In recent years drug regulatory agencies have required drug companies to prepare risk management plans, however these plans are predicated on known risks. The revelation of risks occurs, far too slowly, over time. Better postmarketing surveillance would need to involve more than 10% of adverse drug reactions being reported to the FDA. It would then be sooner rather than later that the required number of adverse reactions occurred to force a change in the product information or the withdrawal of the drug.

Drugs which have been available for more than seven years have already gone through the tests of time and the amount of information about their risks has expanded enormously from what was available when they were initially approved. The worst offenders have either been removed from the market or have important new information about harm that will aid prescribers and patients concerning safer use. As a result, for most patients using older drugs for their approved indications, the benefits will hopefully outweigh the risks.

Conflict of interest: none declared

REFERENCES

1. Wolfe SM. Worst Pills, Best Pills. 3rd ed. New York: Simon & Schuster Pocket Books; 1999.
2. Lasser KE, Allen PD, Woolhandler SJ, Himmelstein DU, Wolfe SM, Bor DH. Timing of new black box warnings and withdrawals for prescription medications. JAMA 2002;287:2215-20.
3. Wolfe SM. Worst Pills, Best Pills. 4th ed. New York: Simon & Schuster Pocket Books; 2005.
4. Wolfe SM, Sasich LD, Barbehenn E. Petition to ban the diet drug sibutramine (Meridia) [letter]. Public Citizen; 2002 Mar 19. www.citizen.org/Page.aspx?pid=2605 [cited 2012 Sep 3]
5. Parkinson J, Wolfe SM. Petition for a black box warning on fluoroquinolone antibiotics [letter]. Public Citizen; 2006 Aug 29. www.citizen.org/Page.aspx?pid=693 [cited 2012 Sep 3]

Letters to the Editor

Safe prescribing of opioids for persistent non-cancer pain

Editor, – The article by Michael McDonough (Aust Prescr 2012;35:20-4) was well written and includes some good material. However, I consider many statements to be incorrect and dangerous such as:

- 'Every prescription for opioids is fraught with danger'
- 'Before prescribing long-term therapy, there should be a trial period of one month'. By that time many people are already dependent.
- 'If prescribing beyond 12 months a second opinion should be obtained'. This person is dependent.

Donald Beard
Surgeon
Norwood, SA

Michael McDonough, author of the article, comments:

While I find myself agreeing with many of the sentiments expressed in the letter, there is no evidence to support the broader generalisation that after a month or even 12 months many patients are already dependent. However, there is some evidence to support that at least some patients may benefit from extended opioid therapy.[1] Dr Beard is referring to the state of physiological dependence rather than the dependence syndrome as described in DSM IV-TR[2] which is synonymous with the term addiction.

Most people who develop a form of physiological dependence to opioids in the context of medical treatment can be withdrawn from opioids without significant risk of developing persistent craving for opioids or chronic, relapsing and remitting opioid use disorder. Further, there are patients who may derive benefit from continued opioid therapy but within the caveats that both I and others have described.[3]

Having concern about opioid use is always appropriate. However, this concern should not, of itself, justify the absolute avoidance approach, especially in appropriately selected and monitored patients.

REFERENCES

1. Furlan AS, Sandoval JA, Mailis-Gagon A, Tunks E. Opioids for chronic non-cancer pain: a meta-analysis of effectiveness and side effects. CMAJ 2006;174:1589-94.
2. Diagnostic and Statistical Manual of Mental Disorders. Fourth Edition: Text Revision. DSM–IV–TR. Arlington, VA: American Psychological Association; 2000.
3. Cohen M, Wodak A. Opioid prescribing in general practice: a proposed approach. Med Today 2012;13:24-32.

The Editorial Executive Committee welcomes letters, which should be less than 250 words. Before a decision to publish is made, letters which refer to a published article may be sent to the author for a response. Any letter may be sent to an expert for comment. Letters are usually published together with their responses or comments in the same issue. The Committee screens out discourteous, inaccurate or libellous statements and sub-edits letters before publication. The Committee's decision on publication is final.

LETTERS

Oxycodone and QTc prolongation

Editor, – Thank you to Michael McDonough for his comprehensive article on the safe prescribing of opioids (Aust Prescr 2012;35:20-4). In particular, Table 1 provides useful recommendations for the monitoring and management of possible emerging adverse effects.

The inclusion of oxycodone as a medication which prolongs QTc was surprising. This precaution does not appear in other sources of information discussing oxycodone, such as the reference cited for Table 1[1], the approved product information for oxycodone, the Australian Medicines Handbook[2], Therapeutic Guidelines[3] or the database which records medications that prolong QTc (www.qtdrugs.org). However, there has been research published which supports the occurrence of prolonged QTc by oxycodone in a dose-dependent manner.[4] Is there any other literature that the author can refer us to which supports the prolongation of QTc by oxycodone?

The suggested strategy to manage this potential adverse effect in his article is to recommend an ECG. Given that the prescribing of oxycodone and oxycodone-related deaths have increased in Australia since 2002,[5] does the author, as a practical consideration, advise that in all cases an ECG be performed before the initiation of all formulations of oxycodone?

Margaret Jordan
NPS facilitator
Illawarra Shoalhaven Medicare Local

Tania Colarco
Clinical pharmacist and NPS facilitator
Drug and Therapeutics Information Service (DATIS)
Repatriation General Hospital, Adelaide

Kirsty Lembke
Program officer
NPS, Sydney

REFERENCES

1. Kalso E, Edwards JE, Moore RA, McQuay HJ. Opioids in chronic non-cancer pain: systematic review of efficacy and safety. Pain 2004;112:372-80.
2. Australian Medicines Handbook. Adelaide: AMH; 2012.
3. eTG complete [internet]. Melbourne: Therapeutic Guidelines Limited; 2012.
4. Fanoe S, Boje Jensen G, Sjøgren P, Korsgaard MP, Grunnet M. Oxycodone is associated with dose-dependent QTc prolongation in patients and low-affinity inhibiting of hERG activity in vitro. Br J Clin Pharmacol 2009;67:172-9.
5. Roxburgh A, Bruno R, Burns L. Prescription of opioid analgesics and related harms in Australia. Med J Aust 2011;195:280-4.

Michael McDonough, author of the article, comments:

Thank you for raising two further questions from my article. As you have noted, I was also referring to the article about dose-dependent QTc prolongation by oxycodone.[1]

The concern is that drugs like oxycodone and others yet to be associated with QT prolongation appear to be identified later rather than sooner. We remain uncertain about the precise mechanism of fatal toxicity in both methadone- and more recently the rising number of oxycodone-related deaths in Victoria[2] and the USA.[3] However, the possibility, even if somewhat small, that QT prolongation may be a predisposing factor together with other arrhythmogenic risk factors – such as hypokalaemia, hypomagnesaemia, other drug interactions and heart disease – should be considered.

I believe baseline ECG recording is not appropriate as a screening recommendation because there is no evidence to guide the implementation of such a strategy. Also, this might give rise to concerns about degrees of variation in the QTc interval in various patients and potentially lead to excessive investigation and possibly over-intervention. Consensus recommendations about QTc monitoring in patients on methadone also draw attention to the controversies surrounding the management of degrees of QTc prolongation and the complexities involved in 'risk versus benefit' analyses in this scenario.[4]

I believe an annual ECG recording in the context of long-term and especially high-dose oxycodone treatment would constitute reasonable care and is preferable to not doing so. Furthermore, undertaking an ECG in any patient on oxycodone and with additional risk factors (mentioned above) would no doubt be a more compelling recommendation.

REFERENCES

1. Fanoe S, Boje Jensen G, Sjøgren P, Korsgaard MP, Grunnet M. Oxycodone is associated with dose-dependent QTc prolongation in patients and low-affinity inhibiting of hERG activity in vitro. Br J Clin Pharmacol 2009;67:172-9.
2. Rintoul AC, Dobbin MD, Drummer OH, Ozanne-Smith J. Increasing deaths involving oxycodone, Victoria, Australia, 2000-09. Inj Prev 2011;17:254-9.
3. Hall WD, Farrell MP. Minimising the misuse of oxycodone and other pharmaceutical opioids in Australia [editorial]. Med J Aust 2011;195:248-9.
4. Krantz MJ, Martin J, Stimmel B, Mehta D, Haigney MC. QTc interval screening in methadone treatment. Ann Intern Med 2009;150:387-95.

The importance of medication reconciliation for patients and practitioners

Editor, – I read the timely article by Ms Duguid on medication reconciliation (Aust Prescr 2012;35:15-9) with great interest. Prescribing is a common but often complex and challenging intervention. With a meteoric rise in the ageing population, its attendant polypharmacy and the shift of chronic disease management to primary care, the majority of prescribing will happen in primary care. The peri-discharge period can be perilous. However the article fails to mention some proven strategies in reconciliation such as:

- referring patients for a home medicines review within a stipulated period of discharge (ideally within two days) thereby avoiding rebound admissions and medication misadventures
- engaging a hospital or consultant pharmacist to liaise with the patient's general practitioner, given that managing patients on multiple drugs can be time consuming and require delicate balancing of guidelines and clinical complexities
- checking for potentially inappropriate medicines using Beers Criteria. An Australian version of this list is currently being considered.[1]

With the proliferation of prescribing rights, relevant curricula (medicine, pharmacy and nursing) need to be restructured to explicitly include therapeutics as a formal part of the training. This will build the knowledge and skill base for the quality use of medicines, ideally in an interdisciplinary milieu.

I wish to thank Ms Duguid for highlighting the magnitude of medication-related problems both in individual patients and as a public health issue. I hope there is a strong political commitment to the quality use of medicines which is a central tenet of Australia's National Medicines Policy.

Jay Ramanathan
Physician trainee
Sydney

REFERENCE

1. Bell SJ, Le Couteur D, McLachlan AJ, Chen TF, Moles RJ, Basger BJ, et al. Improving medicine selection for older people – do we need an Australian classification for inappropriate medicines use? Aust Fam Physician 2012;41:9-10.

Margaret Duguid, author of the article, comments:

I would like to thank Dr Ramanathan for highlighting the risks of medication-related problems occurring following discharge from hospital and the value of hospital and community liaison services and home medicines reviews in the immediate discharge period. Home medicines reviews within 7–10 days of discharge have been shown to decrease the potential for adverse events in at-risk patients discharged home.[1]

To date, timely access to home medicines reviews in the immediate discharge period has been a limitation to their uptake.[2] However, with the ability for general practitioners to refer directly to accredited pharmacists and the proposed hospital home medicines review referral pathway (due to be introduced in late 2012), some of the barriers to early post-discharge medication reviews will be removed.

Patients transferred from hospital to residential aged-care facilities are at particular risk of medication errors. Often their medicines are changed and doses of newly prescribed medicines omitted or delayed. In the case of a resident returning from a hospital admission, ceased medicines were inadvertently administered from a pre-existing medication chart.[3] Checking the medication orders against the medicines list in the discharge summary to identify any discrepancies is an important safety practice. As Dr Ramanathan pointed out, medication reviews early in the admission provide the opportunity to identify and reconcile these discrepancies as well as review those medicines commonly known to cause harm in older patients.

Pharmacists also have an important role in checking the patient's records when new medicines are ordered, ceased or changed and reconciling any discrepancies with the prescriber.

The Australian Commission on Safety and Quality in Health Care has a strong commitment to patient safety. Promoting medication reconciliation is one of its priorities.

REFERENCES

1. Nguyen A, Yu K, Shakib S, Doecke CJ, Boyce M, March G, et al. Classification of findings of home medicines reviews in post-discharge patients at high risk of medication misadventure. J Pharm Pract Res 2007;37:111-4.
2. Angley MA, Ponniah AP, Spurling LK, Sheridan L, Colley D, Nooney VB, et al. Feasibility and timeliness of alternatives to post-discharge home medicines reviews for high-risk patients. J Pharm Pract Res 2011;41:27-32.
3. Elliot RA, Tran T, Taylor SE, Harvey PA, Belfrage MK, Jennings RJ, et al. Gaps in continuity of medication management during transition from hospital to residential care: an observational study (MedGap Study). Australas J Ageing 2012. DOI: 10.1111/j.1741-6612.2011.00586.x

LETTERS

Assessing fever in the returned traveller

Editor, – The article by Anthony Gherardin and Jennifer Sisson (Aust Prescr 2012;35:10-4) provided a good discussion of the issues in this important clinical situation. However, there were several important omissions which I think should be commented upon.

Firstly, measles is a very important cause of fever and rash in the returned traveller, yet this is not mentioned. Many younger Australian doctors will never have seen a case of measles. However, it continues to occur in many resource-poor countries. Measles is one of the most contagious infections known in humans so the importation of even a single case is a public health emergency. It is very important to consider this diagnosis in a returned traveller with fever, respiratory symptoms and a maculopapular (or 'morbilliform') rash. The most rapid and accurate diagnostic test is a polymerase chain reaction on a throat swab or urine, complemented by acute and convalescent serology.

Secondly, in the diagnosis of malaria, rapid antigen tests – immunochromatographic (ICT) card tests – have become standard in nearly all laboratories in Australia, as an addition to the traditional thick and thin blood films. These tests are at least as sensitive as microscopy (by an experienced operator) for malaria caused by *Plasmodium falciparum*, but perform poorly for other species of malaria.

Thirdly, the NS1 antigen test for dengue fever was not mentioned. This test becomes positive earlier than serology and has excellent sensitivity and specificity. Admittedly it is only available in larger laboratories.

Finally, I think the authors have underemphasised the role of the infectious diseases physician. Most infectious diseases departments are very happy to give phone advice and, if necessary, urgent clinical review of any febrile or unwell returned traveller. Furthermore, many of the conditions listed in the article (for example schistosomiasis, yellow fever, trypanosomiasis, leishmaniasis and typhus) are rarely – if ever – seen by general practitioners and should be referred to a specialist regardless of whether or not they are atypical or severe.

Joshua S Davis
Infectious diseases staff specialist
Royal Darwin Hospital

Anthony Gherardin, one of the authors of the article, comments:

We thank Dr Davis for adding to the discussion and would not disagree with anything he has stated. Within the word limit constraints of the article, we could not flesh out too much and the issues raised are very relevant for general practitioners.

Nurturing a close relationship with local infectious disease physicians is also important for safe, high-quality practice.

Undergraduate student prize 2012

Congratulations to Mirjam van den Boom, medical student at the University of Auckland, for winning the Australian and New Zealand Association for Health Professional Educators (ANZAHPE) undergraduate student prize for 2012.

The prize was sponsored by *Australian Prescriber*. It was awarded by the Editor at the ANZAHPE conference in Rotorua in June.

Mirjam's entry topic was 'Supervision of paediatric trainees: effect on patient management and education'.