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Patient Follow-Up and Monitoring Medicines

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Since we are concerned about signals of harm caused during therapy with medicine, we should be interested in the quality and frequency of patient follow-up. There are approximately 186 million hits if one searches the Internet using the term 'patient follow-up', but most of them refer to special studies (as far as I went in my review!); it is far less certain what happens to patients who are treated in routine practice. In the late 1970s, Professor Mike Riley, who was Professor of Clinical Pharmacology at the University of Zimbabwe (formerly Rhodesia), emphasized to students that during the prescribing process one should always think of a plan for follow-up of therapy. According to Professor Riley, a plan needed to consider the following:

- Should the patient be reviewed?
- If so when?
- When is there likely to be a therapeutic response?
- When are adverse reactions likely to occur, common and serious ones in particular?
- What information should the patient have before I hand over the prescription to help their self-assessment of success of treatment and possible adverse effects?

Such advice, so long ago, and all the information from studies since, should have brought us to a point where medical errors and adverse drug reactions (ADRs) should be recognized and reported before any major damage is caused. Not only is there much information, but some of that information has been turned into guidelines for patient follow-up. There are approximately 1.7 million hits on the Internet related to guidelines for good prescribing practices in different diseases; however, it seems that many of these are from the UK. In addition, there are many duplications contained in this figure.

I cannot possibly review all the material on the Internet, even when it comes to the many fewer papers drawing attention to common, continuing treatment problems such as excessive use of NSAIDs and gastrointestinal bleeding, overuse of antibiotics related to local increases in resistant organisms, and adherence and dose issues related to β-blocking drugs. Indeed, my purpose is to point out only that there is an enormous amount of information available on best practices for the use of medicines, in addition to the summaries of product characteristics, which seems neither to reduce the level of iatrogenic disease nor to have an effect on reporting rates of ADRs.

1. Is There Something Wrong with Patient Follow-Up?

An article on therapeutic guidelines[1] makes a number of important and relevant points. In the first paragraph, the authors make the point that medical decision making is becoming increasingly complex, particularly taking into account the myriad therapeutic options. However, that was some time ago and with the plethora of guidelines now available one wonders whether they may themselves add to the bewildering array of advice available on the Internet. Every time I access the Internet I wonder which site will give me the best information, not to consider that there may be contradictory advice; it all takes time and one practical route to take is not to bother to look!

Outright opposition or passive lip service agreement to guidelines are two reasons mentioned in the paper as being problems. Another is that the guidelines may be too idealistic and not seen as suitable for daily clinical practice.[1]

On top of all these general issues, most follow-up guidelines do not fulfill pharmacovigilance needs; they do not explicitly mention what to do in the face of suspected ADRs, but rather they may suggest alternative therapies in the case of drug intolerance (see, for example, the generally excellent UK National Institute for Health and Clinical Excellence [NICE] guideline on secondary prevention following myocardial infarction, where para 1.3.2.6 does give cough as an example relating to ACE inhibitors but it does not mention what intolerance to β-blockers might be in para 1.3.4.6, even though 'the maximum tolerated dose' is mentioned as the target for treatment).[2]

It seems likely that the disease-based guidelines are not designed to tell a health professional how to manage patients in detail, sensibly leaving such matters for clinical judgement, although the general advice to have a patient follow-up plan with the intention of monitoring effectiveness and safety issues could be included.

It is noteworthy that the above NICE guideline does suggest that the dose of β-blocker should be increased to the point of intolerance. An American review of β-blocker use in secondary prevention following myocardial infarction found that usage of those drugs was as follows: "93.2% at discharge: 20.1% received <25% of target dose, 36.5% received 25% of target dose, 26.4% received 26% to 50% of target dose, and 17.0% received >50% of target dose. Between discharge and 3 weeks, 76.4% had no change in β-blocker dose, with 11.9% and 11.6% having their dose reduced and increased, respectively."[3] Such a finding of suboptimal dosing might suggest that more detailed guidance would be useful and/or that patient follow-up, although essential, is not done or is ineffective.

It is not difficult to find many more examples of problems in medication on follow-up of patients, as well as, inevitably, loss of patients to follow-up that could be related to adverse effects of treatment.

2. One Size Does Not Fit All

The need to follow-up patients seems essential, logically, to find the right dose that optimizes effectiveness and avoids dose-related harm. Response to medicines will often follow a normal distribution curve and it is likely that the recommended doses will not include all outliers. This may be particularly true in children, where clinical trials may not have been conducted in all relevant age groups, and also in the elderly who have progressive deterioration in organs as well as obvious concomitant diseases. Thus, the need for individual patient follow-up for optimization of therapy seems very necessary for a sizeable minority of patients, but it is clear that there is a considerable resource implication for healthcare professionals. Nonetheless, Mike Riley had the right idea, i.e. that a plan should be *considered* for every patient; I would suggest that resource implications should be counted at the time of prescription for that particular doctor and patient, and balanced against the benefits for improving that patient's outcome.

Another reason why individual patients cannot be considered as part of a group norm for treatment is the way in which healthcare is increasingly practiced. This is linked to limitations in time and resources to some extent, and to evolution of healthcare teams. Doctors, nurses and pharmacists are all involved in therapy with medicines and roles change; more nurses are prescribers, and pharmacists are increasingly involved in monitoring roles. This is very good, but it does mean that a therapeutic plan, which must be initiated by the prescriber, has to be known by all those involved in the follow-up process. This is even more complicated where patients may be seeing several specialist health professional prescribers, each with a responsibility for the therapy they initiate, and also for any possible interactions with other medicines that a patient may be taking. This is particularly true of the increasing numbers of geriatric patients in the world – a group in which I have an increasing interest!

It can be that prescribers do not even know about the problems that occur from the medication they prescribe. I remember one instance

where a psychiatrist claimed that he had never seen a case of agranulocytosis from mianserin, although four of his patients had been admitted to his own hospital under the care of haematologists.

3. How Do We Manage Follow-Up?

Follow-up of patients is not simple. There have been several studies on falls in geriatric patients, and we have known for years that these falls can be due to medications.[4] How would that secondary risk be picked up and managed in an individual patient? Does the orthopaedic surgeon contact the prescriber, say, of a psychotropic medication that may have been, at least in part, responsible for the fall? Would the surgeon even be aware of the medication, and could he or she safely change a prescription issued by another doctor if the drug was known? In some healthcare situations, general primary care practitioners manage this coordination complexity rather well, but the situation is increasingly problematic with increasing medical specialization. In a recent paper, in the area of geriatrics, where we know elderly people are vulnerable to problems from metabolizing and excreting drugs, as well as frequent polypharmacy and difficulties in handling their medications, there was a strong suggestion that *comprehensive* geriatric assessment might reduce inappropriate medication use.[5] This approach seems to be a useful one, but it assumes that the relevant healthcare practitioners can either be actively involved or allow others to monitor and change medications for them.

Three ways forward occur to me. The first is to further pursue the economics of therapy management. Given that time, and therefore money, needs to be made available for patient follow-up, we need more information than the well known data on the costs of avoidable adverse reactions.[6] We need to know how much individual patient follow-up will result in improved, safer therapy, which should not only reduce healthcare costs, but also costs for the whole society (through less time away from work and the further consequences of this, such as reduced productivity and the implications for domestic economy). Studies in this area need careful design to pick up the secondary effects of adverse drug effects such as falls and other accidents.

The second point relates to the role of clinical pharmacologists and clinical pharmacists. Surely they should be at the fore in medicine therapy follow-up. Some do it now, and surely complex medication regimens and their follow-up are best left to those whose training is most suitable for that role? More money spent on more of these professionals might prove very cost effective.

Finally, pharmacovigilance needs to harness the individual experiences of outcomes of medication, due to drugs or to systematic medication errors. We need to be able to measure good as well as bad outcomes. Patients need to play their part in the process by active reporting of their experiences, and I hope they will do so increasingly if we can show them tangible benefits for their own, and public, health.

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References

1. Haines AH, Hurwitz B. Clinical guidelines: report of a local initiative. Introduction. Occas Pap R Coll Gen Pract 1992 Dec; (58): 1-6 [online]. Available from URL: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2560230/pdf/occpaper00112-0010.pdf [Accessed 2011 Oct 27]
2. National Institute for Health and Clinical Excellence. NICE clinical guideline 48. MI: secondary prevention [online]. Available from URL: http://www.nice.org.uk/nicemedia/live/11008/30493/30493.pdf [Accessed 2011 Sep 27]
3. Goldberger JJ, Bonow RO, Cuffe M, et al. β-blocker use following myocardial infarction: low prevalence of evidence-based dosing. PACE-MI Investigators. Am Heart J 2010 Sep; 160 (3): 435-42.e1
4. Campbell AJ, Reinker J, Allan BC, et al. Falls in old age: a study of frequency and related clinical factors. Age Aging 1981; 10: 264-70
5. Sergi G, De Rui M, Sarti S, et al. Polypharmacy in the elderly: can comprehensive geriatric assessment reduce inappropriate medication use? Drugs Aging 2011; 28 (7): 509-18
6. Pirmohamed M, James S, Meakin S, et al. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. BMJ 2004; 329 (7456): 15-9

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