes, such as patients with a corrected QT of >500 ms on baseline or post treatment ECG or in those receiving repeated high doses of haloperidol (eg, >100 mg).[4] Haloperidol should be discontinued if the corrected QT is >550 ms.[7]

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INTRAVENOUS HALOPERIDOL HAS A LIMITED ROLE IN THE MODERN EMERGENCY DEPARTMENT

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Haloperidol is a butyrophenone-class antipsychotic agent with more than 6 decades of clinical use across most disciplines of medicine. In the emergency department (ED), haloperidol is commonly used to facilitate chemical sedation of acutely agitated patients, ameliorate symptoms of nausea and vomiting, reduce hallucinations and delirium associated with ethanol withdrawal, and more. Only the intramuscular (IM) route is Food and Drug Administration (FDA)-approved for parenteral use, but the same formulation has been used intravenously (IV) for many years. Despite its ubiquity in the ED, there are safer and more effective alternative routes of administration or medications for most indications. Furthermore, regardless of the route of administration, it carries a risk of extrapyramidal symptoms/dystonic side effects. Finally, when administered IV, there is an increased risk of the most feared complication—torsade de pointes—which prompted one of several FDA boxed warnings for the medication. What evidence supports its limited efficacy and increased risk compared to other therapies?

Before 2010, the largest evaluation of electrophysiologic changes and torsade de pointes associated with IV haloperidol was a retrospective review of case reports (n=41) and FDA MedWatch reported data (n=29).[1] The authors identified if cases were associated with the concomitant use of proarrhythmic medications (57% of cases), reported the total cumulative haloperidol dose administered prior to a QT-prolonging or torsade de pointes event, and identified whether other commonly accepted risk factors for torsade de pointes were present (electrolyte abnormalities, history of cardiac disease, and preexisting prolonged QTc>450 ms). Although 97% of the reported cases had a risk factor, no specific risk factor adequately predicted risk. Importantly, 24% of patients were younger than 40 years old. A separate 60% had no reported electrolyte abnormality prior to observed QT prolongation or torsade de pointes. These authors suggest cumulative doses of less than 2 mg are safe. A large randomized controlled trial evaluated the safety of IV haloperidol doses up to 20 mg but limited enrollment to critically ill and risk-stratified patients in the ICU.[2] These results cannot be generalized to an ED setting where sedation is often administered before or in parallel with diagnostic evaluation. A cross-sectional study of medically healthy patients with schizophrenia (n=1,017) being treated with low-dose (2 mg) haloperidol identified an IV route of administration was associated with QTc prolongation (adjusted relative risk 1.18 to 1.43), whereas an oral route of administration was not (relative risk 0.92 to 1.06).[3] Whether this risk results from higher peak plasma concentrations immediately following IV administration (and theoretically greater transient I_{KR} potassium channel blockade) remains unclear. Only 2 cases of sudden death associated with the use of IM haloperidol are published, and neither is presented with electrocardiographic data clearly substantiating a causative etiology.[4] Given the available data, with risk stratification in a well-differentiated patient (eg, inpatient hospital units), IV haloperidol may be an acceptable agent. Still, computer-aided QTc interval calculation has poor sensitivity for predicting torsade de pointes, and the presence of paced rhythms, conduction delays, and challenging baseline waveforms in agitated patients limits their utility.[4] In the ED, where baseline serum electrolyte concentrations, past medical history, and presenting diagnosis are not always available within the first hour of treatment, IM administration or an alternative agent is a more appropriate choice.

Other notable adverse effects of haloperidol include the family of dystonic reactions. In a meta-analysis evaluating the presence of dystonic reactions in agitated patients treated with IM haloperidol, upward of 5% experienced a reaction when not concomitantly treated with an anticholinergic agent.[5] When an agent from the butyrophenone class is desired for sedation, droperidol offers similar results but with a lower incidence of dystonic reactions—approximately 1% when administered through IM route at a median dose of 5 mg in one series.[6] Alternatively, dystonic reactions can be avoided entirely by a selection of agents from other drug classes, including *N*-methyl-D-aspartate-antagonists, benzodiazepines, and barbiturates—each of which necessitates its own risk/benefit analysis. These are especially important when treating medically complex elderly patients, a scenario where haloperidol may occasionally have an advantage.

Intravenous haloperidol has historically served a crucial role in managing acutely ill patients. Although there is no clear evidence of a dose-dependent risk of torsade de pointes and fatal outcomes in appropriately risk-stratified patients, prudence would dictate that clinicians evaluate the presence of proarrhythmic medications and baseline electrocardiogram, and ideally, baseline serum electrolyte concentrations before administering IV haloperidol.[7] However, facing an undifferentiated agitated patient in the ED, the delay in obtaining this information may not be tolerable or safe. Given this and the fact that clinical practice now affords the ability to choose from many

other appropriate medications, we see a very limited therapeutic role for IV haloperidol.

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