



Therapeutics Today

*Nollaig Shona dár léitheoirí go léir!
Happy Christmas to all our readers!*



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Go easy on the salt! – A recent meta-analysis assessed the relationship between salt intake and the risk of stroke or cardiovascular disease (CVD) (*BMJ 2009;339:b4567*). There were 13 cohort studies (n=177,025) included in the study, where follow-up ranged from 3.5-19 years. Outcomes for the analysis were relative risks (RR) for stroke and CVD according to high and low salt intake. The categorisation of salt intake differed among the studies. In total there were 5,346 strokes and 5,161 total CVD events reported. The study found that higher salt intake was associated with a greater risk of stroke (equivalent to 23% increased relative risk [RR 1.23] P=0.007). Although there was significant heterogeneity between the studies there was no indication of publication bias and sensitivity analysis showed no significant difference in the overall relative risk with removal of any individual study. There was a strong trend (not statistically significant) to an association between higher salt intake and CVD (RR 1.14), with significant heterogeneity between the studies. An accompanying editorial (*BMJ 2009;339:b4980*) concluded that this study showed that **higher salt intake was associated with an increased risk of stroke and probably CVD** and that the study is a further addition to the medical evidence on this topic.



Clonidogrel and PPIs. The NMIC has continued to receive a number of queries in relation to concomitant use of clonidogrel and PPIs, following the statement issued by the Irish Medicines Board (IMB) in June 2009 (www.imb.ie). This notified healthcare professionals of a possible interaction between PPIs and clonidogrel, resulting in a potential to increase cardiac events such as acute myocardial infarction (see *Therapeutics Today* newsletters 2009: 5, 6). The IMB has recommended that concomitant use should be avoided unless absolutely necessary. Many enquirers have requested information on alternatives to PPIs when gastroprotection is required for patients taking clonidogrel. The Summary of Product Characteristics for Plavix® contains the following information in Section 4.5:

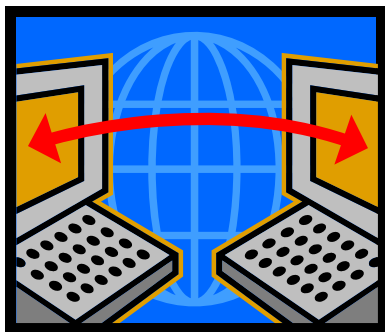
- "Since clonidogrel is metabolised to its active metabolite partly by CYP2C19, use of drugs that inhibit the activity of this enzyme would be expected to result in reduced drug levels of the active metabolite of clonidogrel and a reduction in clinical efficacy. Concomitant use of drugs that inhibit CYP2C19 should be discouraged... Drugs that inhibit CYP2C19 include omeprazole, esomeprazole, fluvoxamine, fluoxetine, moclobemide, voriconazole, fluconazole, ticlopidine, ciprofloxacin, cimetidine, carbamazepine, oxcarbazepine and chloramphenicol... Although the evidence of CYP2C19 inhibition varies within the class of Proton Pump Inhibitors, **clinical studies suggest an interaction between clonidogrel and possibly all members of this class. Therefore, concomitant use of Proton Pump Inhibitors should be avoided unless absolutely necessary. There is no evidence that other drugs that reduce stomach acid such as H2 blockers or antacids interfere with antiplatelet activity of clonidogrel.**"

In view of cimetidine's reported inhibitory effects on CYP2C19 (outlined above), some expert groups have recommended that, where gastroprotection is required for patients taking clonidogrel, a H2-receptor antagonist (but not cimetidine) might be considered instead of a PPI (www.cks.nhs.uk/antiplatelet_treatment; <http://www.mhra.gov.uk/Publications/safetyguidance>). The NMIC will continue to keep this under review and provide updates as they become available. We are happy to help with individual questions in this area – just contact us at nmic@stjames.ie



Public smoking bans are good for the heart! It has been estimated that second-hand smoke (SHS) increases the risk of acute myocardial infarction (AMI) by 25-30%. In countries where smoking prevalence is high, AMI in non-smokers is particularly increased. A recent systematic review sought to estimate the overall effect of public (i.e. workplace and public places) smoking bans on the risk of AMI in the general population (*J Am Coll Cardiol* 2009; 54: 1249-55). A total of 11 studies from 10 locations throughout North America

and Europe were reviewed. These had included approximately 24 million people and observed 215,524 cardiac events, with observation times ranging from 2 months to 3 years. The combined results suggested that community smoking bans were associated with an overall 17% reduction in the risk of AMI. Greater reductions were noted for the US sites and in those studies with longer observation periods. The greatest beneficial effects were noted among younger individuals and non-smokers. An interesting accompanying editorial (*J Am Coll Cardiol* 2009; 54:1256-7) outlines the limitations of the review in terms of heterogeneity of the primary studies, the differences in how the smoking ban has been enforced according to region and differences in the way changes in AMI were tracked. However, it concludes that a 17% risk reduction for AMI is not trivial. It suggests that it is prudent to assume that exposure to SHS may be almost as dangerous to persons with diagnosed or latent coronary disease as active smoking. It recommends that doctors should encourage initiatives like smoking bans and increased taxes on cigarettes to lower the probability of young people starting to smoke, to increase the rate at which smokers quit and lower the frequency of smoking among those not yet willing or able to quit. **The author concludes that decreased exposure to tobacco smoke is fundamental in ensuring a continuing fall in the rate of cardiovascular disease.**



Google Scholar and PubMed go head to head... A recent study compared the search engines Google Scholar and PubMed in terms of their ability to locate primary literature to answer drug-related questions (*Ann Pharmacother* 2009; 43: 478-84). Google Scholar is a beta-phase search engine produced by Google. It retrieves documents such as scholarly literature citations as well as other literature including peer-reviewed publications, books, abstracts and publications from universities and professional organisations for its database. Since its launch in 2004, use has

increased rapidly. PubMed is a free internet database, published by the National Library of Medicine, that serves as an indexing service for biomedical literature. It indexes over 17 million citations in >5,000 biomedical journals. Due to the availability of free full-text articles, it has become the most frequently used biomedical-indexing database. This study used drug information question reviews, published in the journal from Jan 2006 - June 2007, to determine the relative retrieval ability of each of the search facilities. Articles were eligible for inclusion if at least 2 key words, contained in the printed article, were included in the MeSH (PubMed medical Subject Heading) database. These terms were then searched for in Google Scholar and PubMed. A total of 22 drug information reviews, (each containing a median number of 6.5 primary literature articles) were included in the study. Overall, Google Scholar searches retrieved significantly more citations and Web pages compared with PubMed searches, using the MeSH term combinations. However, results showed no significant differences, in terms of the mean number of primary literature articles located within the first 100 citations for both Google Scholar and PubMed. Google Scholar was better at locating older articles (i.e. published prior to 2000) compared with PubMed but there was no difference for articles published after 2000. The authors concluded that while PubMed searches yielded few total citations, it appears to be more specific than Google Scholar for locating relevant primary literature articles.