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SAFER USE OF HIGH RISK MEDICINES

Waitemata District Health Board
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CITALOPRAM AND ESCITALOPRAM - SAME BUT DIFFERENT

- TAKE CARE WITH ESCITALOPRAM – DOSES ARE HALF THAT OF CITALOPRAM
- SCREEN FOR RISK FACTORS OF QT PROLONGATION
- ASK ABOUT ADVERSE EFFECTS
- MONITOR FOR HYPONATRAEMIA

Citalopram and escitalopram are both useful SSRIs (Selective Serotonin Reuptake Inhibitors) for the treatment of adult depression. Escitalopram is the s-enantiomer, and active part of citalopram, which is a mix of s- and r-enantiomers. There is increasing evidence to suggest that escitalopram is more clinically effective than citalopram.[1]

TAKE CARE WITH ESCITALOPRAM – DOSES ARE HALF THAT OF CITALOPRAM

The optimal dose for the treatment of moderate depression is: **citalopram 20mg daily OR escitalopram 10mg daily**[2,3]

It is important that prescribers are aware that there is a dose difference because confusion between these medicines could lead to escitalopram overdosing.

A small proportion of patients may eventually require the *maximum* dose of citalopram 40mg or escitalopram 20 mg.[2] There is no clinical benefit of using higher doses than this, but a greater risk of adverse effects including QT prolongation. Higher doses require informed consent and regular (6 monthly) ECGs.

For older adults, and people with mild to moderate hepatic impairment (Child-Pugh Criteria A and B),[3] the maximum dose should not exceed citalopram 20mg or escitalopram 10mg. Dose adjustment is not necessary for mild or moderate renal impairment; there is no dose information for severe renal impairment (CrCl <20mL/min).[3]

Recommended daily doses of citalopram and escitalopram

Patients	Citalopram		Escitalopram	
	Starting dose	Maximum dose	Starting dose	Maximum dose
Adult 18-65 years without risk factors	20mg	40mg	10mg	20mg
Adult >65 years or impaired hepatic function	10mg	20mg	5mg	10mg
Taking omeprazole*	20mg	20mg	5mg	10mg

Note: It may be helpful to try half the recommended starting dose for the first week if there are concerns about initial adverse effects.

*Omeprazole increases plasma levels of citalopram and escitalopram, increasing the risk of QT prolongation and hyponatraemia.

As with any SSRI, allow at least 2-4 weeks at each dose level to assess efficacy before *increasing* the dose.[4] If there is no response to treatment after 4-6 weeks, consider a different antidepressant. Take care when switching to non-SSRIs, as a wash-out period of 2-7 days is generally recommended.[5] There is a risk of withdrawal effects if doses are *reduced* abruptly; gradually taper down over 2 to 4 week intervals[2,3] Withdrawal effects include agitation, dizziness, anxiety, confusion, insomnia, and headache, gastrointestinal upset and visual disturbances. These symptoms are generally mild to moderate and occur within the first few days of dose reduction or discontinuation. They are usually self-limiting and resolve within 2 weeks.[2,3]

SCREEN FOR RISK FACTORS OF QT PROLONGATION

Citalopram is associated with a dose-dependent increase in QT interval prolongation,[6] which could potentially lead to Torsade de Pointes. For this reason, the recommended maximum dose is 40mg per day. Citalopram is contraindicated if patients have congenital long QT syndrome, or if they are taking other medicines that prolong the QT interval, eg Class 1a and III antiarrhythmic.

There is also a risk of dose-dependent QT prolongation with escitalopram; the maximum daily dose of escitalopram must therefore not exceed 20mg per day.

Patients should be screened for risk factors for QT prolongation before starting treatment.[7] Risk factors include:[2,3,8]

- Female gender
- Older age
- Underlying heart disease
- Recent myocardial infarction
- Congestive heart failure
- Bradyarrhythmias
- Predisposition to hypokalaemia and hypomagnesia
- Renal impairment (CrCl <20ml/min)

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CITALOPRAM AND ESCITALOPRAM

- Hepatic disease
- Starvation or obesity
- Other medicines that can prolong QT interval eg **lithium**, **sotalol**, **omeprazole**

Note: If serum electrolytes are out of range, these should be corrected before therapy begins.[3]

If patients have pre-existing cardiac disease or multiple risk factors for QT prolongation, ECG monitoring should be performed prior to initiating citalopram or escitalopram, after dose increases, and if there are symptoms indicative of arrhythmia (dizziness, palpitation, syncope or seizures).[3] Advise patients about these symptoms so they can seek medical advice immediately if they occur.[8] These patients should have an ECG to assess heart rate and rhythm, and blood tests to check for hypokalaemia and hypomagnesia.[8]

ASK ABOUT ADVERSE EFFECTS

Prior to initiating any SSRI, discuss the possibility of adverse effects with the patient and their family. Inform them that nausea, anxiety, insomnia, agitation, hypomania, worsening of depression and suicidal ideation could occur in the first few days or weeks. Dose-related adverse effects include fatigue, impotence, increased sweating, somnolence, and insomnia, so use the lowest effective dose possible.

Suicidality

All antidepressants are associated with an increased risk of suicidality, particularly in young adults.[2,3] This may be due to an increase in anxiety, restlessness or agitation especially in the first few days of treatment. Contact with the patient in the first week of treatment is important to determine suicidal ideation and any unusual changes in behaviour.[2]

Citalopram and escitalopram are not recommended if under 18 years of age.[2,3]

Bleeding

SSRIs all have the potential to increase the risk of bruising, epistaxis, vaginal and gastrointestinal bleeding. Take special care if also taking aspirin, NSAIDs, warfarin and other anticoagulants, or if patients have a past history of bleeding.[2,3]

Sexual dysfunction

Sexual dysfunction in men and women is associated with depression and with SSRIs.[2] All phases of sexual response can be affected; decreased libido and delayed orgasm are most commonly reported. Discuss these issues openly when considering treatment and as treatment progresses;[2] a dose reduction or an alternative antidepressant may be required.

Note: There is some evidence to suggest that SSRIs are useful for the treatment of premature ejaculation. This is an unregistered indication so make sure that the patient is aware of this, and that SSRIs can affect sperm quality in case the patient is currently hoping to conceive.

Serotonin syndrome

This potentially life-threatening drug reaction results from an excess of serotonergic activity, and can develop from high doses of a single serotonergic medicine, or if a combination of them are used together. Serotonergic medicines include antidepressants, **lithium**, **St John's wort**, **sumatriptan**, **tramadol** and **pethidine**.[9]

Serotonin syndrome can also occur when switching between antidepressants without an adequate 'washout period'. A triad of neuromuscular, autonomic and mental status changes occur, which may include myoclonus, shivering and agitation.[9] In all suspected cases, discontinue serotonergic medicines and seek specialist advice.

Note: In cases of severe depression, psychiatrists may use higher than recommended doses of SSRIs or combinations serotonergic medicines.

MONITOR FOR HYPONATRAEMIA

Hyponatraemia is considered a rare adverse reaction that is associated with all SSRIs.[2] Take special care when prescribing them to patients with existing risk factors for hyponatraemia including:

- Female gender
- Older age
- Low body weight
- Cirrhosis
- Previous history of hyponatraemia
- Reduced renal function
- Concurrent use of other hyponatraemic medicines (eg diuretics, **omeprazole**)[10,11,12]

Hyponatraemia is most likely to occur during the first 4 weeks of treatment. Observe for signs of hyponatraemia which include dizziness, nausea, lethargy, confusion, cramps and seizures.[11]

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CITALOPRAM AND ESCITALOPRAM

For high risk patients:

- Check baseline sodium before starting the SSRI and correct it if necessary
- Check sodium after the first 2 weeks of treatment and again after 3 months
- Consider checking sodium after a dose increase or following the addition of any other potentially hyponatraemic medicine
- If a drop in sodium is observed without clinical symptoms, monitor sodium closely, as it may return to normal.[10,11]

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