

Selective Serotonin Re-uptake Inhibitor (SSRI) prescribing in the elderly

Pharmacological treatment of depression in old age can be difficult. Elderly patients tend to have age-related physiological changes, multiple diseases and consequently polypharmacy. Elderly patients are also predisposed to adverse events. The aim of this bulletin is to highlight some of the adverse effects and drug interactions that might occur when SSRIs are used in the elderly.

Starting SSRIs – “start low, go slow”

Physiological changes associated with aging affect the pharmacokinetics and/or pharmacodynamics of almost all drugs. Conventional doses produce higher serum concentrations than are seen in younger adults. Older adults are often more sensitive to particular serum concentrations. Therefore, it is best to prescribe small initial doses and make conservative dose increases.

Therapeutic response

The elderly show a similar time course of response to antidepressant therapy to that of younger adults. At least 4 to 8 weeks of SSRI therapy should be allowed for a clinical response. In general, if SSRI therapy is discontinued, the dose should be tapered gradually to minimise the risk of withdrawal symptoms such as dizziness, anxiety and headache.

Adverse effects

The elderly are more prone to experiencing adverse drug reactions. Those most commonly associated with SSRIs include gastrointestinal disturbances and bleeds, headache, insomnia and somnolence. These can be minimised by slow dose escalation. Some adverse effects particularly relevant to the elderly include:

Hyponatraemia. Most cases of SSRI-induced hyponatraemia have occurred in elderly individuals, usually within the first few weeks of therapy. Hyponatraemia resolves once the SSRI is discontinued but may recur if the patient is rechallenged with the same or different SSRI. (see previous Bulletin: Drug Induced Hyponatraemia February 2006 on intranet)

Increased risk of gastrointestinal bleeding. The risk of bleeding appears to be increased over 3-fold (a direct serotonin effect). Concurrent use of a proton pump inhibitor should be considered in those patients at increased risk of gastrointestinal injury.

Increased risk of falls. Sedation, agitation, post-prandial hypotension, bradycardia, orthostatic hypotension and syncope have all been proposed as possible explanations.

Decreased bone density. In a prospective population based study, daily SSRI use was associated with a 2-fold increased risk of fracture, increased odds of falling and lower bone mineral density at the hip. The risk was dose dependent. Depression does not appear to be a confounding factor causing lower bone density.

Drug Interactions:

Pharmacokinetic - affect drug concentrations

All SSRIs have the potential to interact with drugs metabolised by the cytochrome P450 system (see following table). Potential interactions should be considered when prescribing drugs that are metabolised by this system. These interactions are dose-dependent and are especially important for drugs with a narrow therapeutic window.

Inhibition of cytochrome P450 isoenzymes by SSRIs

SSRIs funded in NZ	Cytochrome P450 isoenzyme				
	3A4	2D6	2C19	2C9	A12
Citalopram	0	+	0	0	0
Fluoxetine	+ to ++	+++	+ to ++	++	+
Paroxetine	+	+++	+	+	+

0 = minimal or no inhibition, + = mild inhibition, ++ = moderate inhibition, +++ = potent inhibition

Pharmacodynamic - affect drug action

The most serious pharmacodynamic interaction involving SSRIs is Serotonin Syndrome. This can occur when SSRIs are used alone but more usually occurs when they are co-prescribed with other serotonergic agents (see table below). Symptoms (in order of increasing severity) include: restlessness, sweating, tremor, shivering, myoclonus, confusion, convulsions, death. Elderly patients are more at risk, in part, because they have more comorbidities and tend to be prescribed more drugs.

Clinically significant SSRI drug interactions in the elderly

Interacting drug/class	Possible effects
Irreversible MAOIs, tricyclic antidepressants (TCAs), lithium, tramadol, pethidine, selegiline, moclobemide, dextromethorphan	Serotonin Syndrome
Diuretics	SIADH and hyponatraemia
NSAIDs, warfarin	Gastrointestinal bleeding, bruising, stroke
Antipsychotics, particularly haloperidol and fluphenazine	Extrapyramidal adverse effects e.g. parkinsonism and dyskinesias
Tamoxifen	Reduced tamoxifen activity
Anticholinergics	Delirium, urinary retention
TCAs, theophylline	Seizures, coma
Codeine	↓ metabolism to morphine

Summary

Overall, SSRIs are generally effective and well tolerated in the elderly. However, there are some potential drug interactions and adverse events that are particularly relevant in this patient group. The use of SSRIs in the elderly should therefore include the “start low, go slow” philosophy, suitable monitoring and awareness of drug interactions.