

# Pharmacy Research Review

Making Education Easy

Issue 9 - 2009

## In this issue:

- > *Amlodipine-induced angioedema?*
- > *Cases of confusion with sodium valproate*
- > *OTC medication dosing errors in children*
- > *Clopidogrel and PPIs: reinfarction risk*
- > *INR, warfarin and the influenza vaccination*
- > *Supplementary prescribing by pharmacists*
- > *Communicating essential medication-related facts*
- > *ACE inhibitors and ARBs: dosing suboptimal*
- > *Paracetamol: pro-survival effects on neurons*
- > *Annual zoledronic acid in hip fracture prevention*

## Welcome to the ninth issue of Pharmacy Review.

In this edition, an investigation revealing incongruent beliefs about medication-related counselling among older patients, pharmacists, and physicians should remind us all about the importance of routinely informing patients about new medications.

Our last study discusses the pros and cons of once-yearly IV zoledronic acid for the prevention of hip fractures in the elderly. Although the review supports the use of infusions over oral dosing of zoledronic acid, it may pay to remember that the safety profile of IV infusions of zoledronic acid have not yet been well established (e.g. concerns exist over atrial fibrillation).

I hope you enjoy this edition and I welcome your comments and feedback.

Kind regards,

**Andi Shirtcliffe**

[andishirtcliffe@researchreview.co.nz](mailto:andishirtcliffe@researchreview.co.nz)

## Probable amlodipine-induced angioedema

**Authors:** Southward J et al

**Summary:** These researchers present the case details of a 50-year-old woman who experienced angioedema during hospitalisation for a right thalamic haemorrhagic stroke. She had no past history of angioedema. After evaluating all of her medications for risk of angioedema, case reports linking calcium channel blockers verapamil, diltiazem, and nifedipine with angioedema led to further examination of amlodipine as a cause. Amlodipine therapy had been initiated 24 hours prior to the development of angioedema, which then resolved 72 hours after discontinuation of the drug. In total, the patient experienced oropharyngeal swelling for 10 days.

**Comment:** It's always hard to keep up with those rare adverse drug reactions that really only seem to populate the literature as isolated case reports. That's why I like to comment on them here when I come across them. It looks like this is something to watch for in amlodipine-naive patients (this case occurred within 24 hours of therapy initiation). Interesting to see that verapamil, diltiazem and nifedipine have also been implicated.

**Reference:** *Ann Pharmacother.* 2009;43(4):772-6.

<http://www.theannals.com/cgi/content/abstract/43/4/772>

# COMING SOON to South Africa

## SUBSCRIBE NOW TO RECEIVE YOUR COPY

This publication is a sample copy from New Zealand. The opinions expressed are specific to the New Zealand health environment. South African versions will be available soon.

## Confusion, a rather serious adverse drug reaction with valproic acid: a review of the French Pharmacovigilance Database

**Authors:** Bondon-Guitton E et al

**Summary:** An examination of the French Pharmacovigilance database for all cases of confusion reported since 1985 with sodium valproate [valproic acid] revealed a total of 272 cases (153 women and 119 men). Most (39.7%) occurred during the first two weeks following sodium valproate exposure. The confusion was rated as "serious" for 62.5% of patients and following treatment discontinuation, outcomes were favourable in the majority (82%). Sodium valproate-induced confusion was more common among patients aged between 61 and 80 years.

**Comment:** Interesting that if you look at the data sheet for sodium valproate it refers to 'rare cases of confusion' being possible. This work looks at data from the French Pharmacovigilance database and reports on 272 cases (admittedly from 1985), but you do have to wonder how many cases are not identified given how frequently sodium valproate is given with sedating agents, not to mention potential post-seizure drowsiness in epileptics and recent increased use in the demented elderly population. According to this work, up to 82% may have a favourable outcome if treatment withdrawal is attempted. Although never an easy decision to make, treatment withdrawal should obviously be in the decision melting pot at the very least.

**Reference:** *Pharmacopsychiatry*. 2009;42(2):61-5.

<http://tinyurl.com/dca7dc>



PHARMACY GUILD OF NEW ZEALAND (INC)

## Therapeutic errors among children in the community setting: nature, causes and outcomes

**Authors:** McD Taylor D et al

**Summary:** These researchers report findings from a telephone survey of 450 parents/caregivers who had reported medication dosing errors in their children; parents/carers were followed-up approximately 48 hours after the initial call placed to the Victorian Poisons Information Centre. The majority of children (68.0%) were aged  $\leq 3$  years. Incorrect and double dosage accounted for 56.8% and 26.1% cases, respectively. Almost all errors occurred in the home (98.2%), involved a single medication (98.8%), and oral dosing (98.4%). Close family members were responsible in 83.1% of cases. Analgesics and cough and cold preparations were mistakenly given in 52.0% of cases. Causal factors included human (rushing, distraction, carelessness) and communication issues in 38.4% and 12.7% of cases, respectively. In 96.5% of cases, the caller was advised to observe the child at home, and no child experienced significant morbidity. Preventive strategies included attention to administration care and routine, communication, medication storage, administration devices, packaging and labelling issues.

**Comment:** I have two small children and readily acknowledge how easy it is to make a mistake when attempting to administer medicines in the wee small hours when no-one in the house has had a decent sleep for days. It must be even more difficult for those with little or no knowledge of medicines. It is no surprise that in this work close family members were found to be most likely to be responsible. Analgesics and cough cold preparations were most likely to be implicated. Sometimes I wonder if paediatric medicines should have mandatory 48-point font for the dose to help out those blurry-eyed sleep-deprived parents!

**Reference:** *J Paediatr Child Health*. 2009 Mar 23. [Epub ahead of print]

<http://www3.interscience.wiley.com/journal/122269374/abstract>

## A population-based study of the drug interaction between proton pump inhibitors and clopidogrel

**Authors:** Juurlink DN et al

**Summary:** Among 13,636 patients aged  $\geq 66$  years prescribed clopidogrel following hospital discharge after treatment of acute myocardial infarction, these researchers identified 734 cases readmitted with myocardial infarction within 90 days after discharge and 2057 event-free controls matched based on age, percutaneous coronary intervention and risk score. Concurrent use of proton pump inhibitors and clopidogrel was associated with a 27% greater risk of reinfarction within 90 days compared with patients using clopidogrel only. The risk was limited to patients currently using a proton pump inhibitor and was not associated with pantoprazole, a drug that does not interfere with the conversion of clopidogrel to its active form.

**Comment:** This study reports on an association that is possibly explained by yet another cytochrome interaction, giving us yet another reason (as if we needed one) to review PPI use. We've all got those patients who probably don't need to be on the PPI at all. For those clopidogrel patients that do, it looks like pantoprazole is a possibly less risky option – and it's fully funded!

**CPD:** identify patients on the combination of omeprazole and clopidogrel and do some proactive counselling to see if they really need that PPI, and if they do refer to their GP for consideration of alternative therapy?

**Reference:** *CMAJ*. 2009;180(7):713-8.

<http://tinyurl.com/cbpyku>

COMING SOON  
to South Africa

SUBSCRIBE NOW TO RECEIVE YOUR COPY

This publication is a sample copy from New Zealand. The opinions expressed are specific to the New Zealand health environment. South African versions will be available soon.

## Fatal intracranial bleed potentially due to a warfarin and influenza vaccine interaction

**Authors:** Carroll DN and Carroll DG

**Summary:** A case is reported of fatal intracranial bleeding possibly due to an interaction between warfarin and inactivated influenza vaccination. A 64-year-old white male was admitted to the hospital after becoming unresponsive. He had a 2-day history of rectum bleeding prior to admission. He had no recent changes in medical conditions or medication regimen, which included warfarin for stroke prophylaxis secondary to atrial fibrillation. The patient had received an inactivated influenza vaccine 4 1/2 weeks prior to presentation, at which time his international normalised ratio (INR) was 2.0 and had been relatively stable for  $\geq 6$  months. Upon admission, his INR values were  $>15$ . A noncontrast computed tomography scan of the head revealed a large parenchymal haemorrhagic infarction involving the left temporal, parietal, and occipital lobes. In the emergency department, the patient received a nitroglycerin infusion to maintain systolic blood pressure in the range of 140–160 mmHg as well as an infusion of 4 units of fresh frozen plasma and 10mg of vitamin K. A neurosurgery evaluation considered that no further action could improve the patient's outcome, and he died approximately 17 hours after admission.

**Comment:** This is a curious interaction that appears to vary in potential from year to year (due to variation in vaccine content) and can take several weeks to manifest itself. So, not the easiest to identify. I guess it's a pretty safe guess that most patients who qualify for warfarin therapy are reasonably likely to get a flu jab, so why not use this time of the year as a prompt to gently remind those patients that any change in medicines (including vaccinations) should prompt a consideration for closer INR monitoring.

**Reference:** *Ann Pharmacother.* 2009;43(4):754-60.

<http://www.theannals.com/cgi/content/abstract/aph.1L413v1>

## Views of pharmacist prescribers, doctors and patients on pharmacist prescribing implementation

**Authors:** Stewart DC et al

**Summary:** Patients' perspectives and experiences of pharmacist supplementary prescribing are reported by this survey conducted in Scotland. Each of 10 pharmacist supplementary prescribers distributed questionnaires to 20 consecutive patients as they attended appointments during October to December 2006. Reminders were mailed to patients by each pharmacist 2 weeks after initial distribution. A total of 103 patients responded. The median age was 67 years. Most (76, 73.8%) consulted with the pharmacist in a general practice setting. Most patients (89.3%) were satisfied with the consultation, 78.7% thought the pharmacist told them everything about their treatment and 72.9% felt the pharmacist was interested in them as a person. Most patients were positive in their attitudes, agreeing that they would recommend a pharmacist prescriber to others and that they had trust in the pharmacist. However, 65% would prefer to consult a doctor.

**Comment:** This is an interesting piece of research looking at an area that is pretty topical here in New Zealand with our own pharmacist prescribing potential on the horizon. Although conducted in Scotland, I would be surprised if the attitudes were all that different to what would be expected back here. I was intrigued that in this study, patients raised no concerns about the potential new role and doctor and pharmacist concerns appeared to be very similar!

**Reference:** *Pharm World Sci.* 2008;30(6):892-7.

<http://www.springerlink.com/content/y12v3h3513227181/>

## Which providers should communicate which critical information about a new medication? patient, pharmacist, and physician perspectives

**Authors:** Tarn DM et al

**Summary:** Qualitative focus group discussions were conducted with 42 patients aged  $\geq 65$  years, 13 pharmacists, and 17 physicians, to clarify their perspectives about what information is essential to impart to patients receiving new medication prescriptions and who should provide the information. All groups affirmed the importance of discussing medication directions and side effects and said that physicians should educate about side effects and that pharmacists could adequately counsel about certain important issues. However, substantial disagreement existed between groups about which provider could communicate which critical elements of medication-related information. Some pharmacists felt that they were best equipped to discuss medication-related issues but acknowledged that many patients want physicians to do this. Physicians felt that they should provide most new-medication education for patients. Patients had mixed preferences. Patients aged  $\geq 80$  years listed fewer critical topics of discussion than younger patients.

**Comment:** This is a constant dilemma in pharmacy practice, and I like the author's conclusion that a potential strategy is to work out (between the doctor and the pharmacist), within reason, who is going to cover what! Wouldn't that save us all trying to elicit what's been covered already before we can even start out counselling? I was interested to see that younger patients seem to want to know more; the younger patients in this study were over 65 years. Anyway, the prescriber would be forgiven for not being able to fit in any medicine counselling at all – given how much they already have to cover during the course of a consultation.

**Reference:** *J Am Geriatr Soc.* 2009;57(3):462-9.

<http://tinyurl.com/d2a7kp>

COMING SOON  
to South Africa

SUBSCRIBE NOW TO RECEIVE YOUR COPY

This publication is a sample copy from New Zealand. The opinions expressed are specific to the New Zealand health environment. South African versions will be available soon.

## Are angiotensin-blocking drugs being used in adequate doses?

**Authors:** Randhawa SK et al

**Summary:** Dosage levels were investigated for angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers among 60 hospitalised patients. Only 23 (38%) were receiving the top recommended dose and the average daily dose was 63.1% of the recommended dose.

**Comment:** I came across this write-up of an audit on ACE doses in an acute hospital in Birmingham at the same time as I saw a cross-sectional study on exactly the same issue in another journal. Although in some patient groups it can obviously be difficult to get the dose right up to that used in the heart failure trials, figures like 38% achieving half the dose used in the evidence has got to mean there's some room for improvement.

**Reference:** *Br J Cardiol.* 2009;16:102-4.

<http://www.bjcardio.co.uk/download/2958>

*Independent commentary by  
Andi Shirtcliffe*

COMING  
SOON  
to South  
Africa

SUBSCRIBE NOW TO  
RECEIVE YOUR COPY

This publication is a sample copy from New Zealand. The opinions expressed are specific to the New Zealand health environment. South African versions will be available soon.

## Acetaminophen inhibits neuronal inflammation and protects neurons from oxidative stress

**Authors:** Tripathy D and Grammas P

**Summary:** These researchers report the effects of pretreatment with paracetamol [acetaminophen] (50 µM) on cerebral cortical cultured neurons that were then exposed to the superoxide-generating compound menadione (5 µM). Pretreatment with paracetamol increased neuronal cell survival and inhibited the expression of cytokines and chemokines. Paracetamol also increased expression of the anti-apoptotic protein Bcl2 in brain neurons and decreased the menadione-induced elevation of the pro-apoptotic protein, cleaved caspase-3.

**Comment:** This is a fascinating *in vitro* study looking at a potential for an antioxidant and anti-inflammatory role for paracetamol on neuronal tissue. Although this is still 'lab stuff' it's potentially a 'watch this space'. A new trick for an old dog (so to speak)? This is available free on-line at <http://www.jneuroinflammation.com/content/6/1/10> for those who wouldn't mind a science fix!

**Reference:** *J Neuroinflammation.* 2009;16:6:10.

<http://www.jneuroinflammation.com/content/6/1/10>

## Once-yearly zoledronic acid in hip fracture prevention

**Authors:** Demontiero O and Duque G

**Summary:** This review assessed the current evidence on the use of once-yearly IV zoledronic acid for the prevention of hip fractures in the elderly. Annual infusions of zoledronic acid have recently been approved for osteoporosis and have proven to be safe and generally well tolerated, producing significant effect on bone mass and micro-architecture. Adherence has also been shown to be better with IV infusions than with the oral formulation. Two large trials have demonstrated significant anti-osteoporotic effect (-59% relative risk reduction of hip fractures) and mortality benefit (28% reduction in mortality) of IV zoledronic acid in older persons with recent hip fractures. The reviewers discuss the pharmacological characteristics and the advantages and disadvantages of zoledronic acid in this patient population.

**Comment:** For those of you looking for a retirement project look no further (and you can send me the cheque in the mail!). It looks like sometime in the not too distant future there is going to be a market for a mobile IV zoledronic acid rest home service! So far, no drug interactions (but don't forget the calcium and vitamin D...as we are all wont to do) and at 60% availability along with actual evidence of reduced mortality it all looks pretty promising. We all certainly know many of those patients who can't tolerate the oral agents. However, I do think the authors of this study might have overstated the 'convenience factor' just a tad. An annual 15-minute IV infusion may have its benefits, but I didn't see much mention of things like invasive therapy, infection potential or other such issues.

**Reference:** *Clin Interv Aging.* 2009;4:153-64.

[www.dovepress.com/getfile.php?fileID=4627](http://www.dovepress.com/getfile.php?fileID=4627)

**Privacy Policy:** Research Review will record your email details on a secure database and will not release it to anyone without your prior approval. Research Review and you have the right to inspect, update or delete your details at any time.

**Disclaimer:** This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits.

## OUT NOW

Sexual Health RESEARCH REVIEW

Eye Health RESEARCH REVIEW

Oral Health RESEARCH REVIEW

Travel Health RESEARCH REVIEW



Go to [www.researchreview.co.za](http://www.researchreview.co.za) to update your subscriptions