Tertiary research applied to primary care

I was intrigued by Dr Ogle’s1 inference that, since our first duty is to our patients, participating in clinical research in practice is somehow abusing them. I completely agree that our first duty is to our patients, but I believe it is unethical to continue to treat them with outdated therapies or to use treatments without evidence of their effectiveness.

We are aware that treatments derived for purified populations in quaternary teaching hospitals are often inadequate, inappropriate, or simply ineffective for our patients in family practice. This might be because our patients have more than one condition at the same time or are just at an earlier, poorly-defined, stage of the disease. I believe we have an ethical duty to take part in clinical trials of the effectiveness (not efficacy) of new medications thrust upon primary care without any testing there.2

The extrapolation of benefit from the specialized, highly controlled hospital clinical trial to primary care practice is often not justified.

Some pharmaceutical companies are aware of this and more are recruiting family practitioners into studies. Admittedly, some of these studies are undoubtedly questionable. Physicians should check whether these studies are funded by a company’s research and development division or the sales division.

Agencies such as the Alberta Heritage Foundation for Medical Research, which support family practice research, are few and far between.3 The government-initiated Canadian Institutes of Health Research refused to have an Institute of Primary Care despite the population involved, because primary care did not have a big enough history of Medical Research Council grants. In the meantime, family physicians might have to go to the marketplace for funding if they are to do any research of their own.

Certainly we should be careful which dances we choose and who we dance with, but we have to stay on the dance floor for the benefit of our patients.

—Andrew J. Cave, MB, CCFP, FRCP, FCFP
Edmonton, Alta
by e-mail

References

Know your “MeSH” terms

In regard to the CyberSearch column,1 “Grapefruit” in the September issue, I would guess that your search on the National Library of Medicine’s (NLM) PubMed utility failed because you did not use the proper search terms or “MeSH” headings as the NLM calls them. Unfortunately, you have to be familiar with the correct terms for a given topic, which is not always easy. When I cannot find something on MEDLINE, my next step is invariably to check for MeSH terms.

Statins are, of course, hepatic hydroxymethyl glutaryl (HMG) reductase inhibitors, but unlike “statin” or “statins,” this is a proper MeSH term. A search using “grapefruit juice” and “HMG reductase inhibitors” on both PubMed and the newer (and I think preferable) NLM Gateway (http://gateway.nlm.nih.gov/gw/Cmd) returned seven articles, of which the second was “Grapefruit juice has minimal effects on plasma concentrations of lovastatin-derived 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors.”2

In a randomized crossover study, 16 healthy subjects received a single 40-mg dose of lovastatin in the evening after each consumed a 240-mL (8-ounce) glass of regular-strength grapefruit juice or water with breakfast for 3 consecutive days. The authors concluded that “Daily consumption of a glass of regular-strength grapefruit juice has a minimal effect on plasma concentrations of HMG-CoA reductase inhibitors (approximately 30% to 40% increase) after a 40-mg evening dose of lovastatin.”2

It took me less than a minute to find the article using NLM Gateway, but I had the advantage of knowing the...
proper MeSH term to use for this particular subject. I doubt I am the first one to point out why your MEDLINE search did not produce the desired results.

—Allan I. Aizenman, MD
Ottawa, Ont
by e-mail

Overdrugged patients: enough is enough

I am surprised that Dr Frank¹ implies that up-to-date physicians almost automatically put eligible seniors with heart disease on ramipril, based on the HOPE trial. Yes, I have heard of this study, and yes, I am aware that many physicians are stampeding to use angiotensin-converting enzyme (ACE) inhibitors in its aftermath, but I have to demur, because most of my elderly patients are already overdrugged by me and other consultants they see.

The ACE-inhibitor cough is far more common and dangerous than it seems from drug monographs, and unwary practitioners can lead patients through many unnecessary tests and treatments for this cough. This is but one of the hazards our patients face through polypharmacy. In fact, I have been around long enough to see some of the most common diseases turn from benign to lethal or disabling through the introduction of modern drugs.

For example, arthritis always hurt, but it seldom killed until nonsteroidal anti-inflammatory drugs (NSAIDs) entered the scene and caused upper gastrointestinal hemorrhage. Cyclooxygenase-2 inhibitors, supposedly gastrointestinal-safe, are not. Numerous patients complain of pain, nausea, or diarrhea. Fenfluramine, or “Fen-Fen” (not available in Canada), a weight reduction drug, had to be discontinued after heart-valve damage was discovered.

If abused, asthma inhalers can lead to an unexpected increase in asthma deaths. Earlier antiarrhythmic drugs caused fatal arrhythmias were banned, while amiodarone (Cordarone), though safer, can create a catalog of important illnesses, such as pulmonary fibrosis and thyroid disorders. Simple allergies became lethal on occasion when terfenadine (Seldane) was used; hiatus hernia treatment with cisapride (Prepulsid) led to heart ailments and was banned. Elevated lipids, if treated with cerivastatin (Baycol), led at times to rhabdomyolysis, while others of the now ubiquitous statins become hazardous with grapefruit juice, and recent research from Denmark describes statin-induced neuropathy.

Consider what female patients must think when told that long-term use of replacement hormones for menopause was recently discovered to cause an increase in all three dreaded female cancers: ovarian, breast, and, as was previously known, uterine. These same hormones also cause an increase in heart disease and stroke, as well as blood clots. This covers most of the causes of death and debility in women, and I do not blame women for being disappointed with their physicians at this point.

Men also are now being told that testosterone drugs might help them for some of the same vague reasons estrogens were once given to women, for example, sense of well-being, improved mood, and better cholesterol ratios with a debatable lower risk of heart disease. Will men also have an increase in cancer and vascular disease that we will have to explain later?

We physicians know that adverse drug reactions occur commonly in the gastrointestinal tract but sometimes forget that the central nervous system is equally vulnerable: anxiolytic drugs, such as benzodiazepines, cause depression because they are central nervous system depressants, but virtually any sort of drug can be mood-altering and might convert compliant patients into polypharmacy zombies. We often hear our patients complain of fatigue, asthma, irritability, insomnia, anxiety, headache, and dizziness—all disabling and often due to prescribed drugs. Patients do not know about this relationship, but we do.

We physicians now have the ability to alter personalities and mimic many disease states through careless prescribing. Will we remember that the simple act of discontinuing a drug might make these puzzling disease states disappear? Or do we launch a prescription cascade to treat the adverse drug reactions and cause more adverse drug reactions?

—D. Rapoport, MD, CCFP
North York, Ont
by fax

Reference

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