LETTERS TO THE EDITOR

Fellowship in Medical Editing

The Section of Scientific Publications of the Mayo Foundation for Medical Education and Research is initiating a 1-year fellowship in medical editing and publishing beginning July 1, 2004, in Rochester, Minnesota. The Foundation publishes the monthly Mayo Clinic Proceedings and a variety of other publications. The fellow will receive hands-on training and orientation in all aspects of medical editing and publishing. This fellowship is open to candidates holding a PharmD degree, as well as those with medical degrees.

Unfortunately, the deadline for applications for this inaugural year has just passed. However, interested Canadian candidates may wish to keep this fellowship in mind for next year. The contact person is Rosemary Perry, Section of Scientific Publications, Mayo Foundation, 200 First Street SW, Rochester MN 55905.

This is a unique opportunity for those interested in a full-time or part-time career in health care writing and editing. As far as I know, the only other journal that offers this type of fellowship is the Lancet, but I’m uncertain whether the latter is open to candidates with a pharmacy education.

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Quinolone Hyperglycemia and Hypoglycemia

In their article about hypoglycemia and hyperglycemia associated with marketed fluoroquinolones, Sandra Tailor and others’ state that the number of case reports of hypoglycemia, hyperglycemia, or both was significantly higher for gatifloxacin than for either levofloxacin or moxifloxacin, noting that this may identify a safety signal for gatifloxacin. While this conclusion may indeed be valid, the data from the Canadian Adverse Drug Reaction Monitoring Program (CADRMP), a spontaneous surveillance system through which adverse reactions to health products are voluntarily reported, must be interpreted with caution. As stated on the Web site for the Canadian Adverse Drug Reaction Information System (CADRIS), the data in the CADRIS database should not be used as the basis for numeric comparisons of reactions associated with different health products, since neither the total number of reactions occurring nor the number of patients exposed to the health product is known.

The issue of exposure is important. For example, if gatifloxacin is used more frequently than either levofloxacin or moxifloxacin, there may be an increased likelihood of seeing adverse reactions with this drug. I contacted the manufacturers of each of the 3 respiratory fluoroquinolones compared in the study by Tailor and others’ to obtain information on drug usage trends, but the information available from each company was not directly comparable.

In addition, although Health Canada records the occurrence of adverse drug reactions reported by health care professionals, the number of patients exposed to the health products, since neither the total number of reactions nor the number of patients exposed to the health product is known. Adverse drug reactions with this drug. I contacted the manufacturers of each of the 3 respiratory fluoroquinolones compared in the study by Tailor and others’ to obtain information on drug usage trends, but the information available from each company was not directly comparable.

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References

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The authors respond:

We thank Zahra Kanji for her comments further highlighting our own acknowledgment of the limitations of the CADRMP reports. We agree, and stated in our paper, that no conclusions can be drawn from these reports regarding differences in overall incidence or prevalence of hypoglycemia or hyperglycemia with the various respiratory fluoroquinolones. However, identifying a signal requires some means of quantification, such as our analysis, and we hope that our findings will provide an impetus for further evaluation of the possibility that the incidence of hypoglycemia or hyperglycemia is greater with gatifloxacin than with levofloxacin or moxifloxacin. The recent review of CADRMP reports by Letourneau and others agrees with our observations.

We agree with Kanji that the issue of exposure is important, as we acknowledged in our paper, but this importance lies in identifying prevalence and causality, not in identifying a safety signal. Levofloxacin has been on the market in Canada since 1998, whereas gatifloxacin was first marketed here in 2001. Kanji’s supposition that gatifloxacin may have been used more frequently than levofloxacin during the period of our analysis (2 years for gatifloxacin and 5 years for levofloxacin) is extremely unlikely. In fact, the IMS database, which reflects national volumes of retail pharmacy prescriptions, indicates exactly the reverse: in every month from May 1998 through December 2002 (approximately the same as the 5-year period for which we analyzed spontaneous adverse reaction reports for levofloxacin), levofloxacin (Levaquin) and moxifloxacin (Avelox) were both prescribed more frequently than gatifloxacin (Tequin) (Figure 1, panel A). The significantly greater number of spontaneous reports of hypoglycemia or hyperglycemia for gatifloxacin, which had a total prescription use approximately one-tenth that of levofloxacin and one-third that of moxifloxacin (Figure 1, panel B), further highlights the importance of the gatifloxacin safety signal.

Although there may be a reporting bias for spontaneous adverse reaction reports for hospital patients, the more intense monitoring in the hospital environment provides the ability to detect adverse reactions with low overall frequency. This does not make the observation of hypoglycemia or hyperglycemia any less significant and should serve to heighten the awareness among community practitioners of the need to monitor patients for this reaction. As pointed out by Letourneau and others, 90% of CADRMP case reports from February 2001 to February 2003 were for patients with type 2 diabetes, which agrees with our findings. Therefore, Kanji’s suggestion that changes in blood glucose levels documented in the CADRMP reports might be due to more intensive monitoring of nondiabetic patients is not valid. Furthermore, the gatifloxacin product monograph suggests, on the basis of surveillance of 15,000 patients, that the incidence of hypoglycemia or hyperglycemia is higher among those with diabetes. Kanji also comments that changes in blood glucose levels might occur because of the infection. However, hyperglycemia due to infection is usually seen early in the course of the infection, before patients have a clinical response to antibiotic therapy. In contrast, the gatifloxacin product monograph indicates that gatifloxacin-induced hypoglycemia tends to occur early in treatment (initial 1 to 3 days), whereas hyperglycemia occurs late in treatment (4 to 10 days after initiation). The early occurrence of hyperglycemia related to infection and the later occurrence of hyperglycemia associated with gatifloxacin makes it less likely that the reports of hyperglycemia found in the CADRMP were due to infection. Similarly, hypoglycemia may be seen in the setting of severe septic shock. However, a review of the concomitant medications for patients described in the CADRMP reports that we reviewed indicated that the patients with hypoglycemia were not in septic shock.

We agree with Kanji that spontaneous reporting of adverse drug reactions to the CADRMP is extremely important, especially given that surveillance of thousands of patients is necessary to detect adverse reactions that occur only rarely (i.e., in less than 1% of patients). In fact, this form of reporting may be one of the few ways of tracking these reactions. Although it is not yet known whether the risk of hypoglycemia or hyperglycemia is higher with gatifloxacin than with levofloxacin or moxifloxacin, the published literature and the CADRMP reports indicate a safety signal for hypoglycemia or hyperglycemia in association with gatifloxacin. In contrast, our review of the literature and 2 independent analyses of...
CADRMP spontaneous reports\textsuperscript{1,2} did not identify such a signal for either levofloxacin or moxifloxacin. Only with continued surveillance, reporting, and evaluation of these adverse reactions by health care workers and pharmaceutical companies will the question of a potential difference among the fluoroquinolones in terms of the risk of hypoglycemia and hyperglycemia be answered.

References

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Canadian Society of Hospital Pharmacists
Société canadienne des pharmaciens d’hôpitaux

2004/2005 Membership Renewal

The Executive, Council, and staff of the Canadian Society of Hospital Pharmacists are pleased to invite you to renew your membership for the 2004/2005 year. As we work toward our Vision 2006 — “A revitalized Society; The influential voice for hospital pharmacy; Inspiring and supporting our members” — please consider renewing your membership for 2004/2005. Together we can continue to build an association and a profession that are bold leaders in our industry.