Controlled-Release Methylphenidate Improves Attention During On-Road Driving by Adolescents with Attention-Deficit/Hyperactivity Disorder

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Background: **Attention-deficit/hyperactivity disorder (ADHD) is associated with a 3- to 4-fold increase in both driving-related accidents and associated injuries. Methylphenidate (MPH) is the most commonly prescribed psychostimulant medication for ADHD. It has been demonstrated to improve performance on a driving simulator. This study investigated whether a once-daily, long-acting, osmotic, controlled-release MPH formulation improves the driving performance of ADHD adolescents while driving their own car on an actual road segment.**

Methods: **Twelve ADHD-diagnosed male adolescent drivers (mean age, 17.8 years) prescribed a standard dose of 1.0 mg/kg (if they were not already taking methylphenidate) of controlled-release MPH participated in this repeated-measures crossover study. On 2 separate occasions (off/on medication randomized), participants drove a standard 16-mile road course incorporating rural, highway, and urban streets. A rater, blind to medication conditions, sat in the back seat and rated impulsive (eg, "cutting off" another driver) and inattentive (eg, drove past designated turn) driving errors.**

Results: **Impulsive driving errors were observed to occur rarely under both medication and no medication conditions. Inattentive driving errors were more common and were significantly reduced while the subject was on medication (4.6 versus 7.8; $P < .01$). The improvement in driving performance (change in number of errors recorded) from first to second testing was positively correlated with medication dosage ($r = 0.60$; $P < .01$).**

Conclusions: **Once-daily controlled-release MPH improves real-life driving performance of adolescent males diagnosed with ADHD. In particular, it significantly reduces driving errors arising from inattention. (J Am Board Fam Pract 2004;17:235–9.)**

Attention-deficit/hyperactivity disorder (ADHD) is a chronic disorder characterized by inattention, impulsivity, and overactivity.[1] Between 40% and 80% of ADHD-diagnosed children continue to suffer as adolescents.[2,3] Among children, ADHD is associated with an increased risk for accidents (especially bicycle and pedestrian).[4–6] Adolescents with ADHD are 2 to 4 times more likely to experience a motor vehicle accident,[7–10] and more than 3 times more likely to incur associated injuries.[8]

Submitted, revised, 6 January 2004.

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This study was funded by a grant from McNeil Consumer & Specialty Pharmaceuticals

Immediate-release methylphenidate (IR MPH) is the most frequently prescribed psychostimulant for the treatment of ADHD. It is a short-acting drug that reaches peak plasma concentration at approximately 2 hours after administration and has an elimination half-life of approximately 4.5 hours (95% confidence interval, 3.1 to 8.1 hours).[11] The current standard of care for daily symptom control is 12 hours.[12] To achieve this standard of care, IR MPH must be administered 3 times daily, dosed at 4-hour intervals. However, such dosing does not cover evening hours. Given its short duration of action, multiple daily dosing of IR MPH results in drug plasma concentrations that rapidly reach peak effects and then quickly dissipate over 4 hours. Symptoms are reported to wax and wane throughout the day as a result of the variations in plasma concentrations that are associated with multiple daily doses.[13]

Driving performance of adolescents with ADHD seems to improve with psychostimulant medication. Cox et al[9] compared the effects of 1 dose of IR MPH and placebo on the simulated driving performances of men with ADHD (ages 19 to 26 years) with that of matched control subjects. When placebo was administered to both groups, ADHD-diagnosed participants demonstrated significantly poorer driving scores than did controls ($P < .05$). However, 1.5 hours after administration of IR MPH, the driving performance of the ADHD-diagnosed group significantly improved ($P < .05$) compared with that of control subjects.

In a subsequent study, Cox et al[14] compared thrice-daily dosing of IR MPH (Ritalin) with once-daily, controlled-release MPH (Concerta). Controlled-release MPH delivers methylphenidate via an osmotic pump to produce a smooth, ascending profile with duration of treatment effect through 12 hours.[15] Once-daily dosing of controlled-release MPH at 8 AM is equivalent to thrice-daily MPH dosed at 8 AM, 12 PM, and 4 PM. In this crossover design study, driving performance of ADHD-diagnosed adolescents (age range, 16 to 18 years) was assessed using a sophisticated driving simulator at 2 PM, 5 PM, 8 PM, and 11 PM Driving performance worsened by a factor of 5 at 8 PM and 11 PM when subjects received IR MPH. Simulated driving performance on controlled-release MPH remained stable from 2 PM to 11 PM. Not only was driving performance significantly better among subjects receiving controlled-release MPH ($P < .001$), but subjects demonstrated significantly less variability in driving performance ($P < .001$).

Given this evidence on simulated driving performance, we hypothesized that ADHD-diagnosed adolescents who received once-daily controlled-release MPH would experience fewer impulsive and inattentive driving errors than when they received no medication.

Methods

Subjects

Twelve male drivers with a mean age of 17.8 ± 1.7 years, 21 ± 15 months of driving experience, and an average of 1 crash and 1 moving vehicle violation participated in this repeated measure, randomized, crossover study. Subjects were recruited through high school nurses and a newspaper advertisement. Inclusion criteria were: diagnosis of current ADHD as determined by parent-report questionnaire and structured clinical interview; positive history of MPH responsiveness disclosed by patient and parent reports; and current daily driving activity. Exclusion criteria were: a history of tics or other adverse reactions to MPH or a history of substance abuse disclosed by patient or parent. Comorbid psychiatric diagnoses were determined by clinical interview for 3 participants (1 subject satisfied the DSM IV criteria for social phobia and 2 the criteria for oppositional defiant disorder).

Procedure

After informed consent was obtained from parents and subjects, parents completed the DuPaul ADHD Rating Scale IV[16] A clinical psychologist (JKP) then administered the Diagnostic Interview Schedule for Children (DISC-IV).[17] Subjects next met with a psychiatrist (RLM) who administered a physical examination and further confirmed the ADHD diagnosis by the Standardized Interview for Adult ADHD.[18] Using a random numbers table, each subject was assigned to receive a single dose of once-daily, controlled-release MPH (Concerta). All the subjects had previously taken MPH products and had been shown to be responsive to MPH. Five of the subjects were taking controlled-release MPH at the time of enrollment in the study, so their dosage was maintained. The remaining subjects were placed on a dose of controlled-release MPH based on the formula of 1 mg/kg. Two subjects received 72 mg, 1 subject received 54 mg, 6 subjects received 36 mg, and 3 subjects received 18 mg controlled-release MPH in the study. The average daily dose of controlled-release MPH was 39 mg. The average milligrams per kilogram was 0.74, so subjects were possibly underdosed.[19] None of the subjects reported side effects or complications from treatment. Three subjects were taking other medications for hypertension, for constipation, and social phobia. All these medications were continued during the study at their prescribed doses.

At the same time of day (some time between 10 AM and 4 PM, depending on the subject's schedule) on 2 separate days, separated by approximately 1 week, subjects were randomly assigned to drive after taking controlled-release MPH at 8 AM or taking no medication on the day of testing. Subjects drove a road course, approved by the Virginia Department of Motor Vehicles, to adequately assess driving competency. This 16-mile road course in-

Table 1. Driving Performance Variables and Total Incidence for Both Conditions

Performance Variables	Controlled-Release MPH	No Medication
Control variables		
Driving significantly faster than traffic	36	37
Driving significantly slower than traffic	2	4
Impulsivity		
Cut someone off	2	2
Pulled out in front of person	0	1
Following traffic too close, 'tail gating'	4	4
Got angry at traffic	1	2
Inattentiveness		
Distracted by inside: CD/radio, examiner, etc.	7	12
Distracted by outside: traffic, pedestrians, etc.	6	5
Missed turn	4	8
Failed to see signal and ran a red light or stop sign	2	5
Inappropriate hesitation, balking	7	12
Inappropriate or unwarranted braking	2	11
Failed to yield to signals or right of way	1	4
Failed to signal when turning	18	29
Drove across midline	2	5
Drove off road or over curb	3	2

cluded rural, highway, and urban driving, and took approximately 45 minutes. The rater (JWH), who was blind to the medication/no medication condition, sat in the back seat of the subject's car on both drives. He continuously observed the subject's driving performance, noting any errors in driving performance on a standard checklist. Items on this checklist were based on our driving simulation findings.[9,14] Because speed control was not previously affected by stimulant medications using the driving simulator,[9,14] speed control (speeding and driving too slow relative to traffic) were used as a control variable for any placebo effect and were not anticipated to change in this study. The remaining variables were positively affected by stimulant medication and this was anticipated to be the case for this study. Variables were clustered into 2 categories: impulsive and inattentive driving errors (see Table 1).

Results

Driving performance is shown in Table 1. The total number of errors for the driving variables (control variables, impulsive and inattentive variables) is shown for both controlled-release MPH and no medication.

Consistent with our hypothesis, the control variables were not affected by medication ($t = 0.48$, $P = .64$), demonstrating that vehicle speed control during both simulation and on-road evaluations is not affected by stimulant treatment.

Impulsive driving behaviors did not occur frequently: while on medication, none of the subjects pulled out in front of another driver, only 1 subject got angry, and 2 subjects cut off another driver. Although impulsive driving errors were more common off medication, this did not reach statistical significance ($t = 0.48$, $P = .64$).

Inattentive driving errors were in general more common. The mean number of inattentive driving errors on/off medication was 4.6 vs 7.8 ($t = 3.06$, $P = .01$). Performance across the on/off medication conditions correlated + 0.53 ($P < .04$), demonstrating that driving was parallel across conditions. To determine whether there was a medication dose effect while controlling for any practice effects, an inattentive improvement score was calculated by subtracting the total number of inattentive errors during test day 2 from the total number of errors during test day 1. This improvement score was then correlated with medication dosage (milligram per kilogram) during test day 2, where 0 = no medication. Improvement in driving performance (change in number of errors recorded) from the first to the second testing was positively correlated with medication dosage ($r = 0.60$, $P < .01$).

Discussion

Although previous research has demonstrated that MPH improves driving performance on a simulator,[9,14] this is the first study to demonstrate that controlled-release MPH is effective in reducing inattention while adolescent male subjects with ADHD drive their own cars on an actual road segment. Specifically, controlled-release MPH seemed to reduce inattention while driving. Inat-

tention to traffic signals, pedestrians, or other distractions could lead to driving-related accidents and may account for the increased incidence of crashes and violations among ADHD drivers.

Impulsivity while driving was not significantly improved on medication, perhaps because of the very low frequency of impulsive driving behaviors witnessed. This low frequency of impulsive driving behaviors may have been caused in part by having an adult experimenter observing and rating driving performance, which may have discouraged impulsive driving behavior. A more unobtrusive monitoring system may have been more sensitive.

It is interesting to note that the control variables in this study, as observed in the previous simulator driving study,[14] were not affected by treatment with stimulants. This can be interpreted in 2 possible ways: given the high number of speeding errors, either adolescents typically engage in speeding, or alternatively, treatment with MPH does not address issues related to speed control. Because a control group of adolescent male subjects without ADHD was not used, it is unclear whether MPH treatment reduced inattention errors to "within normal limits" or whether speeding or impulsive errors were elevated relative to adolescent male drivers without ADHD.

Further studies are required to determine whether routine treatment of ADHD drivers with an MPH formulation that provides comprehensive coverage would reduce driving-related accidents, associated injuries, and costs. It is reasonable to assume, however, that reducing inattentive errors, such as crossing the midline, merging into oncoming traffic, or failure to respond to traffic signals, could reduce the risk of dangerous driving collisions.

Because this study did included no adolescent female subjects or adults with ADHD with greater driving experience, these findings cannot be generalized to these populations. This study has shown that real-life driving performance is improved in adolescent male subjects with ADHD; in particular, it significantly reduces driving errors arising from inattention. Physicians often have opportunities to encourage patients' safe behaviors.[20] Data suggest that physicians should consider discussing with their ADHD patients the increased risk of driving mishaps associated with ADHD, the potential benefits of MPH, and the need to have MPH pharmacologically active at the time of driving.

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