Use of OxyContin by adolescent students

Although increases in the nonmedical use of OxyContin (oxycodone) in the United States have been reported recently,[1,2] few data are available to assess whether such use has diffused into general populations in Canada.

In a school survey of 7726 Ontario students in grades 7 to 12,[3] 1.3% of the students (95% confidence interval [CI] 0.9% to 1.7%) reported lifetime use of OxyContin, and 1.0% (95% CI 0.7% to 1.5%) reported use in the past year. Similar to the situation for other illegal drugs,[3] the majority (69%) of past-year users had used the drug only once or twice. Reported use did not vary significantly by sex or grade but did vary by region, with the highest past-year use occurring among students in Northern Ontario (3.3%; 95% CI 1.8% to 6.1%).

To assess whether OxyContin users differ from the users of other illicit drugs, we compared the drug-use profiles of 105 lifetime OxyContin users and 909 users of illicit drugs other than cannabis and OxyContin. The results suggested that OxyContin is merely an addition to the repertoire of drugs used by adolescents. Among 13 illicit drugs examined (e.g., cannabis, heroin, methamphetamine, barbiturates, stimulants, tranquilizers, LSD, phencyclidine [PCP], hallucinogens, cocaine, crack, ecstasy and methylphenidate). OxyContin users were significantly more likely than nonusers to use only 4 of these drugs (heroin, barbiturates, tranquilizers and methylphenidate). This finding raises the spectre of potential polydrug reactions.

Of course, such data are not without limitations. For example, as for other illicit drugs, we would expect some degree of underreporting of OxyContin use. Also, our question was restricted to OxyContin use and thus did not yield information about the use of oxycodone in general and other opioids.

Still, these data, which constitute one of the first reports of OxyContin use within a general Canadian population, allow 2 important observations. First, at this point, there is no evidence of the diffusion of OxyContin into mainstream adolescent populations. Second, our Ontario estimates are lower than the most comparable ones available from the United States. According to US data for 2005,[2] 1.8% of 8th-graders, 3.2% of 10th-graders and 5.5% of 12th-graders reported past-year use of OxyContin; the corresponding data for Ontario students were 0.7% (95% CI 0.3% to 1.6%), 0.7% (95% CI 0.3% to 1.5%) and 1.4% (95% CI 0.7% to 2.7%).

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DOI:10.1503/cmaj.1060037

Questions about Adderall XR

As reported by Wayne Kondro,[1] Health Canada's February 2005 decision to withdraw Adderall XR (a mixture of 4 amphetamine salts marketed by Shire Biochem for the treatment of attention deficit hyperactivity disorders [ADHD]) was reversed in August by a 3-member New Drug Committee. Stronger labelling has been recommended, and sudden death, myocardial infarction, cerebrovascular accident and convulsion will be added to the list of adverse drug reactions.

This situation raises a number of disturbing questions. Given that Adderall XR was approved by Health Canada after deaths and other problems had been reported to the US Food and Drug Administration, it must be asked whether Health Canada had those reports when it approved the drug. If so, why did approval go ahead? If not, why did it apparently take more than a year for Health Canada to acquire the reports? There is a lack of evidence that Adderall XR is clinically superior to other stimulants used to treat ADHD, the New Drug Committee found that higher risks of sudden cardiac death have "not been ruled out due to limitations in the data currently available,"[2] and there is clear evidence of underreporting of serious adverse events. Given these problems, what is the Canadian public to make of the decision to reintroduce Adderall XR?

The reliance on stronger labelling also raises questions. In the United States, stronger labelling for another ADHD drug, pemoline (Cylert), was ineffective in ensuring safe use.[3] In this type of situation, the precautionary principle — had it been heeded — would have provided clear guidance. With no additional health benefits and reasonable suspicion of harm, public health concerns should trump economic interests, yet the New Drug Committee appears to have decided otherwise. To what extent does this reflect the committee's terms of reference and process? The committee met in private and reviewed only data that had been provided by Shire and Health Canada. The committee's mandate appears not to have included issues such as the imprecise diagnosis of ADHD, evidence of overdiagnosis of the condi-

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tion in North America, and whether a net public health benefit was expected from reintroduction of this amphetamine product.

Why are the scientific data that form the basis of regulatory decisions in Canada considered proprietary? The New Drug Committee should have met in public, its reports and transcripts should have been posted on the Web, and other scientists, health care professionals and members of the public should have been allowed to make submissions. The committee's report provides a glimpse of the thinking behind regulatory decision-making. A glimpse is not enough: full participation and access to information are needed.

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Competing interests: None declared.

DOI:10.1503/cmaj.1060004

Questioning the evidence

I am writing about a recent article in the CMA Leadership Series on Elder Care, distributed with the Nov. 8, 2005, issue of *CMAJ*.[1]

As one who has been studying the research and marketing related to Alzheimer's disease (AD) treatments for nearly a decade, I found the article disturbing. The discussion on the benefits of the AD drugs are nearly opposite to what the best evidence says.

The writer states that "In numerous randomized clinical trials (RCTs), cholinesterase inhibitors (ChEIs) have consistently been shown to improve or delay the decline of cognitive functioning, delay the emergence of challenging behaviours and slow the loss of activities of daily living. In RCTs, benefits have been shown to last over a period of up to 2 years, with data from open-label trials suggesting a longer benefit."[1]

However, the company-sponsored trials upon which this statement relies are problematic and overstate the case for the role of these drugs in managing AD. The latest meta-analyses find that the effects of ChEIs are marginal to non-existent.[2]

I found the discussion of side effects almost laughable: "Before initiating treatment, physicians should discuss reasonable expectations with the patient and their caregiver. Patients should be warned of possible side effects, noting that they are often mild and fleeting."[1]

When I have read the monographs of the key AD drugs, the effects such as nausea, vomiting, anorexia and stomach upset are as high as 30%. In fact some commentators have joked that these drugs are more effective as weight-loss pills than altering the rate of cognitive decline. Here is an example of some of the side effects related to an AD drug, rivastigmine (taken from the product monograph):

> Exelon's use is associated with significant gastrointestinal adverse reactions, including nausea and vomiting, anorexia, and weight loss. In the controlled clinical trials, 47% of the patients treated with an Exelon dose in the therapeutic range of 6 to 12 mg/day developed nausea (compared with 12% in placebo). A total of 31% of Exelon-treated patients developed at least one episode of vomiting (compared with 6% for placebo). The rate of vomiting was higher during the titration phase ... than in the maintenance phase ... Five percent of patients discontinued for vomiting, compared to less than 1% for patients on placebo.[3]

I don't know any physician who would dismiss these effects as "mild and fleeting."

I would echo the words of one researcher, Jason Karlawish, who remarked on a flawed study on donepezil with: "Would it be churlish to wonder out loud how this paper is different from an advertisement?"[4] I have to admit I am on the verge of losing a lot of respect for the *CMAJ* unless it stops distributing this kind of clearly biased and non–evidence-based fluff. I cannot see how it is in the best interests of physicians to have such articles published under the banner of *CMAJ*.

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DOI:10.1503/cmaj.1050255

[The author responds:]

Mr. Cassels raises 2 major objections relating to comments I made about the treatment of AD with ChEIs.[1] His first objection refers to the quality of the evidence supporting the use of these medications. The second objection relates to the tolerability of these drugs, specifically, addressing the issue of gastrointestinal side effects.

With regards to the evidence supporting the use of ChEIs, to date there are 22 RCTs with ChEIs published in leading peer-reviewed journals, including the *New England Journal of Medicine*, the *Journal of the American Medical Association*, the *Lancet*, *Neurology* and *JAGS*, that have consistently shown a modest benefit for patients with AD. All these trials were carried out under