Adverse reporting on adverse reactions

Namrata Bains, MSc; Duncan Hunter, PhD

Is there an epidemic of deaths in Canadian hospitals arising from adverse drug reactions? A recent meta-analysis undertaken by researchers at the University of Toronto and published in the *Journal of the American Medical Association* estimated the number of deaths caused by adverse drug reactions in hospital patients.[1] The investigators were quoted in the *Globe and Mail* as saying that the results could be extrapolated to Canada "with very little danger" and that about 10 000 deaths occur in Canada each year as a result of adverse drug reactions.[2]

We examined hospital separation and mortality data for the province of Ontario to estimate the in-hospital mortality associated with adverse drug reactions. The most recent available hospital separation data, i.e., for the fiscal years 1992/93 to 1996/97, were used. These data are processed by the Canadian Institute for Health Information and are maintained by the Ontario Ministry of Health Provincial Health Planning Data Base. "Drugs Medicaments and Biological Substances Causing Adverse Effects in Therapeutic Use" are assigned a supplementary code (E-code 930-949) on a patient's hospital record.[3] Admissions to hospital for patients who live outside of the province and for those whose place of residence was unknown were excluded from the analysis.

Of the 6.6 million discharges from Ontario hospitals between 1992/93 and 1996/97, we identified an average of 16 344 hospital admissions per year in which an adverse drug reaction was recorded. In other words, adverse drug reactions were recorded in approximately 1.2% of hospital admissions over this period. Each year, on average, 680 (4.2%) of the persons who experienced an adverse drug reaction died in hospital. We calculated the overall incidence of in-hospital mortality associated with adverse drug reactions to be 0.05%. Assuming that rates in other provinces are similar to those observed in Ontario, we estimate that approximately 1824 deaths annually could be attributed to adverse drug reactions in Canada; this is substantially lower than the estimate of 10 000 deaths per year cited in the *Globe and Mail*

We also compared our mortality estimates with data on the leading causes of death published in annual reports by Statistics Canada.[4–7] The average number of deaths per year between 1992 and 1995 (the most recent years for which data were available) was 76 256 (305 025 deaths of Ontario residents over the 4-year period). If we assume that fatal adverse drug reactions contributed to less than 1% of these, then mortality associated with adverse drug reactions would be ranked approximately 19th on the list. This is far below causes such as ischemic heart disease, cerebrovascular disease, lung cancer, pneumonia and diabetes and, contrary to what Lazarou and colleagues suggest,[1] is certainly not among the top 4 to 6 leading causes.

Although this preliminary look at the data is likely to contain biases that affect the precision of our estimates, many of these are shared by the studies that contributed to the original meta-analysis. Our results are based on an extrapolation of Ontario data to all of Canada, but rates of adverse drug reactions in Ontario hospitals may be different from those in other provinces and the territories. We were unable to distinguish between adverse reactions that occurred because of drugs administered *in* hospital, and those that *resulted* in hospital admission. Although we were able to estimate the number of patients who experienced an adverse drug reaction and who also died, we could not establish whether the drug reaction actually caused their death. In addition, it is possible that some adverse drug reactions were not recognized and thus not recorded. Furthermore, our estimates are higher than those based on data collected by the Canadian Adverse Drug Reaction Monitoring Program,[8] a voluntary reporting system operated by the Health Protection Branch of Health Canada. In a study that examined data from this program for the years 1984 to 1994, the investigators found only 1417 cases of drug-related deaths over the 10-year period. Given the voluntary nature of the reporting system, the extent of underreporting (and hence the actual incidence) is impossible to determine. Only reabstraction studies in which the original patient history is reviewed in detail would determine the extent and direction of bias in our estimates.

So who has got it right? The truth probably lies somewhere in the middle. On the one hand, we believe that the results of the meta-analysis substantially overestimate the number of deaths that can be attributed to adverse drug reactions and that it is inappropriate to speculate on the basis of these data about the extent of the problem in Canada. On the other hand, it is possible that some deaths do result from adverse drug reactions, and we congratu-

late the authors for having drawn attention to this issue. Future research should rely not on meta-analyses of a small number of dated studies, but on careful analyses of routinely collected hospital separation data by researchers who are experienced in using administrative data, combined with detailed re-abstraction studies supplemented with expert clinical opinion.

Ms. Bains is a Research Associate with the Health Information Partnership, Eastern Ontario Region, Kingston, Ont. Dr. Hunter is Director of the Health Information Partnership and an Assistant Professor with the Department of Community Health and Epidemiology, Queen's University, Kingston, Ont., and the Department of Epidemiology and Community Medicine, University of Ottawa, Ottawa, Ont.

The Health Information Partnership is funded by the Ontario Ministry of Health. The views expressed in this article are the authors' and do not necessarily reflect the position of the Ministry.

Competing interests: None declared.

References

1. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *JAMA* 1998;279 (15):1200-5.
2. Abraham C, Taylor P. Drug reactions kill thousands: researchers. *Globe and Mail* [Toronto] 1998;Apr 15:A3.
3. World Health Organization. *Manual of the international statistical classification of diseases, injuries, and causes of death*. Geneva: WHO; 1977.
4. Statistics Canada. *Mortality—summary list of causes, 1992*. Ottawa: Minister of Industry, Science and Technology; 1993.
5. Statistics Canada. *Mortality—summary list of causes, 1993*. Ottawa: Minister of Industry, Science and Technology; 1994.
6. Statistics Canada. *Mortality—summary list of causes, 1994*. Ottawa: Minister of Industry, Science and Technology; 1995.
7. Statistics Canada. *Mortality—summary list of causes, 1995*. Ottawa: Minister of Industry, Science and Technology; 1996.
8. Mittman, Liu BA, Iskedjian M, Bradley CA, Pless R, Shear NH, et al. Drug-related mortality in Canada (1984–1994). *Pharmaco Drug Saf* 1997;6:157-68.

Reprint requests to: *Ms. Namrata Bains, 221 Portsmouth Rd., Kingston ON K7M 1V5*

Discussing complementary therapies: There's more than efficacy to consider

Tracy Truant, RN, MSN; Michael McKenzie, MD

? See related article page 365

In this issue (page 365) Dr. Neill A. Iscoe and colleagues identify evidence of efficacy, questions of cost and the potential for toxicity as important factors for physicians to discuss with cancer patients who are considering the use of complementary therapies.[1] Dr. Elizabeth Kaegi's decision-making tool for patients, published in *CMAJ* last year, conveyed much of the same information and stimulated a heated debate in the journal.[2–4] No matter what position they take on the issue, it is likely that most physicians would concur with Iscoe and colleagues' statement that "Whatever transpires, the physician should continue to provide support and comfort to the patient and his family through this difficult time." The ability to provide that support and comfort depends on an understanding of the patient's perspective, not least with respect to complementary therapies.

Research on patients' decisions about complementary therapies is still in its infancy, and such research involving patients with prostate cancer has yet to be done. What we know so far comes from qualitative studies involving patients with other types of cancer; these have shown that such decision-making is complex and is influenced by many factors, of which physicians need to be aware. One of us (TT) conducted a study in which 16 women with breast cancer, at varying points along the disease trajectory and from various cultural backgrounds, were interviewed to determine how they made decisions about using complementary therapies. Qualitative analysis of their accounts revealed a dynamic three-phase process of decision-making that was closely linked with the trajectory of their illness. This and other studies have shown that, rather than being based solely on statistical data about treatment outcomes, decisions about both complementary and conventional therapies often reflect lifestyle preferences as well as beliefs about health and illness.[5–7] Other factors that influence decisions include the quality of the relationship with the health care provider as well as the patient's preferred role in making decisions, desire for control, physical status and degree of fatigue, prospects for cure and the need to sustain hope.[5,8–12]