Clinical Practice Regarding Dopamine-Agonist Use and Driving in Parkinson's Disease

R.M.A. de Bie, J. Miyasaki, A.E. Lang, S.H. Fox

ABSTRACT: *Background:* Current Health Canada instructions for use of the dopamine agonists (DA), pramipexole and ropinirole, state that Parkinson's disease (PD) patients should be told not to drive. The objective was to assess neurologists' actual clinical practice concerning driving advice they give to PD patients starting a DA. *Methods:* An online survey was created consisting of 4 items regarding demographics, 5 regarding PD and driving, and 9 regarding DA use and driving. The survey was distributed to 563 neurologists. *Results:* In total 96 neurologists (17.9%) responded. 4.4% tell patients with PD not to drive, solely because they are taking a DA. Respondents assess the patient's tendency for excessive daytime sleepiness and sleep attacks after starting a DA more frequently than after starting other dopaminergic drugs (p<0.001). *Discussion:* A minor proportion of the clinicians responding to our survey advise PD patients not to drive, solely because they use a DA. Such being the case, we propose that current Health Canada guidelines need revision.

RÉSUMÉ: Les agonistes de la dopamine et la conduite automobile chez les patients atteints de la maladie de Parkinson. Contexte: Les directives de Santé Canada concernant l'utilisation des agonistes de la dopamine (AD), soit le pramipexole et le ropinirole, mentionnent qu'on devrait dire aux patients atteints de la maladie de Parkinson (MP) de ne pas conduire s'ils prennent ces médicaments. Le but de cette étude était de vérifier ce que les neurologues conseillent en clinique à leurs patients atteints de la MP lorsqu'ils commencent à prendre un AD. Méthodes: Nous avons effectué une enquête par courrier électronique dont 4 items portaient sur la démographie, 5 sur la MP et la conduite automobile, et 9 sur l'utilisation d'un AD et la conduite automobile. Le questionnaire a été envoyé à 563 neurologues. Résultats: 96 neurologues ont répondu au questionnaire (17,9%). Parmi eux, 4,4% disent à leurs patients atteints de la MP de ne pas conduire parce qu'ils prennent un AD. Les répondants vérifient plus souvent si les patients ont tendance à présenter une somnolence diurne excessive et des attaques de sommeil lorsqu'ils commencent à prendre un AD plutôt qu'un autre médicament dopaminergique (p < 0,001). Discussion: Une faible proportion des cliniciens qui ont participé à notre enquête prévient leurs patients de ne pas conduire simplement parce qu'ils prennent un AD. Devant cet état de fait, nous suggérons que les lignes directrices actuelles devraient être révisées.

Can. J. Neurol. Sci. 2007; 34: 438-442

Current Health Canada instructions for use of the dopamine agonists (DA), pramipexole and ropinirole, state that Parkinson's disease (PD) patients should be told not to drive. This has clear implications for patients' quality of life. The objective was to assess neurologists' actual clinical practice concerning driving advice they give to PD patients starting a DA.

METHODS

An online survey was created with www.monkeysurvey.com consisting of four items regarding demographics, five regarding PD and driving, and nine regarding DA use and driving. The introductory statement to the questionnaire was as follows: "The questionnaire concerns patients with Parkinson's disease and driving safety. Drive or driving refers to all activities where

From the Movement Disorders Centre, Division of Neurology (RMAdB, JM, AEL, SHF), University of Toronto, Toronto, Ontario, Canada; Department of Neurology, Academic Medical Center (RMAdB), Amsterdam, The Netherlands.

RECEIVED APRIL 16, 2007. ACCEPTED IN FINAL FORM JULY 23, 2007. Reprint requests to: R.M.A. de Bie, Department of Neurology H2-236, Academic Medical Center, PO Box 22660, 1100 DD Amsterdam, The Netherlands. impaired alertness could put people at risk of serious injury or death e.g. operating machines. We are interested in your current practice, rather than what you believe is the correct answer or the legally appropriate thing to do."

The survey was distributed to 530 neurologists by the Canadian Neurological Society (CNS) via letter with directions to the website; 437 of these also received follow-up e-mails. In addition, the Canadian Movement Disorders Group (CMDG) sent an e-mail to 37 members (of whom six were not a member of the CNS). Responses were provided anonymously and to maintain anonymity, it was not recorded whether responders were a member of the CMDG. The survey was distributed between March and June 2006 and responses were collected up to August 2006.

RESULTS

In total 536 neurologists were contacted and 96 (17.9%) responded. Responses came from all provinces and most of the responders work in an urban population-dense area (Tables 1 and 2). Only 4.4% (95% confidence interval 0.3%-8.5%) advise patients with PD not to drive, solely because they are taking a DA (Table 3). Respondents assess the patient's tendency for excessive daytime sleepiness and sleep attacks after starting a

Table 1: Demographic variables of responders

	Number of respondents
Total	96
Population-density area	
Urban	91
Rural	5
Province	
Alberta	18
British Columbia	12
Manitoba	4
Newfoundland and Labrador	4
Nova Scotia	2
Ontario	38
Quebec	16
Saskatchewan	2

Table 2: Answers regarding PD and driving

		Category of practice	2	
	Special interest	University		
	in MD	Hospital	Community	Totals (%)
Number of respondents	27 (28.1%)	41 (42.7%)	28 (29.2%)	96 (100%)
5. Asks if patient actually drives?				
(Almost) all patients	10	17	17	44 (46.8)
Most patients	12	14	8	34 (36.2)
Occasionally	4	6	3	13 (13.8)
(Almost) never	0	3	0	3 (3.2)
6. Evaluates if patients are safe to drive?				
(Almost) every visit	1	3	6	10 (10.6)
Most of the times	15	16	16	47 (50.0)
Occasionally	9	15	5	29 (30.9)
(Almost) never	1	6	1	8 (8.5)
7. Predictor for driving safety?*				
Self report	17	17	17	51 (54.3)
Neurological exam	23	29	23	75 (80.0)
Evaluation of cognitive function	22	33	23	78 (83.0)
None	0	1	0	1 (1.0)
Other	12	12	13	37 (39.4)
9. Estimated percentage of patients who were				
involved in accidents				
5% or less	13	17	16	46 (50.5)
>5% and <25%	3	1	1	5 (5.2)
>25% and <50%	0	0	0	0
>50%	0	0	0	0
I don't know	10	19	11	40 (44.0)

PD Parkinson's disease; MD Movement Disorders; * More than one answer possible.

Table 3: Answers regarding DA use and driving

10. Considers dependency on driving before starting DA (Almost) always Most of the times Occasionally		,		
0. Considers dependency on driving before starting DA (Almost) always Most of the times Occasionally	Special interest in MD	University Hospital	Community	Totals (%)
(Almost) always Most of the times Occasionally				
Most of the times Occasionally	∞	11	10	29 (31.9)
Occasionally	9	12	11	29 (31.9)
	∞	6	5	22 (24.2)
(Almost) never	4	5	2	11 (12.1)
11. Assesses patients tendency for EDS and SA before starting DA*				
Yes, by history taking	16	28	21	65 (72.2)
Yes, with Epworth Sleepiness Scale	2	9	9	14 (15.6)
Yes, with formal sleep studies	0	1	0	1 (1.1)
I do not	7	∞	3	18 (20.0)
12. How often not started DA because it could interfere with driving				
5% or less	19	30	18	67 (74.4)
> 5% and <25%	4	3	9	13 (14.4)
>25% and <50%	2 3	2 0	ω,	7 (7.8)
	0	7	1	3 (3.3)
15. Tells patients trief must not unive solely because trief take DA	_	_	ŗ	2
No.	1 2 4 5	36	26	86 (95 5)
14. Assess patients tendency for EDS and SA after starting DA))	
At each follow-up	15	14	17	46 (51.7)
Once after stable dose, early treatment	8	S	9	14 (15.7)
Occasionally	9	13	2	21 (23.6)
If patients brings up subject	0	1	8	4 (4.5)
Not at all	0	4	0	4 (4.5)
15. How assesses tendency for EDS and SA*	Ç	((6
By history taking	23	3.7	56	81 (91.0)
Epworm Steepiness Scale Formal sleep studies	\ <u>-</u>	y 4	1.1	6 (6.7)
I do not	1 0	+ 4	0	4 (4.5)
16. Estimated percentage of patients using DA that have EDS or SA				`
making driving inappropriate				
5% or less	13	18	18	49 (55.0)
>5% and <25%	11	17	10	38 (42.7)
>25% and <50%	0 (7 0	0 0	2 (2.2)
52U%	0	D	>	-
. Assesses patients tenuency for EDS and SA on outer doparitimetate incurcation. At each follow-in	7	7	٠,	19 (21 3)
Once after stable dose, early treatment	. m	-	, 4	8 (9.0)
Occasionally	12	18	13	43 (48.3)
If patients brings up subject	0	4	4	8 (9.0)
Not at all	2	7	2	11 (12.4)
18. Estimated percentage of patients using any dopaminergic therapy have EDS or SA				
making driving inappropriate	Ç	6	-	į (
3% OI JESS	13	77	19	22 (27.1)
>3% and <50%	v c	CI	A C	2 (2 (2)
>50%	10	0	0	(i: -i) -i 0

DA Dopamine Agonist; MD Movement Disorders; EDS Excessive Daytime Sleepiness; SA Sleep Attacks; * More than one answer possible.

DA3. more frequently than after starting other dopaminergic drugs, including levodopa (Chi-square test p<0.001). Most respondents (91.0%, 83.1%-96.7%) assess the patient's tendency for excessive daytime sleepiness and sleep attacks by history taking; 30.3% (21.1%-39.5%) use the Epworth Sleepiness Scale, 6.7% (1.7%-11.7%) use formal sleep studies and 4.5% (0.3%-8.7%) do not assess this symptom. Fifty-five percent (45.1%-65.1%) of respondents believe that <5% of PD patients using a DA have excessive daytime sleepiness to such an extent that it makes driving inappropriate. There were no differences in responses according to where the neurologist practiced, e.g. clinical practice, province, and population-density.

DISCUSSION

Although our study is limited by a low response rate, it is likely to be biased towards those respondents with a greater interest in PD and driving, indeed 27 out of 96 indicated a special interest in movement disorders. Reasons for the low response rate to our survey could be that the neurologists were wary of giving an opinion or had already made up their mind. It is also very likely that a proportion of the CNS members do not treat PD patients, which would affect the response rate. Another reason could be that, as the survey shows, clinicians do not perceive these side effects as a major problem. Only a small proportion of the clinicians responding to our survey advise patients not to drive, solely because they are taking a DA. This contrasts with the current Therapeutic Products Directorate Canada guidelines stating that PD patients using a DA "should be warned not to drive" based on reports of sudden onset of sleep ("sleep attacks") resulting in motor vehicle accidents.¹⁻⁴ Driving restrictions have clear implications for patients' quality of life.

A number of factors intrinsic to PD might affect driving safety, including motor symptoms, mood disturbances, cognitive impairments, and visual deficits. Nevertheless, general accident rates in PD are low. Ritter and Steinberg found PD patients to be involved in fewer accidents and traffic violation than the general population.

An important aspect of PD and driving safety is that dopaminergic drugs can cause drowsiness and rarely, sudden onset of sleep. 8.9 The use of DA is associated with excessive daytime sleepiness. 10.11 However, the frequency of excessive daytime sleepiness is nearly as high among patients who have never used a DA. 10 The use of dopaminergic drugs in early PD may even improve driving safety in a number of patients because it may improve movement, result in better sleep 12-13 — thus improve alertness during the day — and it may improve cognition. 14-16

In accordance with the above, neurologists assess the patient's tendency for excessive daytime sleepiness and sleep attacks after starting a DA more frequently than after starting other dopaminergic drugs. However, neurologists' approach regarding excessive daytime sleepiness and driving safety in general is varied, including the frequency of assessments.

We advise regular assessment of patients regarding their sleepiness¹¹ and, if indicated, informing drivers to stop driving.¹⁷ Drivers' awareness of their sleepiness while driving is not sufficient to prevent road traffic accidents.¹⁷ Additionally, standardized visual and neuropsychological testing, including spatial perception, visuoconstructional abilities, nonverbal

memory, and executive functioning, provide indices of key functional abilities in PD important for driving.⁵

Overall, our study suggests that advising patients not to drive solely because they have PD and use a DA is too rigid in the opinion of most neurologists, who are caring for these patients. We propose that current Health Canada guidelines need revision in light of neurologists' current clinical practice.

ACKNOWLEDGEMENTS

The authors thank the staff at CNS and Dr. Richard Camicioli (CMDG) for their help with the survey.

REFERENCES

- Moller H. Antiparkinsonian drugs and "sleep attacks." Canadian ADR newsletter. 2001;11:3-4.
- Frucht S, Rogers JD, Greene PE, Gordon MF, Fahn S. Falling asleep at the wheel: motor vehicle mishaps in persons taking pramipexole and ropinirole. Neurology. 1999;52:1908-10.
- Olanow CW, Schapira AHV, Roth T. Falling asleep at the wheel: motor vehicle mishaps in persons taking pramipexole and ropinirole [letter]. Neurology. 2000;54:274.
- Weiner WJ. Falling asleep at the wheel: motor vehicle mishaps in persons taking pramipexole and ropinirole [letter]. Neurology. 2000;54:274-5.
- Uc EY, Rizzo M, Anderson SW, Sparks JD, Rodnitzky RL, Dawson JD. Impaired visual search in drivers with Parkinson's disease. Ann Neurol. 2006;60:407-13.
- Homann CN, Suppan K, Homann B, Crevenna R, Ivanic G, Ruzicka E. Driving in Parkinson's disease – a health hazard? J Neurol. 2003;250:1439-46.
- Ritter G, Steinberg H. Parkinsonism and driving fitness. Munch Med Wochenschr. 1979;121:1329-30.
- Bassi S, Albizzati MG, Frattola L, Passerini D, Trabucchi M. Dopamine receptors and sleep induction in man. J Neurol Neurosurg Psychiatry. 1997;42:458-60.
- Ferreira JJ, Galitzky M, Thalamas C, Tiberge M, Montastruc JL, Sampaio C, et al. Effect of ropinirole on sleep onset: a randomized placebo controlled study in healthy volunteers. Neurology. 2002;58:460-2.
- Gjerstad MD, Alves G, Wentzel-Larsen T, Aarsland D, Larsen JP. Excessive daytime sleepiness in Parkinson disease. Is it the drug or the disease? Neurology. 2006;67:853-8.
- Hobson DE, Lang AE, Martin WRW, Razmy A, Rivest J, Fleming J. Excessive daytime sleepiness and sudden-onset sleep in Parkinson disease. A survey by the Canadian Movement Disorders Group. JAMA. 2002;287:455-63.
- Clarenbach P. Parkinson's disease and sleep. J Neurol. 2000;247(Suppl):20-3.
- Schafer D, Greulich W. Effects of parkinsonian medication on sleep. J Neurol. 2000;247 Suppl:24-7.
- Bowen FP, Kamienny RS, Burns MM, Yahr M. Parkinsonism: effects of levodopa treatment on concept formation. Neurology. 1975;25:701-4.
- Downes JJ, Roberts AC, Sahakian BJ, Evenden JL, Morris RG, Robbins TW. Impaired extra-dimensial shift performance in medicated and unmedicated Parkinson's disease: evidence for a specific attentional dysfunction. Neuropsychologia. 1989;27:1329-43.
- Kulisevsky J, Garcia-Sanchez C, Berthier ML, Barbanoj M, Pascual-Sedano B, Gironell A, et al. Chronic effects of dopaminergic replacement on cognitive function in Parkinson's disease: a two-year follow-up study of previously untreated patients. Mov Disord. 2000;15:613-26.
- Nabi H, Guéguen A, Chiron M, Lafont S, Zins M, Lagarde E. Awareness of driving while sleepy and road traffic accidents: prospective study in GAZEL cohort. BMJ. 2006;333:75-7.

Additional Material Items of the Survey

- 1. To what category do you belong?
- 2. In what population-density area do you work as a neurologist?
- 3. In which province do you work?
- 4. Do you perform medico-legal assessments; work-disability, lawsuits, driving?
- 5. In general, do you ASK patients with Parkinson's disease whether they actually drive?
- 6. In general, do you EVALUATE whether Parkinson's disease patients who actually drive are safe to do so?
- 7. Which of the following do you consider a PREDICTOR for driving safety in patients with Parkinson's disease (more than one answer possible)?
- 8. If in your opinion, driving safety is questionable in a patient with Parkinson's disease who continuous to drive, what action would you undertake?
- 9. How many of your patients with Parkinson's disease who drive have been involved in a traffic accident or caused a traffic accident (to the best of your knowledge)?
- 10. If you consider starting a dopamine agonist, do you take into account whether a patient's quality of life is dependent on his or her ability to drive (e.g. socially, work-related, for household purposes)?
- 11. In general, do you assess the patient's tendency for excessive daytime sleepiness and sleep attacks BEFORE starting the dopamine agonist (more than one answer possible)?

- 12. In a patient who has NO current excessive daytime sleepiness, how often did you decide not to start a dopamine agonist because it could interfere with a patient's ability to drive?
- 13. Do you tell patients that while taking a dopamine agonist they must not drive, SOLELY because they are taking the dopamine agonist?
- 14. Do you assess the patient's tendency for excessive daytime sleepiness and sleep attacks after starting the DOPAMINE AGONIST?
- 15. How do you assess the patient's tendency for excessive daytime sleepiness and sleep attacks mostly (more than one answer possible)?
- 16. What percentage of patients using a DOPAMINE AGONIST do you think have excessive daytime sleepiness due to the dopamine agonist to such an extent that it makes driving inappropriate?
- 17. Do you assess the patient's tendency for excessive daytime sleepiness and sleep attacks after starting treatment with OTHER DOPAMINERGIC MEDICATION (particularly levodopa)?
- 18. What percentage of patients using ANY DOPAMINERGIC THERAPY do you think have excessive daytime sleepiness due to such an extent that it makes driving inappropriate?