"DRUG MAY HAVE CAUSED HUGE NUMBER OF DEATHS": LESSONS LEARNED DURING AN ENCOUNTER WITH *THE FIFTH ESTATE*

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In Brief • En bref

A recent television program raised questions about how the media deal with complex medical issues. In this case, concerns about the safety of nifedipine and other calcium-channel blockers became the subject of an investigative report for a television program, which alleged that many patients were dying because of these drugs. The program prompted numerous calls to family physicians by patients concerned about the safety of their antihypertensive medications. Cardiologist Martin Myers believes the scientific community should respond when it believes reporting on medical and scientific issues has been biased and inaccurate.

Une émission de télévision récente a soulevé des questions sur l'attitude des médias face aux questions médicales complexes. Dans ce cas, les préoccupations soulevées par la sécurité de la nifédipine et d'autres inhibiteurs calciques a fait l'objet d'une enquête pour une émission de télévision au cours de laquelle on a soutenu que ces médicaments entraînaient la mort de nombreux patients. À cause de l'émission, des médecins de famille ont reçu de nombreux appels de patients inquiets au sujet de la sécurité de leurs médicaments hypertenseurs. Le Dr Martin Myers, cardiologue, croit que les milieux scientifiques devraient réagir activement lorsqu'ils sont d'avis que les comptes rendus portant sur des questions médicales et scientifiques sont biaisés et inexacts.

Imagine sitting down to breakfast with the morning paper and reading this headline: "Tens of thousands of patients have died from taking blood-pressure pills — past president of Canadian Hypertension Society not concerned".

Imagine further that you are that past president and that the accompanying story accuses you of participating in a cover-up of these deaths. The article is on the front page and is read by more than one million Canadians. The next day the story disappears completely from the media. Not a single television, radio or newspaper report mentions anything about the drug or the "tens of thousands of deaths."

This Kafkaeque scenario actually occurred to me on Feb. 27, 1996. The only difference was that the story appeared on a CBC public-affairs program, *the fifth estate*, and not in a morning newspaper.

Academic physicians working in high-profile specialities are frequently contacted by the media to comment on new research or controversial subjects of public interest. I have received hundreds of such requests over the last 20 years on topics such as hypertension, caffeine and treatments for heart disease. The content of most interviews is generally transcribed accurately into newspaper articles or other media reports. Exceptions occur, but these are invariably minor and often unintentional on the part of the writer or commentator. However, my past media encounters could never have prepared even the most experienced academic specialist for events such as the Feb. 27 edition of *the fifth estate*.

BASIS FOR PERCEIVED CONFLICT OF INTEREST

The story began in December 1994. I was asked by Bayer Inc. (formerly Miles Canada Inc.) to attend a meeting of the Health Protection Branch (HPB) in Ottawa to clarify a sentence in the product monograph for a new formulation of a commonly prescribed antihypertensive medication, nifedipine. During earlier discussions, the pharmaceutical company and the head of the cardiovascular section at the HPB, Dr. Tomasz Uscinowicz, agreed that I should assist in the deliberations, since I had been the principal investigator of the research study upon which the sentence in the product

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monograph was based. The meeting was over in less than 10 minutes, and the outcome was that the conversion of Adalat-PA to Adalat-XL was to be done this way: "Patients switched from Adalat-PA 10 or 20 mg to Adalat-XL should receive an initial dose of Adalat-XL 30 mg once daily. If clinically warranted, the dosage should be increased to 60 mg once daily. Blood pressure and patient symptoms should be monitored closely."

Nine months later, in September 1995, I received a letter from Dr. Vincent Krupa of the HPB, who invited me to participate in an ad hoc advisory committee on "the safety of calcium-channel blockers in the treatment of hypertension and heart disease." I agreed to participate and to attend a Sept. 18 meeting in Ottawa to review the existing literature on calcium-channel blockers and advise the HPB of any concerns regarding the use or safety of these drugs in clinical practice.

I had been chair of the Canadian Hypertension Society Consensus Conference on the Treatment of Hypertension in 1988, which first recommended the use of ß-blockers and diuretics as initial therapy for patients with uncomplicated essential hypertension.[1] Calcium-channel blockers and angiotensin converting enzyme inhibitors were designated as second-line therapy in these recommendations. I was also a member of the 1992 Canadian Hypertension Society committee that reaffirmed the 1988 recommendations.[2] I was also known as an advocate of the use of diuretics and ß-blockers as first-line therapy because of their proven beneficial effects in reducing morbidity and mortality. The rationale for this approach was the subject of an editorial I wrote for *CMAJ* in 1990.[3] I had also published studies raising concerns about the nifedipine capsule in patients with unstable angina as far back as 1988[4] and had conducted several research studies on the different dihydropyridine calcium antagonists currently available in Canada.[5-8]

The meeting of the advisory committee

The four-member Cardiovascular Advisory Committee met with representatives of the HPB in Ottawa on Sept. 18. The chair made it clear that any recommendations would be based upon scientific evidence, not opinion. During the 4-hour meeting all aspects of calcium-channel-blocker use in hypertension and coronary heart disease were discussed, including the recent publications of Drs. Psaty [9] and Furberg,[10] which had sparked controversy earlier in the year.

From a safety perspective, the committee did not believe that Dr. Psaty's case-control study or Dr. Furberg's meta-analysis provided sufficient evidence to withdraw any product from the market, including the nifedipine capsule. The committee did recommend that the HPB encourage Canadian physicians to use the longer-acting calcium-channel blockers because they possess superior pharmacokinetic and pharmacodynamic properties, have fewer side effects and promote better compliance with therapy. Overall, there was general agreement that Canadian physicians should treat hypertension in accordance with the guidelines of the Canadian Hypertension Society,[1,2] with diuretics and ß-blockers used as first-line therapy.

In the absence of existing guidelines for the treatment of coronary heart disease, ß-blockers were preferred, although diltiazem and verapamil were suggested as supplementary or alternate therapies based upon evidence from studies performed in postmyocardial-infarction patients, which showed that these agents provided benefit if left ventricular function was not impaired.[11,12]

At the end of October, the committee submitted its final recommendations to the HPB. Three months later, on Jan. 23, 1996, the HPB mailed a letter to all physicians in Canada that outlined the controversy surrounding calcium-channel blockers and made a series of recommendations for their use in patients with hypertension and heart disease. The advisory committee did not see the final letter before its distribution to physicians.

Background to the fifth estate program

Meanwhile, *the fifth estate* had been alerted to a potential "cover-up" at the HPB concerning nifedipine. In early December, I was asked to give an interview on the scientific issues surrounding the calcium-channel-blocker controversy, based upon the recent papers by Drs. Furberg and Psaty. I provided the CBC researcher with copies of the Canadian Hypertension Society Consensus Conference reports and other related articles that described Canadian recommendations for treating hypertension and my involvement in advocating them.

My interview took place Dec. 12, 1995. Although the visit was to have lasted 1 hour, the television crew stayed for almost 4 hours, with more than 1 hour of on-camera interview time. The interviewer, Trish Wood, was aggressive. Numerous issues were raised, but I confined my comments to the scientific issues and the Canadian recommendations. The HPB was not mentioned during the interview. At the conclusion, although not pleased with the intensity of the interrogation, I was satisfied that I had presented a balanced view of the subject and the Canadian perspective.

Over the next few weeks, it became apparent that *the fifth estate* was interested in more than just issues related to the use of calcium-channel blockers in the treatment of hyper-

tension or coronary heart disease. In late January I was asked to complete a second interview. I refused because I had already spent a half-day answering all reasonable questions.

THE PROGRAM AIRS

Feb. 27 arrived, and *the fifth estate* was on the air. In her introduction, Trish Wood told viewers about a medication for high blood pressure, nifedipine, "taken every day in this country by hundreds of thousands of people" which "may have caused a huge number of deaths." This statement was followed by a comment from Dr. Michelle Brill-Edwards, who according to the program had been a drug reviewer at the HPB when short-acting nifedipine had been approved for the treatment of angina. She said "the numbers [of deaths] involved are off the scale. . . . We're talking here thousands, tens of thousands, maybe more than that worldwide certainly."

Subsequently, Dr. Curt Furberg was interviewed in North Carolina, and stated that "we're probably talking tens of thousands of patients" dying as a result of taking these pills (short-acting nifedipine). Dr. Salim Yusuf from Hamilton was interviewed next. He generally supported Dr. Furberg's position and described how he had attempted to alert people about potential harm from nifedipine as far back as 1989.

Excerpts from my 1-hour interview appeared twice during the program. In one clip I said that there was some circumstantial evidence that nifedipine capsule may be harmful, but that there is no evidence whatsoever that the longer-acting drugs are harmful (referring to amlodipine and felodipine, as well as nifedipine-XL). Later on, I described the pharmacologic differences between the nifedipine capsule and nifedipine-XL. Another Canadian expert then commented on the two formulations, dismissing any difference between the nifedipine capsule and nifedipine-XL by equating nifedipine with a skunk — the implication was that it smells no matter how it is formulated. The "scientific discussion" about the nifedipine capsule versus XL was now over.

Wood then interviewed Dr. Agnes Klein, acting director of the HPB's Bureau of Human Prescription Drugs; conflict of interest on the advisory committee was the focus of that intense cross-examination. Dr. Brill-Edwards' story concluded the program. The reviewer explored her sacrifice in making her concerns about nifedipine public and how it has resulted in the loss of her job.

WHAT THE PROGRAM LEFT OUT

It is beyond the scope of this article to recite in full the contents of the 50-minute program. However, it is worth noting what *the fifth estate* chose not to reveal.

The program made it appear that the HPB, assisted by its medical advisory committee, had covered up a major scandal involving tens of thousands of deaths. The program did not tell the viewer that the Food and Drug Administration (FDA) in Washington had convened an open hearing on Jan. 25, 1996, to listen to different viewpoints on the calcium-channel-blocker debate. The FDA concluded that the long-acting calcium-channel blockers are safe and should continue to be used in accordance with their product monographs. Concerned about "off-label" uses of the nifedipine capsule, the FDA emphasized that it should be restricted to the specific indications in the original product monograph and should not be used for other conditions such as unstable angina, postmyocardial infarction or hypertension.

The program never told its viewers exactly what the letter from the HPB recommended to Canadian physicians — that calcium-channel blockers not be used as primary therapy for hypertension or heart disease and that the Canadian Hypertension Society's guidelines for treating hypertension should be followed. The letter also listed calcium-channel blockers as third-line therapy for coronary heart disease after ß-blockers and long-acting nitrates, hardly a positive recommendation for nifedipine.

The fifth estate never stated my position on-air about the use of calcium-channel blockers in hypertension, even though there was considerable footage on the subject. They chose not to mention the guidelines of the Canadian Hypertension Society or my role in their creation. *The fifth estate* knew all sides of the calcium-channel-blocker story several weeks before the program was aired and yet chose to omit anything that would have detracted from a sensational story.

Even though the program was totally ignored by other media, Canadian physicians were flooded with telephone calls from anxious patients who had taken its contents seriously and were concerned about the "tens of thousands of deaths" being caused by nifedipine and possibly other calcium-channel blockers. After all, this was the CBC speaking.

It must be true.

MEDICINE AS ENTERTAINMENT

What is the role of the media in dealing with complex medical issues? Should television programs be allowed to create fear and anxiety among patients? Should a publicly funded network be involved in such activities? Should public affairs be portrayed as entertainment, with science and drama interwoven? How do tearful emotions measure up against data from randomized, placebo-controlled clinical trials? When should pharmaceutical prod-

ucts be compared with a skunk? How can practising physicians protect their patients against biased reporting in the media, especially if it is tacitly sanctioned by its appearance on a government-funded network?

Finally, why should academic physicians agree to speak with reporters or appear on television or radio and risk a repetition of my experience with *the fifth estate*? Previously, it seemed to be the right thing to do: it was a public service. Are we now seeing a shift from the ethical reporting of medical issues to sensationalism? Is medicine becoming another form of mass entertainment, with physicians serving as actors in million-dollar productions?

I believe there is good reason to be concerned about these developments. In this instance, *the fifth estate* clearly benefited from its 50-minute foray into the medical field. At least one million Canadians saw the program and "the hundreds of thousands" of patients throughout the country receiving calcium-channel blockers must still be thinking about the dire mortality statistics.

The *fifth estate*'s attempt at medical coverage may have been good for television ratings, but it could have a serious and deleterious impact on the care of hypertensive patients and their willingness to accept medical therapy.

In this instance, the program provoked little response from the medical media. In future, the scientific community must take a more prominent role in responding to this type of reporting so that our patients are not left anxious, confused and disillusioned when confronted with medical issues that are presented as entertainment.

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