Snippets

CALCIUM SUPPLEMENTATION AND THE RISK OF MYOCARDIAL INFARCTION

The recent Auckland Calcium Study revealed an association of a daily one gram calcium supplement in elderly women with an increased risk of myocardial infarction. As a result, many doctors and patients have requested advice regarding the use of calcium supplements for the treatment and prevention of osteoporosis.

The data from the Auckland study have been presented at an Australasian and an American Meeting, but are not yet published. Three other recent studies of calcium supplementation in older women show similar trends, but do not reach statistical significance.

It is possible that high doses of calcium accelerate vascular calcification. There is no international consensus around the subject at present. While further research is being done in this area, the Greenlane Bone Clinic suggests the following:

- Daily one gram calcium supplementation be avoided for people over the age of 70 years and those known to have coronary heart disease.

It is likely that the association is mainly a problem for people with high risk of coronary heart disease. Calcium intake should probably be maintained at a total of approximately one gram per day (equivalent to four servings of dairy products). For instance, in a person consuming a dietary intake of ~0.5g, calcium supplementation should not exceed 0.5g.

There are very few data relating to the cardiovascular effects of calcium supplements in older men. What are available show similar non-significant adverse trends, so the same cautions suggested for older women may be appropriate.

- All people over age 70 years receive regular sunlight exposure or vitamin D supplementation.
- A total calcium intake of one gram per day should be advised for patients taking bisphosphonates for osteoporosis or Paget's disease, as there is a theoretical risk of mild hypocalcaemia. Higher intakes may be optimal in those under 70 years without coronary heart disease.
- Calcium supplements continue to be used, where indicated, for younger women.
- There is no reason on the basis of the Auckland Calcium Study, to advise reduced calcium intakes in children, adolescents or young and middle-aged adults.

Supplied by Professor Ian Reid, University of Auckland

USE OF eGFR FOR DRUG DOSE ADJUSTMENT

The new version of the BNF states:
"BNF 54 continues to provide drug dose adjustments based on creatinine clearance but also gives the advice that, in practice, for most drugs and for most patients of average build and height, the estimated glomerular filtration rate (eGFR calculated from a formula derived from the Modification of Diet in Renal Disease study) can be used to determine dose adjustments in place of creatinine clearance. However, for potentially toxic drugs with a small margin of safety and in some patients (e.g. those at both extremes of weight) the creatinine clearance should be used or the dose should be adjusted according to plasma-drug concentration and clinical response. Work is underway to remove the current BNF categorisation of renal impairment, which focuses on drug elimination, so that there is no confusion with the grading used to determine chronic kidney disease."

Comment

Creatinine Clearance is calculated from the Cockcroft Gault equation. The difference between this and eGFR was explained in BPJ 6. We agree that creatinine clearance and eGFR will be very similar in most people as described above but reiterate that significant differences may be observed in:

1. Ethnic groups for which the MDRD equation has not been validated (Māori, Pacific Island, Asian People) BPJ 6
2. Extremes of body size or muscle bulk
3. Combinations of the above factors
4. eGFR above 60 ml/min. This does not accurately reflect actual GFR and will not correlate well with creatinine clearance calculated by Cockcroft Gault. However, this is unlikely to affect drug prescribing

As more experience is gained in the interpretation of eGFR its utility in drug dose adjustment will become clearer.

Comments endorsed by Professor Rob Walker, University of Otago

Snippets

COMPULSIVE GAMBLING AND DOPAMINE AGONISTS

In BPJ 8 we discussed the drug management of Parkinson's Disease. The main therapies increase the availability of dopamine with levodopa or stimulate dopamine receptors with dopamine agonists such as bromocriptine, ropinirole, cabergoline and pergolide.

Recent cases described in the literature and from spontaneous reporting schemes suggest an association with pathological gambling, increased libido and hypersexuality.[1] Although rare, product information for these drugs includes, or is being updated to warn of, the potential for such effects especially at high doses. Patients or their carers are advised to report any unusual or atypical behaviour.

To some extent these unexpected events may be explained by the role of dopamine as the "reward chemical" and its role in addictive disorders.

PSYCHIATRIC REACTIONS WITH CORTICOSTEROIDS.

Systemic corticosteroids can cause a range of neuropsychiatric reactions from mood changes to psychoses.

The latest BNF carries a reminder about this reaction and the possible risk factors which include; high doses, tablet preparations and a history or family history of psychiatric illness. Psychiatric reactions occur in up to 6 % of people and include affective disorders, irritability, anxiety, sleep disorders, psychotic reactions, behavioural disturbances and cognitive dysfunction. Onset varies from a few days to weeks after starting treatment. Interestingly, reactions have also been reported on withdrawal of treatment.[2]

HEARING LOSS AND DRUGS FOR ERECTILE DYSFUNCTION

The FDA has recently announced a revision to the labeling of sildenafil (Viagra), tadalafil (Cialis) and vardenafil (Levitra) to warn more prominently of the potential risk of sudden hearing loss.

This warning is based on a total of 29 postmarketing reports of sudden hearing loss associated with these drugs, with or without tinnitus, vertigo or dizziness. A further trigger was a recent report of a man who developed bilateral, profound sensorineural hearing loss after taking sildenafil daily for 15 days. In most cases the hearing loss was one side only. In about a third of cases, the hearing loss was temporary.

The warning advises that if a there is a sudden loss of hearing while taking one of these drugs it should be stopped immediately and medical advice sought.[3]

WARNINGS FOR LUMIRACOXIB AND TERBINAFINE

The Medicines Adverse Reactions Committee (MARC) reminds all prescribers of the importance of monthly liver function monitoring in patients taking lumiracoxib (see BPJ 8 for more information). Any abnormal results should be forwarded to the Centre for Adverse Reactions Monitoring. Prescribers are also reminded to dispose of any 400mg sample stock they may have, and remove references to the 400mg strength from their computer.

Oral terbinafine is associated with serious hepatic and haematological reactions. MARC has concerns that oral terbinafine is often prescribed for conditions that are either clinically inappropriate or where the risk of harm outweighs the benefits. To maximise the safety and efficacy of oral terbinafine, prescribers should ensure that the infection is caused by susceptible fungal organisms before prescribing.[4]

References

1. MHRA. Drug Safety Update Vol 1 (1), August, 2007. Available from; http://www.mhra.gov.uk/mhra/drugsafetyupdate. (Accessed 28 October 2007)

2. MHRA. Drug Safety Update, Vol 1 (2), September, 2007. Available from; http://www.mhra.gov.uk/mhra/drugsafetyupdate. (Accessed 28 October 2007)

3. FDA News. October 18, 2007. Available from; http://www.fda.gov/bbs/topics/NEWS/2007/NEW01730.html (accessed, 28 October 2007)

4. Prescriber Update, Medsafe. Nov 2006. Available from; http://www.medsafe.govt.nz/profs/PUarticles/watchingbriefsNov06.htm#Terbinafine (accessed 28 October 2007)