MIL

Oxford University Hospitals NHS
NHS Foundation Trust

Volume 3, No. 1 **September 2016**

This Medicines Information Leaflet is produced locally to optimise the use of medicines by encouraging prescribing that is safe, clinically appropriate and cost-effective to the NHS.

Initiating antidepressants for the treatment of depression in adults in hospital

Depression is two to three times more common in people with chronic physical illness than in the general population.[1]

Diagnosis: persistent low mood and biological features (low energy, psychomotor retardation, poor sleep, poor appetite, poor concentration) or cognitive features (loss of interest, amotivation, guilt, sucidiality).

Symptoms must have been present for a minimum period of two weeks.

Diagnosis can be difficult as biological features may be confounded by the presence of severe physical illness (eg hypoactive delirium in the elderly). Collateral history from families, GPs or advice from a psychiatrist is often necessary.

NICE has published guidance for the treatment of mild, moderate and severe depression[2]:

- Antidepressants are indicated as first line treatment for moderate and severe depression.
- First line treatment for mild depression is non-pharmacological, usually accessed through primary care.

Ideally, starting antidepressants is a decision made with a fully informed patient. In general, in a hospital setting, this may not always be possible and appropriate follow-up either with the GP or psychiatric team improves treatment adherence and outcome.[3]

Starting antidepressants

The choice of antidepressant should be based on the following:

- **Patient preference**
- **Past response (effectiveness, side effects)**
- **Side effect profile**
- **Risk of overdose**
- **Co-morbid medical conditions**
- **Drug interactions**

NICE recommends that SSRIs (Selective serotonin reuptake inhibitors) are generally used as first-line as

TABLE 1 : Antidepressants that can be initiated at OUH (unless advise from psychiatric medicine): confirm diagnosis, if moderate or severe start antidepressant and titrate over 1-2 weeks to minimum effective dose.[4]

Drug of choice	Starting dose	Starting dose in the elderly	Minimum effective dose **(Assess response after 2 weeks at minimum effective dose)**	Time of dose	If drug **poorly tolerated** switch to another in same class or different class **Titrate up to minimum effective dose.** Assess weekly for further 1-2 weeks and if no improvement consider asking psychiatrist advice or increase dose. If discharged request GP review. **Drug Effective** – If first episode continue for 6-9 months after symptom resolution. If recurrent depression consider using for at least 2 years after symptom resolution.
Sertraline	50mg	25mg	50 -100mg	Morning	
Mirtazapine **(1st choice if sedation required)**	15mg	7.5mg	15mg	Night time	
Citalopram	10mg	10mg	20mg	Morning	

they are safer in overdose and generally better tolerated than other classes of antidepressant.

Age

Under 18s - psychological therapy should be offered as a first line treatment. An antidepressant can only be prescribed following assessment and diagnosis by a child and adolescent psychiatrist.

Side effects

The majority of these are mild and transient. Most side effects are a class effect arising from effects on other neuroreceptors such as muscarinic, histamine, $5HT_3$, α_1.

In summary;

1) **SSRIs** cause more GI upset, headaches, stimulation/agitation and sexual side effects (although all antidepressants have sexual side effects)

2) **TCAs'** (Tricyclic antidepressants) common side effects are mediated through their anticholinergic effects (blurred vision, dry mouth, confusion, constipation, urinary retention). TCAs are also prone to cause weight gain.

Individual antidepressants are also associated with specific side effects. **Mirtazapine**, for example, is sedative and causes weight gain through increased appetite. **Venlafaxine** should be used with caution in people with high blood pressure.

Safety in overdose

SSRIs are highly unlikely to be lethal in overdose, and their relative safety over TCAs is the main reason for their first-line use.

Hunter serotonin toxicity criteria.[5] (84% sensitive, 97% specificity)

IN THE PRESENCE OF 1 OR MORE SEROTONERGIC DRUGS (WITHIN THE PAST 5 WEEKS)	Serotonin toxicity or syndrome
If patients have spontaneous clonus	YES
If patients have inducible clonus *and* either agitation *or* diaphoresis	YES
If patients have ocular clonus *and* agitation *or* diaphoresis	YES
If patients have tremor *and* hyperreflexia	YES
If patients are hypertonic *and* have a temperature > 38°C *and* have ocular clonus *or* inducible clonus	YES

Like all drugs that reduce 5-HT breakdown they can cause the 'serotonin syndrome'. This can occur at therapeutic doses of SSRI if the patient is on or has recently received other agents affecting serotonin metabolism.

Treatment of SSRI overdose is supportive including use of supplemental oxygen, IV fluids and cardiac monitoring. Benzodiazepines can be used for short term management of agitation. Serotonergic drugs should be stopped.

TCAs have anticholinergic and arrythmogenic properties, and are cardiotoxic in overdose. TCAs cause tachycardia, reduce blood pressure and prolong the QTc interval. Torsades des pointes, is associated. TCA overdose must be managed as a potential emergency with senior input and liaison with intensive care physicians.

Co-morbid medical illness & antidepressants

Depression co-morbid with chronic physical illness can lead to poorer treatment response and worse prognosis for both. There is also the risk of drug interactions, especially with SSRIs.

TCAs should only be used with caution in cardiac disease due to their anticholinergic and arrythmogenic actions.

- Only the three antidepressants listed in table 1 should be initiated at the OUH foundation trust.
- In cardiac patients who are already on TCAs and are stable, the TCA should not be stopped unless clinically indicated. The reason for doing so should be clearly documented in the medical notes/discharge summary.
- Evidence indicates mirtazapine and sertraline (other SSRIs are also safe) are safest in cardiac disease.
- SSRIs can increase the risk of upper gastrointestinal bleeds. The risk is elevated in the elderly, those with bleeding disorders or co-prescribed aspirin, NSAIDs, steroids or warfarin. It is important to consider stomach-protective medication.
- Hyponatraemia is a risk with all antidepressants, especially in medically ill, elderly, female patients. This is usually an early side effect of treatment, probably mediated through SIADH. Monitoring in elderly patients is recommended.[4]
- Antidepressants are associated with postural hypotension and should therefore be used with caution in the elderly at risk of falls.[3]

- TCAs are associated with weight gain and should be used with caution in patients with diabetes.[3]

For any woman who is pregnant or breast-feeding, specialist psychiatric advice must be sought when prescribing antidepressants.

Stopping

There is a risk of "discontinuation symptoms", experienced by up to a third of patients.[4] These are usually a benign and self-limiting phenomena but can be uncomfortable. Discontinuation symptoms are more likely with long term treatment, higher doses of medication and shorter half-life drugs such as paroxetine and venlafaxine. Symptoms include flu-like symptoms, 'electric shock like' sensations, dizziness exacerbated by movement, insomnia, excessive (vivid) dreaming, irritability, crying spells.

Stopping antidepressants before the depressive episode has resolved increases the risk of relapse. Stopping antidepressants should therefore always be discussed with the prescriber and be a joint decision between doctor and patient. Alternative management of the depressive illness, if indicated, should ideally be established beforehand.

Switching antidepressants

Switching antidepressants can be a complex process due to variations in half-life, the potential for interactions and risks of serotonin syndrome. Switching should be managed with specialist advice from a psychiatrist and/or Medicine Information.

References

1. NICE Clinical Guideline 91 Oct 2009
2. NICE Clinical Guideline 90 Oct 2009
3. *Anderson,IM Selective serotonin reuptake inhibitors vs tricyclic antidepressants: a meta-analysis of efficacy and tolerability. Journal of Affective Disorders,*
4. Taylor D, Paton C, Kapur S *The Maudsley Prescribing Guidelines in Psychiatry, 12th Edition* (2015) Wiley-Blackwell
5. Whyte, IM et al, QJM: monthly journal of Association of Physicians 2003 Sep;96(9):635-42 The Hunter Serotonin Toxicity Criteria: simple and accurate diagnostic decision rules for serotonin toxicity.

Prepared by: ***Zehanah Izmeth (Consultant in Psychiatry) on behalf of Psychological Medicine Team***

With advice from: *Katharine Westcott (Medicine Information Pharmacist)*

Review date: *September 2019*