

Dear Dave

Dave and other members of the bpac^{nz} team answer your clinical questions

Can **SUMATRIPTAN** be used safely with **SSRIs**

Many drug interaction programmes and texts warn against concurrent use or advise caution when sumatriptan is used with an SSRI (fluoxetine, paroxetine or citalopram). What is the basis of this interaction and can these drugs be used safely together?

Migraine and depression are common conditions and often co-exist so there is a significant potential for these drugs to be used together. Sumatriptan is a serotonin agonist and the SSRIs inhibit the re-uptake of serotonin therefore there is a theoretical potential for the drugs to increase serotonergic activity leading to serotonin syndrome. Serotonin syndrome comprises a cluster of symptoms, including altered mental status, autonomic instability, and neuromuscular abnormalities. However, milder symptoms of serotonin 'overload' may occur without the full blown syndrome.

There have been a few reports of symptoms of serotonin syndrome when sumatriptan has been given together with an SSRI.¹ Symptoms attributed to increased serotonergic activity include, restlessness, anxiety, weakness, myoclonus, loss of co-ordination, tachycardia and sweating.² Postmarketing surveillance^{1,3} has also identified cases of serotonin syndrome but such reports appear to be very rare.

Several studies have looked at the evidence of safety for the use of Sumatriptan with an SSRI. A large prospective study followed over 12,000 patients who were using subcutaneous sumatriptan for migraine. Almost 1800 of these patients also took an SSRI during the study and there was no increase in adverse effects within 24 hours of taking sumatriptan.⁴

www.bpac.org.nz keyword: "sumatriptanssri"

Who is Dave?

Pharmaceutical Programme Manager Dave Woods is a graduate of Manchester University (B.Sc. [Hons]) and the University of Otago (MPharm). Dave has extensive experience in hospital pharmacy, drug information, rational use of drugs and quality assurance. He has published on a range of subjects and holds editorial positions for several international journals.

If you have a clinical question email it to dave@bpac.org.nz

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Concurrent use of triptans (drugs in the same group as sumatriptan) and SSRIs is widespread and there has been no epidemic of the syndrome in practice even though almost 50,000 people in the USA are taking these drugs at the same time.⁵ Our analysis of Pharmhouse data using patient NHI numbers indicates that approximately 10% of people taking sumatriptan (about 1000) are also taking an SSRI.

In other countries, up to six different triptans are available, e.g. zolmitriptan, almotriptan and naratriptan. Some of these may have a greater potential to interact with SSRIs as they have different pharmacokinetic properties. In New Zealand, only sumatriptan and rizatriptan (not subsidised) are available but there is no indication that the latter has a different potential to interact than sumatriptan. Venlafaxine (a serotonin and noradrenaline re-uptake inhibitor) also has the potential to interact with sumatriptan and the same cautions apply, as with the SSRIs.

Other agents which increase serotonin levels, may also interact with sumatriptan. One such agent is St John's Wort which is freely available without prescription and in supermarkets. Authorities in the UK and Sweden have advised that St John's Wort should not be used by people taking triptans.⁶

In summary, there have been reports of serotonergic symptoms and serotonin syndrome when sumatriptan and SSRIs have been used together. In practice, such reports appear to be rare and the drugs can be used safely together in the vast majority of people. However, all people taking this combination should be advised to report symptoms of increased serotonergic activity (e.g. restlessness, tremor, sweating, shivering) particularly with initiation of treatment or with dose increases. The same cautions apply to the use of venlafaxine and sumatriptan. It is advisable to avoid St John's Wort in people taking sumatriptan or an SSRI and especially if they are taking both.

References

1. Stockley IH, Textbook of Drug Interactions. 6th ed. London, Pharmaceutical Press, 2002.
2. Gardner DM, Lynd LD. Sumatriptan contraindications and the serotonin syndrome. *Ann Pharmacother* 1998; 32:33–8.
3. Medsafe. Imigran. Data sheet 2006. Available from <http://snipurl.com/1ohaz>. Accessed July 2007.
4. Putnam GP, O'Quinn S, Bolden-Watson CP, et al. Migraine polypharmacy and the tolerability of sumatriptan: a large scale prospective study. *Cephalalgia* 1999;19:688–75.
5. Tepper S, Millson D. Safety profile of the triptans. *Expert Opin Drug Saf* 2003;2:1–9.
6. Henderson L, Yue QY, Bergquist C, et al. St John's Wort (*Hypericum perforatum*): drug interactions and clinical outcomes. *Br J Clin Pharmacol* 2002;54:349–356.



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Can you ever use **BETA-BLOCKERS** in someone with a history of **ASTHMA**



Media attention has focused recently on the tragic case of a fatal reaction to propranolol, used for migraine in a 37-year-old woman with a history of asthma.

GPs providing advice in this case expressed their unanimous opinion that it was inappropriate to prescribe a beta-blocker to an asthmatic.¹ Drug manufacturers² and almost all commonly used texts say that their use is contraindicated in asthma.

The key point in this recent case was that the history of asthma was not obtained from the patient or the notes. The take home message primarily revolves around accurate history and note taking. The HDC commissioner commented that if the information needed is not available in the notes, it is vital that the doctor concerned obtain the relevant history from the patient. “Patients cannot be relied on to volunteer all relevant details, and indeed do not have the training and experience to know what may be important. They rely on their GP to elicit key information.”³

The question remains though – can a person with asthma safely use a beta-blocker?

The answer is probably that some patients can sometimes safely take some beta-blockers, but this is not a good basis for safe prescribing!

In the 1960's, studies on earlier generations of beta-blockers, which were non-cardioselective, showed acute reductions in FEV1 and led to the recommendation that their use is contraindicated in asthma patients.^{4,5} Propranolol is non-cardioselective, that is, it not only blocks beta-1 adrenoceptors but also beta-2 adrenoceptors in the smooth muscle of the airways, potentially leading to bronchospasm.⁶

Most of the recent studies and analyses have focused on the use of cardioselective beta-blockers because of their huge potential in the treatment of cardiovascular disease, particularly in COPD patients.^{7,8} Both cardio-selective and nonselective beta-blockers have been shown to increase emergency department visits and hospitalisations in asthma patients while decreasing admissions for COPD patients.⁹

A recent article concludes “current evidence indicates that cardioselective beta-blockers are not contraindicated in patients with airways disease.”¹⁰ However, this statement is then followed by the advice that “it is still appropriate to apply certain provisos, which are themselves not evidence-based, to minimise the risk of adverse reactions”. The authors also point out that conclusions drawn from meta-analyses apply to populations and not individuals.

There are varying opinions as to whether the contraindication is absolute. In general, beta-blockers, selective or non-selective, should not be used in people with asthma. However, if there is a compelling reason for prescribing a beta-blocker to a person with asthma, such as heart failure, then consultation with a respiratory specialist is recommended. Cardioselective beta-blockers may be used for people with COPD, if they do not have concomitant asthma.

References:

1. Health and Disability Commissioner. A Report by the Health and Disability Commissioner. Case 04HDC199380. Available on line at <http://snipurl.com/1ohb4>. Accessed July 2007.
2. Medsafe. Apo-Propranolol. Data Sheet 2006. Available on line at <http://snipurl.com/1ohcc>. Accessed July 2007.
3. Paterson R. Health & Disability Commissioner. NZ Doctor Oct 2006
4. Zaid G, Beall GN. Bronchial response to beta-adrenergic blockade. N Engl J Med 1966;275:580-4
5. McNeill RS. Effect of a Beta-adrenergic-Blocking Agent, Propranolol, on Asthmatics. Lancet 1964;13:1101-2
6. van der Woude H J, Zaagsma J, Postma DS, et al. Detrimental Effects of Beta-Blockers in COPD. A concern for nonselective Beta-blockers. Chest 2005;127(3):818-824.
7. Saltpeter S, Ormiston T, Salpeter E. Cardioselective beta-blockers for reversible airway disease. Cochrane Database Syst Rev 2002:CD002992
8. Saltpeter S, Ormiston T, Salpeter E. Cardioselective beta-blockers of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2005:CD003566
9. Brooks TW, Creekmore FM, Young DC, et al. Rates of Hospitalisations and Emergency Department Visits in Patients with Asthma and Chronic Obstructive Pulmonary Disease taking Beta-blockers. Pharmacotherapy 2007;27(5):684-90
10. Sutherland T, Taylor R. Beta-blockers in asthma and chronic obstructive pulmonary disease – shouldn't be used or underused? NZFP 2007;34(1):35-37