The Effect of IM Droperidol on Driving Performance

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ABSTRACT

Objectives: Droperidol (DROP) is used in the emergency department (ED) for several indications, but its effect on psychomotor performance is unclear. The purpose of this study was to evaluate the effects of DROP, 2.5 mg intramuscular (IM), on driving performance.

Methods: This was a randomized, double-blinded, two-period, placebo-controlled crossover trial that utilized a standard driver-training program with computerized scoring. We solicited 20 paid volunteers who were pre-screened with a 12-lead EKG to evaluate QT length. For the first driving simulation, subjects were randomly assigned to receive either 2.5 mg of DROP IM or an equal volume of normal saline (NS). At least 72 hours later, the same subjects participated in a second driving simulation. For the second driving simulation, the assignment of DROP, 2.5 mg IM, or normal saline was reversed: (If a subject received DROP, 2.5 mg IM, in the first simulation, the subject received normal saline in the second simulation; conversely, if a subject received normal saline in the first simulation, the subject received DROP, 2.5 mg IM, in the second simulation). Thirty minutes later, participants drove the 20-minute simulation and received an average score based on the errors made in 4 categories: accelerating, braking, steering, and signaling. Post-testing, participants evaluated their degree of drowsiness and driving impairment using a visual analog scale and compared their perception of impairment to that caused by alcohol ingestion. Data were analyzed using analysis-of-variance, Pearson chi-square and Fischer's exact test with alpha set at $p = 0.05$.

Results: Twenty subjects (11 males and 9 females) completed the protocol. The mean age was 30 years with a range of 20 to 46 years, and the mean weight was 80 kg. The mean driving experience was 12 years. Participants who received DROP felt significantly drowsier (38.6 mm $\pm$ 9.0) than those receiving NS (13.2 mm $\pm$ 9.0), the mean difference was 25.4 mm $p = .009$. Subjects receiving DROP were also more likely to feel that their driving would be impaired as rated on the VAS (DROP: 34.6 $\pm$ 5.2; NS: 3.2 $\pm$ 5.2; $p = .0005$), and DROP subjects reported impairment equivalent to 1–4 drinks more frequently than those receiving placebo (61% vs. 16.7%, $p < .001$). These subjective feelings of impairment were confirmed by their driving performance on the simulator. The mean driving score, using the driving simulator, was 68.8% with DROP vs. 73.6% with NS; $p = .013$.

Conclusions: Subjects receiving modest doses of IM DROP report increased perceptions of drowsiness, driving impairment, and intoxication; these perceptions are confirmed on objective testing.

INTRODUCTION

Acute presentations of nausea and vomiting, headache, and agitation all provide frequent therapeutic challenges for the clinician. IM Droperidol (DROP) has been effectively used in the emergency

department (ED) setting to treat these complaints [1–5]. When given IM, DROP's onset of action is from 3 to 10 minutes with a peak effect at 30 minutes. Sedative effects generally last 2 to 4 hours [6]. Therefore, it is likely that a patient will be discharged from a healthcare facility while the sedative effects of DROP

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persist; this impairment may interfere with the complex psychomotor tasks of driving a car.

The goal of our study was to examine the effect of IM DROP on simulated driving performances. Although many agents must carry warning labels that explain the possible effects on driving or the operating of heavy machinery, no previous study has evaluated the effect of IM DROP on driving performance.

METHODS

We compared the effects of DROP, a neuroleptic butyrophenone tranquilizer, on simulated driving performances [6]. Since the likelihood of driving, after receiving any agent, is greater if the person does not recognize their impairment, we also investigated the subjects' perceptions of drowsiness compared to their actual driving impairment. This study was a randomized, double-blinded, two-period, placebo-controlled crossover trial. The Institutional Review Board (IRB) approved the study, and all participants signed a consent form prior to participating in the study. Although this study was approved prior to the FDA Black Box Warning on droperidol, we advised the IRB of this development and a 12-lead EKG pre-screening of all participants was mandated.

Licensed drivers greater than 18 years of age were eligible to participate; pregnancy was an exclusion criterion. All participants were pre-screened with a 12-lead EKG to evaluate QT length. Each volunteer was required to participate in 2 simulations that were scheduled at least 72 hours apart. Each participant was driven to and from the study site by one of the study investigators.

To objectively assess driving in a controlled environment, driving simulators were employed (L-300 Car Simulator System, Doron Precision Systems Inc., Binghamton, NY). The simulators were mounted on a fixed platform and incorporated a typical size steering wheel, gas and brake pedals, seat, and seat belt. Participants had a practice run on the "Destination Driving" course and a test run on the more demanding "Crash Avoidance" course. Both courses tested the participants' abilities to accelerate, brake, steer, and signal in response to images that were projected onto a large screen located in the front of the room. The simulator recorded 50 data points during each of the two driving tests and generated scores based on the number of errors in each of four driving skill areas: acceleration, braking, steering, and signaling. The number of errors was automatically recorded and the final score calculated by comparison to the total number of expected responses. Therefore, the final score represented the total percentage of correct driving responses. Although there is no fixed "passing" or "failing" grade, competent drivers without simulator experience are expected to score approximately 70-75 percent. Driving performance feedback was not provided to the participant by the simulator or by the investigators.

First, participants used the driving simulator for a practice run on the "Destination Driving" course. They were then randomized through a computer-generated random number table to receive either 2.5 mg of IM DROP or an equal volume (1cc) of normal saline (NS). The dosage of DROP is the maximum initial

dose recommended by the drug's manufacturer (Taylor Pharmaceuticals, an Akorn Company, Decatur, Illinois) [1].

In order to assess the subjective effects of DROP versus NS, participants completed a pre-simulator questionnaire 20 minutes after the injection. The five questions were:

- 1) Do you think you received a placebo or DROP?
- 2) Rating of drowsiness on a visual analog scale (VAS)
- 3) Do you feel that your driving will be impaired?
- 4) Rating of how much you feel your driving will be impaired on VAS
- 5) Compare your level of impairment to that which you have experienced after consuming alcoholic beverages (0, 1, 2, 3, >3 drinks, or "don't know").

Thirty minutes after the injection, and coincident with the expected peak effects of DROP, participants performed the first test drive. Immediately following the 20-minute simulated drive, participants completed a post-simulator questionnaire that was identical to the pre-simulator questionnaire. At least 72 hours later, the same subjects participated in a second driving simulation. For the second driving simulation, the assignment of DROP, 2.5 mg IM, or normal saline was reversed: (If a subject received DROP, 2.5 mg IM, in the first simulation, the subject received normal saline in the second simulation; conversely, if a subject received normal saline in the first simulation, the subject received DROP, 2.5 mg IM, in the second simulation).

Data were analyzed using SAS PROC MIXED. Pearson's chi-square and Fisher's exact test were used to test for significance between binomial parameters. Assuming a 5-point difference on the driving simulator test and a common standard deviation of 2.5, with alpha at 0.05 and power = 0.80, a sample size of 12 was needed. We enrolled 20 paid volunteers to allow for the potential loss of some volunteers.

RESULTS

Twenty qualifying volunteers, 11 men and 9 women, completed the protocol. The mean age was 30 years with a range of 20 to 46 years, and the mean weight was 80 kg. The mean driving experience was 12 years.

As indicated in *Table 1*, the participants' subjective impressions of drowsiness and level of impairment (post-injection) were similar before and after the test drive, indicating that the act of simulated driving itself did not change their perception of impairment. Approximately three-quarters of each group correctly identified the solution they had received. Participants receiving DROP rated their drowsiness as significantly greater (38.6 mm $\pm$ 9.0 versus 13.2 mm $\pm$ 9.0, $p < .01$) than those in the NS group. When receiving DROP, 60% felt that their driving would be impaired, while only 10% (and 0% post simulator) felt that their driving would be impaired after an injection of NS ($p = 0.001$). This was consistent with the VAS, which confirmed the perception of a much greater level of impairment when receiving DROP ($p = 0.0005$). Nine of 20 participants (45%) (pre

TABLE 1. Results of Subjects Receiving DROP vs. Normal Saline Pre and Post Simulation

	Pre Simulator	Post Simulator
Proportion correctly identifying injection given		
Droperidol	75% (15/20)	70% (14/20)
Normal Saline	74% (14/19)	80% (16/20)
Drowsiness VAS (mm ± SD) (0-not drowsy; 100-most drowsy)		
Droperidol	37.4 ± 4.6	38.6 ± 9.0
Normal Saline	8.6 ± 4.6	13.2 ± 9.0
Mean Difference	28.8; p = .0001	25.4; p < .009
Proportion perceiving that driving was impaired		
Droperidol	60% (12/20)	60% (12/20)
Normal Saline	10% (2/20)	0% (0/20)
p value	p = .001	p = .0001
Level of Impairment VAS (0-not impaired; 100 most impaired)		
Droperidol	30.4 ± 4.3	34.6 ± 5.2
Normal Saline	5.0 ± 4.3	3.2 ± 5.2
Mean Difference	25.4; p = .0005	31.4; p = .0005

and post simulator) who received DROP compared their expected level of impairment to the equivalent of consuming 2–4 drinks; only one (5%) NS participant ($p < .02$) compared his expected level of impairment to the equivalent of 2–4 drinks.

There was not a significant difference between the DROP participants and the NS participants in the individual scores for accelerating, braking, steering, and signaling. There was, however, a significant difference between the DROP participants and the NS participants in the overall mean score. The mean driving score with DROP was 68.8% $\pm$ 1.7, and the NS driving score was 73.6% $\pm$ 1.7 (Δ 4.8; $p < .015$).

DISCUSSION

This study confirms the overall adverse effects (degree of drowsiness) of clinically utilized doses of Droperidol on driving performance. The perception of drowsiness, while driving, may well be of clinical significance. Using a simulator, Weiler, et al. compared the effects of fexofenadine, diphenhydramine, alcohol, and a placebo on driving performance. He found that subjects' perceptions of drowsiness was a weak predictor of accident occurrence, but perceptions of drowsiness did correlate with the inability to

maintain a safe minimal following distance, steering instability, and left-lane excursions [7]. Although visual analog scales have been previously used in evaluating drug induced drowsiness and have been shown to correlate with other assessments of sleepiness, the inherent nature of the VAS makes interpretation and statistical analysis of specific VAS values problematic [8,9]. Given the accepted clinical significance of a 13 mm difference on a VAS assessing pain scale, it is likely that our relatively large VAS difference of more than 25 mm would be meaningful as well as statistically significant [10].

The deleterious effects of droperidol on driving performance may be relevant to the physician. Prior to the FDA's warning regarding the use of DROP, the drug was commonly used by emergency physicians in the ED for the treatment of vomiting, agitation, and headache [1–5]. A similar butyrophenone agent, haloperidol, is still commonly used for some of these same indications. Due to their rapid onset and relatively long duration of action, it is likely that patients would be discharged from the ED while still under the influence of these drugs. Because study subjects reported increased perceptions of drowsiness, driving impairment, and intoxication, our data suggests that patients, receiving modest doses of IM DROP, should use caution if they

plan to operate a motor vehicle after discharge from a health-care facility.

LIMITATIONS

There are several limitations to the current study. Although there was a significant difference in the overall mean simulator driving scores, the two groups' mean scores differed by only 4.8 points. Since there is not a clearly defined failing score, it is not possible to determine whether this decrease in driving ability would actually represent a serious hazard on the road. However, the fact remains that nearly half of the DROP subjects reported impairment comparable to 2–4 alcoholic drinks, and the reported impairment is cause for concern. There are no standardized tests, for our simulator, which would allow for direct comparison with alcohol ingestion, and so we were unable to compare DROP use to alcohol ingestion. It should also be noted that the mean driving experience of our participants is 12 years. It is possible that drivers with less experience may be more significantly affected by DROP. The study subjects were healthy volunteers, unlike many patients who received DROP in the ED for nausea, agitation, or migraine. Such patients might experience greater difficulty with complex psychomotor tasks such as driving. The current study evaluated subjects 30 minutes after an injection of DROP. Most patients would leave an ED at least two hours post injection; the effect of DROP, two hours post injection, was not measured.

CONCLUSION

Participants receiving a commonly utilized dose of droperidol (2.5 mg IM) report increased perceptions of drowsiness, driving impairment, and intoxication. These perceptions were objectively confirmed through the use of simulated driving tests.

The author has no potential financial conflicts of interest to report.

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