A Retrospective Review of the Use and Safety of Droperidol in a Large, High-risk, Inner-city Emergency Department Patient Populaton

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Abstract

Droperidol (DROP) is used in the emergency department (ED) for sedation, analgesia, and its antiemetic effect. Its ED safety profile has not yet been reported in patients (pts). **Objectives:** To document the use of DROP in high-risk pts (those with head injury, alcohol or cocaine intoxication, and/or remote or recent seizures), and to determine the number of serious and minor adverse events (AEs)—seizures, hypotension, extrapyramidal side effects (EPSEs)—after DROP. **Methods:** The ED database (EmSTAT) was queried to determine who received intramuscular or intravenous DROP in the ED in 1998; further chart review was done if the patient was considered high risk for or had experienced an AE. Multiple regression analysis using a random-effects model determined the significance of each variable in the occurrence of AEs. **Results:** 2,468 patients (aged 20 months to 98 years; 112 $\leq$17 years; 141 $\geq$66 years) received DROP for agitation (n = 1,357), pain (1,135), anxiety (99), vomiting (173), or other reasons (50). There were 945 pts considered high risk; 933 charts were reviewed (DROP mean dose 4.1 $\pm$ 2.0 mg); of these, 50 patient visits did not meet the criteria for high risk. There were 622 pts with head trauma (401 with alcohol use), including 47 with computed tomography (CT) scans positive for brain injury, 64 with cocaine use, and 197 with recent or remote seizures (137 with alcohol use). Minor AEs such as transient hypotension occurred in 96 pts after DROP (73 with alcohol use); 20 received intravenous fluids, while an additonal 28 pts (8 with alcohol use) received rescue medications for EPSEs. Six possible serious AEs occurred in pts with serious comorbidities; 2 cases of respiratory depression, 3 post-DROP seizures, and 1 cardiac arrest (resuscitated) 11 hours after DROP in a cocaine-intoxicated pt (normal QT interval). There was no significant difference among high-risk groups in the occurrence of AEs. **Conclusions:** The vast majority of pts who received DROP in the ED did not experience an AE. A few serious AEs were noted following DROP in patients with serious comorbidities; it is not clear that DROP was causative. **Key words:** droperidol; dystonic reactions; seizures; adverse events; emergency department. ACADEMIC EMERGENCY MEDICINE 2002; 9:1402–1410.

The use of droperidol (DROP) in the emergency department (ED) as a chemical restraint for extremely agitated and out-of-control patients has been reported.[1,2] Although it is presumed to offer effective sedation, the safety of DROP use in the acutely intoxicated/agitated patient is not known. Its safety is also not known for other select groups, such as elders, patients with a history of seizures, those with cardiovascular or central nervous system (CNS) dysfunction (i.e., hypotension or extrapyramidal symptoms), extremely intoxicated patients, or those abusing cocaine. Information supporting the effectiveness and safety of DROP in reducing acute agitation in patients with acute brain injury is also lacking.

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Droperidol is a butyrophenone used for sedating agitated patients but has also been used for the treatment of headaches,[3,4] nausea,[5] and vertigo,[6] and in augmenting relief of pain when used with opioids.[7] It is generally not recommended in those patients who have a history of seizures or in patients with acute head injury because DROP is thought to lower seizure threshold.[8,9] However, upon arrival to the ED it is often not clear whether an agitated or intoxicated patient has just had a seizure, has a known seizure history, or has a significant brain injury to warrant seizure precautions.

Another potential adverse side effect of DROP is cardiovascular instability. Recently, there have been reports of widened QT complex and torsades de pointes in patients receiving DROP,[10] raising additional concerns about its use in patients whose previous medical history is uncertain or unobtainable because of the patient's current medical condition or agitated state.

The objective of this study was to document the safety of DROP when used in a non-selected patient population for any reason. Our hypothesis

was that DROP would be safe and effective in all patients.

METHODS

Study Design. A retrospective review of DROP use for ED patients during 1998 was performed utilizing the ED database (EmSTAT) at Hennepin County Medical Center (HCMC). This study was reviewed by the institutional review board and considered exempt from informed consent because of its retrospective nature and its use of archival data.

Study Setting and Population. Hennepin County Medical Center is an urban hospital located in downtown Minneapolis, Minnesota, with approximately 95,000 patient ED visits per year. EmSTAT is a computerized database for all ED patients. Data are entered online and can be retrieved directly from EmSTAT as a highly formatted patient record, which includes the following fields: patient's name and hospital record number, age, gender, date and time for all entries (including evaluations, continuing assessments, treatment and diagnostic orders given and completed), chief complaint, primary and secondary discharge diagnoses, medications/fluids, dose and route of delivery, disposition, and vital signs (heart and respiratory rate, blood pressure, and temperature).

All patients treated in the ED with intramuscular (IM) or intravenous (IV) DROP were identified through EmSTAT, and summary data (see above) were collected. In addition, all patients receiving DROP were cross-referenced with patients who also received benztropine mesylate (Cogentin) or diphenhydramine (Benadryl) at the same or next ED visit as an index of dystonic reactions.

Study Protocol. Complete patient charts were obtained and reviewed if the patient had received DROP in the ED and EmSTAT review indicated signs of head trauma, recent or remote seizure, cocaine use, a dystonic reaction, hypotension (systolic blood pressure [SBP] $\leq$90 mm Hg) and the use of alcohol. Head trauma was defined liberally as any contusion, laceration, or any other injury to the head or face documented in the physician's physical examination. Patients who were diagnosed as having recent seizures or were noted as having a previous history of seizures were categorized as seizure patients. Cocaine was noted if the patient admitted to using it just prior to ED arrival or if a positive urine drug screen for cocaine was found. Level of intoxication was usually determined by breath alcohol analysis; on rare occasions, serum alcohol levels were measured.

The DROP observation period (DOP) was defined as the isolated observation time when DROP was the only medication the patient had received in the ED (other than antibiotic, pain, or additional antiemetic medications). As soon as any other drug was given (such as an antiepileptic medication) or when the patient was discharged from the ED, the DOP ended. If the patient received any medication with antiepileptic potential prior to or concurrent with DROP, no DOP time was generated (i.e., 0 minutes). The entire medical record was also reviewed for all admitted patients.

Data Analysis. All charts were identified and data collected in a standardized manner. Means and standard deviations were calculated when appropriate. A random-effects model multiple regression analysis[11,12] was used to account for multiple visits by the same patient and to determine significance of the following variables: age, level of alcohol intoxication, gender, total time in ED, DOP, total amount of DROP, route of delivery, degree of closed head injury (none, injury, injury with negative head computed tomography [CT], injury with positive head CT), under the influence of cocaine, and seizure. A p-value $\leq$0.05 was considered significant.

Chart review was attempted for 945 patients who appeared (by EmSTAT) to have a highest likelihood of being at high risk for adverse events following DROP, or who had apparently experienced a side effect suggested by subsequent ED interventions (i.e., IV fluids, benztropine mesylate, diphenhydramine). Of these 945 cases, 933 charts were available for review. After review, 50 patient visits did not meet our criteria for high risk and, therefore, are not included. None of the 50 charts had an adverse event. Only one of the 12 missing charts was of a hospitalized patient; he was admitted for alcohol withdrawal and his medical record could not be found.

RESULTS

A total of 2,468 ED patients received DROP in our ED in 1998. Indications for its use are summarized in Table 1. Approximately half (46%) of these patients had documented ingestion of ethyl alcohol by breath alcohol levels (BALs). The largest percentage of patients receiving DROP were sent home (55.8%), followed by admission to the hospital (19.7%), being sent to the crisis intervention center (10.6%) or detoxification centers (10.7%), or being taken to jail (3.2%). (The crisis intervention center is the HCMC emergency psychiatry department, and the detoxi-

TABLE 1. Indications for Droperidol,* All Patients (*N* = 2,468)

	n (% Total)
Agitation (including ingestions, e.g., alcohol)	1,333 (54%)
Agitation (trauma)	691 (28%)
Pain†	444 (18%)
Vomiting	173 (7%)
Headache	99 (4%)
Anxiety/psychosis	99 (4%)
Vertigo/dizziness	25 (1%)
Other	25 (1%)

*Multiple diagnoses for some patients result in greater than 100%.
†Includes all causes of pain, except for headache, which is separately listed as a pain indication for droperidol.

fication centers are local community observation units for monitoring intoxicated patients.)

Agitation was the most common reason DROP was given, but vomiting, anxiety, and headache or other pain-related complaints were also common reasons for receiving DROP. Droperidol was given to both adult and pediatric patients. The age range was from 20 months to 98 years, with 112 pediatric patients (age ≤17 years) and 141 elders (≥66 years) receiving DROP.

The results of regression analysis revealed no significant difference among the high-risk groups (head trauma, seizure, and alcohol/cocaine) in terms of amount of DROP given, route (IM or IV), DOP, or age. There was a significant difference among gender, with women spending less total time in the department ($p \leq 0.05$) than men. (This is consistent with easier placement in our available community detoxification facilities for intoxicated/agitated women, compared with such placement for men.) Those patients who received a head CT as part of the ED workup and who were found to have no CT evidence of traumatic brain injury (TBI), and therefore were not admitted, also stayed significantly longer in the ED compared with other patients. Specifically, those patients with CT evidence of TBI spent a shorter time in the ED until admitted, compared with those with a negative head CT who were subsequently discharged to home.

Major or Life-threatening Adverse Events.

High-risk groups. Table 2 summarizes the characteristics of the high-risk patients who received DROP.

Head trauma. Five hundred fifty-six patients who received DROP had signs of head trauma on physical examination (excluding head trauma with cocaine, *n* = 17, or seizure, *n* = 49). The average age (±SD) for head trauma patients was 35.0 ± 10.8 years (range 14–88); the majority (76%) were male. Most patients received IM DROP (88%). More than 60% of the patients were discharged to home; the remaining were admitted to the hospital (*n* = 34) or sent to a local detoxification unit (*n* = 77), the crisis intervention center (*n* = 10), or jail (*n* = 35).

Of those with head injury, 402 (77%) had ingested alcohol. The average level of intoxication (±SD) was 213 ± 78 mg %. None of these intoxicated head-injured patients had a history of seizures or cocaine. Sixty-seven of the intoxicated patients with head injury were of sufficient clinical concern to warrant a head CT; 18 (27%) of these had TBI as shown by positive CT scans.

The remaining 154 patients with head injury had no apparent signs of alcohol or other drug ingestion. Of these, 43% were sent home. The remaining

TABLE 2. High-risk Patient Group

Patient Group (*n*)	Age in Years—Mean (±SD)	Emergency Department Length of Stay in Minutes—Mean (±SD)	Droperidol Dose in mg—Mean (±SD)	DOP* in Minutes—Mean (±SD)	Blood Alcohol Level	Disposition (% Admitted)
Head trauma†	35 (±11)					
+Alcohol (402)		435 (±203)	4.2 (±1.8)	348.5 (±194.6)	0.213	6
−Alcohol (154)		391 (±193)	3.8 (±2.4)	248.7 (±182.1)		42
Cocaine	33 (±8)					
+Alcohol (20)		499 (±299)	4.8 (±2.9)	355.2 (±285.9)	0.176	55
−Alcohol (44)		434 (±264)	4.1 (±1.8)	337.2 (±256.3)		14
Seizures						
+Alcohol (137)	39 (±8)	432 (±214)	4.1 (±1.5)	330.1 (±192.6)	0.250	31
−Alcohol (60)	42 (±16)	384 (±245)	4.0 (±2.9)	187.0 (±158.6)		30

*DOP = droperidol observation period, defined as the duration of time in which the patient had received only droperidol, with the exception of a low percentage of patients (<5%) also receiving other antiemetics.
†Excludes head trauma in cocaine and seizure high-risk patient groups.

TABLE 3. Descriptions of Complications

Case 1 An 81-year-old female nursing home patient was brought to the emergency department (ED) after a possible witnessed seizure and a history of severe chronic obstructive pulmonary disease (COPD) and congestive heart failure (CHF). She was given 2.5 mg of intravenous (IV) droperidol (DROP) for sedation in preparation for a head computed tomography (CT), and a brief seizure or anoxic episode was observed, requiring the patient to be intubated. The patient was found to have an arterial pH of 7.37 and a pCO_2 of 103 torr and a pAO_2 of 36 torr. She was extubated two days later and discharged by day 4 with a diagnosis of severe COPD, pneumonia, and urinary tract infection.

Case 2 A 27-year-old male patient was brought in from jail after a question of having a seizure and a documented fever of 102°F. He received a total of 3 intramuscular (IM) shots of DROP (5 mg, 5 mg, and 2.5 mg) over 72 minutes for sedation in preparation for a head CT and lumbar puncture for presumed meningitis. He was also given 2 grams of IV ceftriaxone (Rocephin) and, after a normal head CT, he had a brief witnessed seizure. He was loaded with IV phenytoin and admitted by neurology to the surgical intensive care unit and was subsequently found to have a positive cerebrospinal fluid (CSF) culture for pneumococcus. His phenytoin was discontinued and he continued to receive a total of 40 mg of IV/IM DROP and 30 mg of prochlorperazine (Compazine) for nausea. The patient did well but left two days later against medical advice with the diagnosis of meningitis.

Case 3 A 39-year-old female with a history of panic attacks and alcohol abuse was in jail for driving while intoxicated. En route for an appearance in court, she became anxious and was noted to be hyperventilating, which required her to be brought to the ED. Fifteen to 20 minutes after receiving 2.5 mg of IM DROP for sedation, she was given 50 mg of IM diphenhydramine and 2 mg of IM benztropine mesylate for what may have been akathisias. Fifteen minutes later or approximately 30–35 minutes post-IM DROP, she was noted to have a 1-minute grand mal seizure. She underwent a full neurological workup for new-onset seizure and no clear etiology for seizures were found, but alcohol withdrawal remains the most likely diagnosis, as per neurology.

Case 4 A 39-year-old male was admitted and monitored for possible cocaine stuffing after being stopped by police. Eleven hours after receiving 2 mg of IM lorazepam and 5 mg of IM DROP for sedation, the patient was observed to have a seizure and undergo a cardiac arrest requiring intubation, 17 cardioversions, and treatment with antiarrhythmics and anticonvulsants. He was placed on a naloxone (Narcan) drip for purposes of maintaining bowel activity (positive for opiates) and received multiple-dose activated charcoal via nasogastric tube. The patient was discharged seven days later neurologically intact and he was diagnosed as having cocaine toxicity, cardiac arrest, and seizure. The patient later admitted to ingesting multiple pieces of ``crack'' cocaine in order to elude the police.

Case 5 A non-intoxicated 65-year-old female fell at home, striking her head and lacerating her scalp. On arrival to the ED, she was given a bolus of 2.5 mg of IV DROP for agitation. Fifteen minutes later, she was given 2 mg of IV lorazepam for continued agitation. Her CT scan was negative for traumatic brain injury, but it was decided to admit her for observation. While waiting in the ED for an inpatient bed assignment, she received additional doses of IV DROP (2.5 mg) at 3 hours 15 minutes, and again at 1 hour 2 minutes prior to admission to the hospital. Shortly after this last dose in the ED, she developed central nervous system depression, which responded to IV flumazenil. She was discharged from the neurosurgery inpatient service the next day with a diagnosis of closed head injury. No evidence of seizures or other potential complications in this group, other than this case, were noted during chart review.

Case 6 A 28-year-old agitated female was physically restrained by police at the scene and, upon ED arrival, she was yelling and hallucinating, with a sinus tachycardia exceeding 200 beats/min. She was given 2 mg IM of lorazepam 12 minutes prior to receiving a 5-mg IM dose of DROP. Nine minutes after the IM injection of DROP, she had a generalized tonic–clonic seizure, and had a rectal temperature of 106.9°F. She was chemically paralyzed, intubated, and treated for possible meningitis, encephalitis, acidosis, and hyperthermia, and was loaded with IV phenytoin. A head CT showed cerebral edema and the patient also ruled in for a myocardial infarction. Her urine drug screen was positive only for cocaine and she had a blood alcohol level of 0.06 mg %. She was discharged five days later with a diagnosis of cocaine toxicity.

patients were admitted (n = 65), transferred to the crisis intervention center (n = 10), returned to a nursing home (n = 3), or taken to jail (n = 10). Of the 154 non-intoxicated head-injured patients receiving DROP, 55 received a head CT; 20 (36%) of these CTs were read as positive for TBI.

Most of the patients with TBI demonstrated by CT were loaded with phenytoin once the results of the scan were known, as is the protocol for most cases of TBI in our institution. By definition, the time at which phenytoin was administered marked the end of the DOP for this patient. All patients with CT-documented TBI were admitted to the neurosurgery service.

Only one possible complication from the use of DROP was identified in this high-risk group of head-injured patients, which is shown in Table 3 (case 5).

Patients with cocaine intoxication. There were 64 patients (25 females) who either admitted to using cocaine (n = 27) or had a positive urine test for cocaine (n = 37), who also received DROP. The average age was 32.8 ± 7.6 years; 31% were also intoxicated with alcohol (BAL = 176 ± 10 mg %). In addition to those positive for cocaine and intoxicated with alcohol (n = 20), nine patients in this group also had signs of head trauma. Two of the nine patients received head CTs, which did not show signs of TBI. The characteristics of the sub-

group of cocaine users are given in Table 2. Nine of the 20 alcohol-intoxicated, cocaine-positive patients subsequently received other antiepileptigenic medications (i.e., lorazepam [Ativan]), thus ending their DOP; 11 were admitted for further observation and treatment.

There were 44 non-alcohol-intoxicated, cocaine-positive patients. Twenty-two received both DROP and an antiepileptic medication at some point during their ED stay (thus ending their DOP). The summary results are shown in Table 2. Eight of the 44 non-alcohol-intoxicated, cocaine-positive patients also had signs of head trauma. Two patients received a head CT, and one had positive CT findings of TBI. Two additional patients with acute mental status changes but no signs of head trauma also underwent CT scanning; both CT scans were positive for brain injury. Among these 44 patients, 14 were admitted to the hospital from the ED, 17 were discharged to home, five were sent to jail, three were taken to a detoxification center, and five were transferred to the crisis intervention center for emergency psychiatric evaluation.

Two possible complications resulting from the administration of DROP occurred in this subgroup of cocaine-intoxicated patients, which are shown in Table 3 (cases 4 and 6).

Patients with observed recent seizures or a history of seizures. There were 197 patients receiving DROP who had either a recently witnessed seizure or a history of a seizure prior to receiving DROP. Approximately two-thirds (n = 137) were also acutely alcohol-intoxicated. Of the patients acutely alcohol-intoxicated (mean BAL = 250 ± 100 mg %) with a history of seizure, 38 had a witnessed seizure just prior to ED arrival. There were 98 men and 39 women in the alcohol-intoxicated group with seizures (age 39.2 ± 8.2 years); 93% (n = 127) had a previous diagnosis of seizure disorder. Ten of the 38 witnessed seizures were thought to be new-onset, due to cocaine (one), head trauma (one), or alcohol withdrawal (eight). There were 49 seizure patients with physical signs of head trauma; 14 had CTs, and three had CT evidence of TBI. Of the 137 intoxicated patients with seizures, 71 patients were thought to have a seizure related to alcohol withdrawal, 26 were subtherapeutic for anticonvulsant medication, and 22 were non-compliant with prescribed anticonvulsants. In addition, there were 18 possible breakthrough seizures in patients with therapeutic antiseizure medication levels: four were thought be due to cocaine, and one due to trauma. Table 2 describes the characteristics of this group. The dispositions of the 137 intoxicated seizure patients included 42 discharged to home, 57 transferred to a detoxification center, 19 admitted to the hospital, 19 transferred to the crisis intervention center, and one taken to jail.

The 60 patients (22 females and 38 males, aged 41.9 ± 16.1 years) with history of seizure but no evidence of alcohol intoxication included 33 patients with witnessed seizures (nine being new-onset). Physical evidence of head trauma was present in 31 of the 60 patients. Head CTs were performed in 21; three were positive for TBI. Twenty-three patients were found to have subtherapeutic anticonvulsant levels, with an additional five patients non-compliant with their antiepileptic medication. Of the remainder, eight patients had a history of alcohol withdrawal seizures, two new-onset seizures were thought to be secondary to cocaine, one patient was found to have a CNS mass, and the etiologies of seizures in 21 others were unknown (although the majority were taking anticonvulsants and were therapeutic). The characteristics of this group are also shown in Table 2. Thirty of the 60 patients (50%) were admitted, 22 were discharged to home, three were transferred to a crisis intervention center, two were sent to a detoxification center, two were sent to jail, and one was returned to his nursing home.

Three patients in this group were found to have a complication after receiving DROP. These patients are briefly described in Table 3 (cases 1–3). No other complications were identified.

Minor Adverse Events.

Dystonic or akathisia reactions. Out of 2,468 patients treated with DROP, 42 also received either diphenhydramine (n = 22), benztropine mesylate (n = 15), or both (n = 5). One of these patients received diphenhydramine before the DROP for purposes of inducing sleep, and one was given DROP/diphenhydramine infusion in combination for an acute allergic skin reaction; these two patients were excluded from the final data analysis. The remaining 40 patients received these medications for presumed dystonic or akathisia reactions. However, further chart review revealed that approximately one-third (n = 14) received either diphenhydramine, benztropine mesylate, or both concurrently with the DROP medication while in the ED because of a known (or presumed) history of dystonic or akathisia reactions and therefore were also excluded as counting as true rescue medications. Of these 14 patients, 11 were alcohol-intoxicated (244 ± 62 mg %). Therefore, only 26 patients required rescue from a known dystonic or akathisia reaction. Six of the 26 patients were also alcohol-intoxicated and received either diphenhydramine (25–50 mg)

(n = 3) or benztropine mesylate (1–2 mg) (n = 3) (Table 4). Eighty-eight percent of the intoxicated patients (n = 17) received IM DROP. Two of the intoxicated patients returned after being discharged to home for treatment of akathisias and their times post-DROP injection were not included in the summary statistics. Both patients required minimal treatment for their discomfort and were subsequently discharged.

In the non-intoxicated group, three of the 23 patients received diphenhydramine (n = 2) or benztropine mesylate (n = 1) concurrently with DROP, while the remainder (n = 20) were rescued from a dystonic or akathisia reaction. The majority of these patients (71%) had received IV DROP and were treated with 25–50 mg of diphenhydramine (65%), 1–2 mg of benztropine mesylate (20%), or both (15%).

Hypotension. Ninety-six out of 2,468 EmSTAT-identified patients met the criteria for having a documented hypotensive episode (SBP $\leq$ 90 mm Hg) after receiving DROP. In those who were alcohol-intoxicated (1,136 patients), 73 patients (BAL = 218 $\pm$ 59 mg %) were noted to have an SBP $\leq$ 90 mm Hg approximately three hours (170.5 $\pm$ 162.3 minutes) after receiving 4.1 $\pm$ 1.8 mg of DROP (Table 4). The average changes in SBP, diastolic blood pressure (DBP), and heart rate (HR) were -29 ± 18 mm Hg, -20 ± 15 mm Hg, and -11 ± 17 beats/min, respectively, from their initial vital signs at arrival. Eight of these patients received IV fluids and one was admitted for a severe arm laceration requiring surgery. There were no admissions for hypotension thought to be associated with DROP administration.

In the alcohol-free group (1,332 patients), 23 patients had an observed episode of hypotension approximately two and a half hours (155.4 $\pm$ 154.5 minutes) after receiving 3.2 $\pm$ 1.4 mg of DROP (Table 4). The average changes in SBP, DBP, and HR were -36 ± 35 mm Hg, -24 ± 25 mm Hg, and -11 ± 24 beats/min, respectively. Twelve patients received IV fluids and six patients were admitted. Seven of those receiving IV fluids had either also received lorazepam (n = 4) or had the diagnosis of urosepsis (n = 3), but no admissions were identified that were thought to be due to hypotension induced by DROP alone.

TABLE 4. Rescue from Dystonic or Akathisia Reactions, and Patients with Hypotension

Patients	Post-injection (Min) (Mean ± SD)	Droperidol (mg) (Mean ± SD)
Dystonic or akathisia		
n = 6* (+alcohol)	161.7 (±232.7)	4.9 (±1.6)
n = 20 (−alcohol)	44.6 (±55.1)	3.3 (±2.4)
Hypotension		
n = 73 (+alcohol)	170.5 (±162.3)	4.1 (±1.8)
n = 23 (−alcohol)	155.4 (±154.5)	3.2 (±1.4)

*Two additional intoxicated patients followed up after discharge with dystonic reaction complaints.

DISCUSSION

Currently in our ED, DROP is administered at the discretion of the staff or residents when it is thought to enhance or expedite patient evaluation and care. In acutely agitated/intoxicated patients, 2.5–5 mg of DROP delivered IV or by IM injection is commonly given and may be repeated as needed, to help sedate the patient, thus expediting medical evaluation. Smaller amounts are also used for treatment of nausea, vertigo, and headaches.

Frequently, DROP is administered to individuals incapable or unwilling to provide a medical history, the overwhelming majority of whom will eventually be discharged from the ED. Given their unpredictable presentation and the need for rapid assessment for serious illness and injury, it is often not possible to prescreen agitated patients for potential drug risk factors prior to sedation with DROP. We subsequently may determine that these patients were at risk for a potential described complication of DROP.

Droperidol is a fluorinated derivative of the phenothiazines, and there are concerns regarding its propensity to cause seizures. Phenothiazines as a group may lower the seizure threshold, especially when used for acute alcohol withdrawal.[13] Early investigations with haloperidol (a congener of DROP) indicated that it lowered the seizure threshold (data on file, McNeil Pharmaceutical, Spring House, PA), although the clinical significance of this reduction was brought into question decades ago by Palestine and Alatorre,[14] as well as by experience from within our own department.[15] A recent meta-analysis of prospectively controlled trials examining the effectiveness of neuroleptic agents in reducing the incidence of seizures in alcoholic patients found that these agents had significant epileptogenic potential.[16] Although DROP was not specifically cited, monotherapy with haloperidol was not recommended. The facilitation of seizure activity by DROP has been reported to occur in epilepsy patients during surgery.[8]

We did not find DROP to be epileptogenic, regardless of the route of delivery, when given in the doses reported here to agitated/intoxicated pa-

tients, patients with closed head injury, epilepsy patients, or patients with CT-documented brain injury. Even in patients with a subsequent admitting diagnosis of alcohol withdrawal, brief exposures to DROP in the ED did not appear to be detrimental. Although we did not specifically address the question of whether DROP was harmful to alcohol withdrawal patients, several patients who ultimately received treatment for alcohol withdrawal were initially given DROP to expedite their ED care. However, no patient who was in clear or florid alcohol withdrawal, such as hallucinating or globally confused, received only DROP in the ED.

The DOP was used in order to document the use of DROP during a time period in which no antiepileptic drug (benzodiazepines, phenytoin, etc.) was also given. The use of a DOP documented that the duration of sedation (overall mean of 312 ± 200 minutes) with DROP (overall mean dose of 4.1 ± 2.0 mg) was safe for patients who later were shown to have significant brain injury. It is important to emphasize that no antiepileptic drug was given during this period, and therefore the lack of seizures cannot be attributed to any other reason other than the lack of epileptigenicity for these doses of DROP. A total of 47 patients with radiographic evidence of brain injury (out of 163 head CTs) secondary to trauma or from spontaneous acute intracranial hemorrhages were given DROP; of these, one patient had a seizure, but it is likely that this seizure was not caused by DROP, but rather by serious comorbidity (i.e., cocaine ingestion). It could also be argued that the sedation of these agitated patients caused by DROP would in fact mask their altered mental status during a neurologic assessment; we speculate that the use of DROP in fact expedited their imaging and subsequently their diagnosis. Although we did not specifically test this hypothesis, patients with CT-documented TBI had a significantly shorter stay in the ED compared with those who had a negative head CT ($p < 0.002$). Our finding that DROP is safe in acutely agitated patients with TBI is consistent with the published work by Stanislav and Childs, who have shown DROP to be safe in patients with chronic brain injury.[17]

Recently, the Food and Drug Administration (FDA) has issued a warning about DROP and its potential to cause prolonged QT syndrome and torsades de pointes,[18] and cardiac dysrhythmias with subsequent hypotension and/or arrest have been reported.[10] Although the vast majority of our patients who received DROP were not on cardiac monitors, all were under continuous ED observation with frequent monitoring of vital signs. Other than the patients we described whose hypertension was temporally related to DROP (most of whom had other likely causes of hypotension), none of our patients were observed to have any other indication of cardiovascular events following DROP while in the ED. This includes a significant number of known alcoholic patients with presumably low body stores of magnesium and other electrolytes as well.

There was one patient (case 4 in Table 3) who ingested (stuffed) ''crack'' cocaine and he was observed, after admission, to have a seizure and go into cardiac arrest 11 hours after receiving both lorazepam (2 mg) and DROP (5 mg). It is our contention that DROP played no role in this patient's seizure or cardiac arrest. This patient had a documented normal cardiac QT interval by electrocardiography and, at the time of seizure/cardiac event, also had nearly surpassed 4 half-lives of the systemic effects of DROP (documented normal kidney and liver function). Most importantly, he had ingested multiple pieces of ''crack'' cocaine, which is known to cause seizures and death.

The potential hazards of DROP to the hypovolemic patient has been postulated,[19] and many of our chronically intoxicated patients may be dehydrated. However, we found no evidence of clinical relevance in our study that would cause us to hesitate in giving DROP to the chronically inebriated. Although a higher number of intoxicated patients have documented hypotension during their DOP, there were no admissions for hypotension, and very few patients required a fluid bolus prior to leaving the department. Even in elders and in pediatric patients, DROP appeared safe. We did, however, observe more frequent episodes of hypotension when both lorazepam and DROP were given. In this circumstance, one should have a heightened level of awareness for possible complications.

Attempts were also made to document the incidence of patient-reported extrapyramidal or dystonic reactions by retrospectively identifying those patients who also received diphenhydramine or benztropine mesylate. Acute intoxication would likely lessen patient recognition and reporting of extrapyramidal or dystonic reactions, and there is some evidence that alcohol may be therapeutic in the treatment of akathisia.[20] The mechanism for this is unclear but might rest in the sedative effects of alcohol. If this is the case, our relatively low incidence of dystonic reactions overall (1%) may be explained in part by the high amount of alcohol consumption in our patient population. Other studies have indicated the rate of dystonic reactions to be 8% to 23%.[21,22]

LIMITATIONS

The primary objective of this study was to document the safety of DROP when given to a large nonselected patient population thought to be representative of those in any ED. Included in this large population of more than 2,400 patients were those thought to be sufficiently agitated to require chemical sedation either with IM or IV DROP. Because this was a retrospective study, we recognize a number of limitations. Several types of bias may have occurred in this study simply because, by its a retrospective nature, data were not collected in a systematic manner. There is also no control group with which to make comparisons. Therefore, comments regarding the incidence and frequency of seizures secondary to DROP are not possible. In addition, it is possible that a small number of patients with a history of seizures (acute or chronic) may have been missed during the chart review. However, unlike most retrospective studies, collection of most of our data was from an entirely electronic ED record (EmSTAT) with defined searchable fields for data entry points. Similarly, the number of dystonic reactions may be greatly underestimated; we based our definition on the associated treatment with the rescue medications diphenhydramine and benztropine mesylate. Some patients who had extrapyramidal side effects after DROP may not have sought treatment if symptoms occurred after their discharge from the ED, or they may have sought care from other local health care facilities. However, our ED serves the great majority of patients in our city who would likely have received DROP for agitation from any cause. This patient population would most likely return to our ED if a delayed reaction occurred. In spite of the above limitations, a very large number of non-selected, high-risk patients received DROP without any documented life-threatening events.

CONCLUSIONS

Those patients most likely to suffer serious sequelae from presumed side effects of DROP (i.e., seizures, hypotension) were specifically evaluated. We included patients with head injury, history of seizure, or agitation secondary to cocaine or alcohol abuse, as well as those having a hypotensive episode. Although benzodiazepines remain the medication of choice for those patients initially seen in the ED after having a seizure or for prevention of seizure, DROP, in the doses and duration reported here, does not appear to be epileptigenic in the acutely agitated patient and may be given even if concerns regarding the possibility of intracranial bleeding exist. Most high-risk patients receiving DROP have no adverse events. The few serious adverse events noted in the high-risk patients who received DROP occurred in patients who had comorbidities; it is not clear that DROP was causative.

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REFLECTIONS

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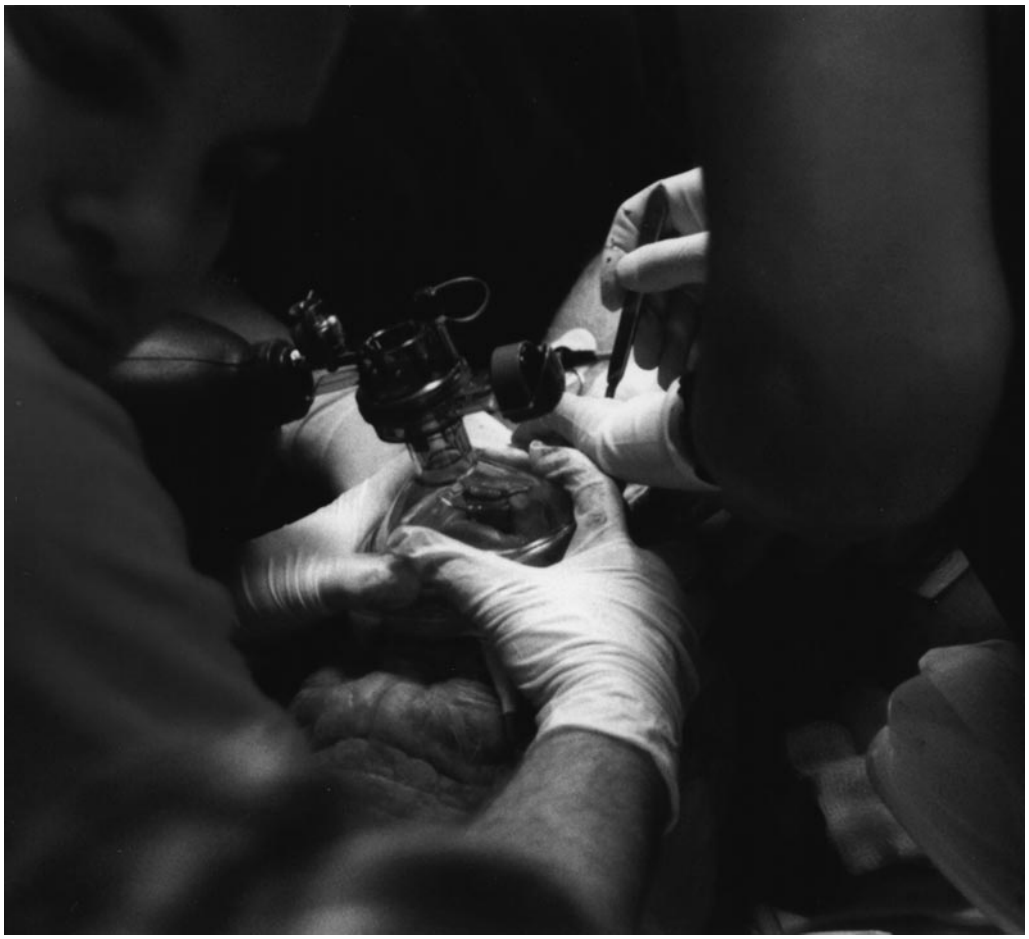

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