New drugs

Should we prescribe them now or should we wait and see?

Roger Ladouceur, MD, FCFP

Even though a range of drugs are already on the market, new drugs are appearing in unprecedented numbers. All this is very confusing for family physicians who want to stay abreast of advances in medical practice.

For hypertension alone, there are 62 drugs and drug combinations, many of which have just been brought to market.[1] Over the next few years, how many other agents for osteoporosis, dyslipidemia, and migraine will be added to the already weighty *Compendium of Pharmaceuticals and Specialties*? How many more cyclooxygenase-2 (COX-2) inhibitors and angiotensin II AT 1 receptor antagonists will emerge?

While many of these new drugs resemble products already on the market, physicians are often faced with the option of prescribing a drug from an entirely new therapeutic class. This is what happened with fluoxetine chlorhydrate (eg, Prozac®), the first selective serotonin reuptake inhibitor, and omeprazole (Losec®), the first proton pump inhibitor. Today, these drugs are widely used, but this was not always so. Prescribing a drug when everyone else is prescribing it is easy; being the first or the only physician to prescribe it is another matter.

This raises the question: As family physicians, should we be among the first to prescribe new drugs? Despite the fact that all drugs go through rigorous testing before approval, some are subsequently withdrawn from the market because of very serious side effects. Four well-known examples are cisapride monohydrate (Prepulsid®),[2] a drug widely prescribed for digestive motility; dexfenfluramine (Redux®),[3] a well-known obesity drug; trovafloxacin (Trovan®),[4,5] a new antibiotic in the quinolone family; and very recently cerivastatine (Baycol®) for lowering cholesterol. So why would family physicians risk prescribing a brand-new drug that could be found to be dangerous a few years down the road? There are many factors at work.

Promotion

First, there is promotion. When a pharmaceutical company markets a new drug, it launches a multifaceted promotional campaign. The campaign uses traditional approaches, such as advertisements in medical journals, visits by pharmaceutical representatives, and booths at events, to extol the virtues of the new product. It also uses much more subtle approaches, such as publication of symposium proceedings, sponsorship of banquets and lectures, and educational workshops developed in cooperation with universities or professional associations. These workshops recruit leaders in the medical community and work down the pyramid to reach the greatest possible number of doctors through continuing medical education networks. It is a well-known fact that these training activities tend to promote use of new products.[6-8]

In addition, drug companies use market introduction tactics, even though they deny doing so. Both doctors and patients wait anxiously for new drugs, even before they are assigned an identification number and approved for sale. Health Canada is criticized for taking so long to approve them. We all knew what a miracle drug sildenafil (Viagra) would be, well before we could prescribe it. It is unsurprising that, as soon as it was on the market, we prescribed so much of it and so quickly. It is very difficult for family physicians not to be influenced by so many messages and not to prescribe a new drug when everyone is talking about it.[9]

Societal influences

We live in a world that puts great faith in science and technology. Most people believe it is just a matter of time before a cure for cancer or AIDS is discovered. As soon as there is a glimmer of hope, the media jump on the story. Newspaper headlines, such as *Le grand livre de la vie dévoilé* ("The great book of life unlocked") and *Vers une médecine personnalisée* ("Made-to-measure medicine")[10,11] about the human genome, or *Un nouveau traitement pour le cancer du pancréas* ("New treatment for pancreatic cancer")[12] appear regularly, leading us to believe that the secret to eternal life is about to be unveiled.

These "discoveries" are often gleaned from research papers presented at international conferences. Even though this research is often in the preliminary stages, communications agencies, usually hired by the same companies that fund research, release these messages of hope to the media for distribution to the general public. It is unsurprising, then, that our patients with metastatic lung cancer or amyotrophic lateral sclerosis or multiple sclerosis cannot understand why we do not have a cure, a vaccine, or another treatment to offer them. They start surfing the World Wide Web in search of a miracle cure. The media have raised their hopes so cruelly.

Publication bias

Are advertising claims and society's expectations justification enough for a family physician to prescribe a new drug? Definitely not. Before prescribing any new substance, physicians must determine its efficacy, safety, and advantages over other drugs already available. The best way to do this is to read the medical literature and review the clinical evidence. And yet, contrary to what the proponents of evidence-based medicine would have us believe, it is difficult to put one's trust in the literature because many data are biased or inaccessible.

The medical literature has a well-known tendency toward what is called publication bias,[13,14] favouring publication of studies with positive findings over studies that have not yielded significant results. Mahoney's study[15] illustrates this point very well; in it, peer reviewers of a medical journal are asked to review manuscripts similar in all regards except for the results and the discussion, which have been changed to make the findings either positive or negative. What the study showed was that the reviewers gave unfavourable scores to the methodology, presentation of data, scientific contribution, and publishability of papers whose findings were negative. In other words, a physician consulting the literature is more likely to find studies favourable to a new medication because studies that do not have significant findings simply are not published.

Similarly, drug companies publicize studies that show the benefits of their product; we would not expect them to do otherwise! On the other hand, blocking access to data critical to assessment of a new drug is unacceptable. And yet, this is common practice in the pharmaceutical industry. Doctors who want to make their own assessments of a new drug and consult the product monograph will find that certain references are marked "data in file." These data are, in fact, inaccessible. They are not to be found in any publication or database, and the drug company reserves the right not to disclose them to doctors.

Basically, the decision to prescribe a new drug depends on three factors: the severity of the illness, the patient's informed wishes, and the doctor's expertise. Prescribing a new drug is appropriate when you have the necessary expertise and are prescribing for a seriously or incurably ill patient who, after learning about the potential advantages and disadvantages of the new drug, still wants it. In every other instance, wait and see.

Dr Ladouceur *practises in the Clinique de médecine familiale at the Centre Hospitalier de Verdun in Quebec.*

Correspondence to: *Dr Roger Ladouceur, Clinique de médecine familiale, Centre Hospitalier de Verdun, Verdun, QC H4G 2A3*

References

1. Société québécoise d'hypertension artérielle. *Guide thérapeutique*. Québec, Qué: Société québécoise d'hypertension artérielle; 1999. p. 117-8.
2. Health Canada, Health Protection Branch. *Letter to health professionals*. Ottawa, Ont: Health Canada; 2000.
3. Health Canada, Health Protection Branch. *Interdiction de vente.* Ottawa, Ont: Health Canada; 15 Septembre 1997.
4. World Health Organization, Information exchange system. *Alert No. 86. Trovafloxacin and alatrofloxacin: suspension and warning: hepatotoxicity.* Geneva, Switz: World Health Organization; 1999.
5. Pfizer. Important information on the safety of Trovan® in tablet form (trovafloxacin mesylate) and Trovan® IV (injectable alatrofloxacin mesylate). In: *Letter to Canadian health professionals*. Kirkland, Que: Pfizer; 1999.
6. Bero LA, Galbraith A, Rennie D. The publication of sponsored symposiums in medical journals. *N Engl J Med* 1992;327:1135-40.
7. Rochon PA, Gurwitz JH, Simms RW, Fortin PR, Felson DT, Minaker KL, et al. A study of manufacturer-supported trials of nonsteroidal anti-inflammatory drugs in the treatment of arthritis. *Arch Intern Med* 1994;272:101-4.
8. Cho KC, Bero LA. The quality of drug studies published in symposium proceedings. *Ann Intern Med* 1996;124:485-9.
9. Avorn J, Chen M, Hartley R. Scientific versus commercial sources of influence on the prescribing behavior of physicians. *Am J Med* 1982;73:4-8.
10. Castelnau B, Agence France-Presse. Le grand livre de la vie dévoilé. *La Presse* 2001 Feb 12:A1.
11. Hachey I. Vers une médecine personnalisée. *La Presse* 2001 Feb 13:A1.
12. Lévesque L, La Presse Canadienne. Un nouveau traitement pour le cancer du pancréas. *La Presse* 1998 Mar 16:A7.
13. Smith ML. Publication bias and meta-analysis. *Eval Educ* 1980;4:22-4.
14. Dickersin K. The existence of publication bias and risk factors for its occurrence. *JAMA* 1990;263(10):1385-9.
15. Mahoney MJ. Publication prejudices: an experimental study of confirmatory bias in the peer review system. *Cog Ther Res* 1977;1:161-75.