Recommended Monitoring for Antidepressants

For General Practitioners

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Introduction

Dear Colleague,

Thank you for your interest and helping to make antidepressants safer.

The following list includes some major potential side effects to look out for in a general practice. I will update this list over time on jonathanhaverkampf.ie. However, it cannot be complete and some information may be outdated or incorrect. If in doubt, please consult the current medical literature.

A baseline at the beginning of therapy is good practice, as is asking routinely for potential side effects.

You may be asked by patients about St. John's Wort as a 'natural' remedy, which has shown to have mild to moderate antidepressant effectiveness. However, besides side effects such as heightened light sensitivity and allergic skin reactions, clinical studies demonstrate that hypericum extracts increased the metabolism of various drugs, including combined oral contraceptives, cyclosporine, and indinavir. Hyperforin, a constituent of St. John's wort with antidepressant activity, has been shown to result in induction of CYP3A4 expression. Because CYP3A4 is involved in the oxidative metabolism of the majority of all drugs, hypericum extracts are likely to interact with a vast number of drugs. [1]

I can be reached by email (jonathanhaverkampf@gmail.com) or by phone (+353 874343347) and am happy to answer any questions you may have.

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All Antidepressants

General Physical Assessment

- blood pressure, heart rate, height, weight, BMI **at least every 6 months**
  Venlafaxine has been associated with elevated blood pressure, especially at high doses (300-375mg/day).
  In one study, the rates for 'postural hypotension' were as follows: Nefazodone (2.8%), tricyclic antidepressants (10.9%), SSRI (1.1%), and placebo (0.8%). [2]
- temperature and respiratory rate as clinically indicated

Pregnancy Status in females of childbearing age

- ask for reproductive status including last menstrual period, last pelvic exam/pap smear and contraceptive use

Renal function testing

- medications excreted renally include
  - bupropion
  - duloxetine/Cymbalta(R)
  - venlafaxine
  - mirtazapine
  - tricyclic antidepressants
  - escitalopram
    and others

Liver enzymes (Aminotransferases)

Although an infrequent event, drug-induced liver injury (DILI) from antidepressant drugs may be irreversible. Aminotransferase surveillance is the most useful tool for detecting DILI, and prompt discontinuation of the drug responsible is essential. [3]

The antidepressants associated with greater risks of hepatotoxicity are iproniazid, nefazodone, phenelzine, imipramine, amitriptyline, duloxetine, bupropion, trazodone, tianeptine, and agomelatine. The antidepressants that seem to have the least potential for hepatotoxicity are citalopram, escitalopram, paroxetine, and fluvoxamine. Cross-toxicity has been described, mainly for tricyclic and tetracyclic antidepressants. [3]

Assess for Risk of Serotonin Syndrome (potentially lethal)

- symptoms include abdominal pain, diarrhoea, flushing, sweating, hyperthermia, lethargy, mental status changes, tremor, renal failure, shock

- be cautious when combining serotonergic medications such as triptans for migraines e.g. Imitrex, synthetic opioids (tramadol/Ultram®, methadone), the antibiotic linezolid/Zyvox®

Other potential side effects that may require action and should be specifically asked for

- changes in appetite
- sleep disturbances
- sexual function (menstrual disturbances, libido disturbances or erectile/ejaculatory disturbances)
- orthostatic hypotension

Abdominal girth **at least every 6 months**

- particularly with the TCAs including
    - amitriptyline
    - clomipramine
    - doxepin
    - imipramine
- mirtazapine

Bone Density

Depression and some treatments including SSRIs have been linked to a decrease in bone density

- If indicated, refer for bone density monitoring and treatment to reduce bone loss (e.g. calcium, vitamin D, weight bearing exercise, etc.)

Review Past Medical History Including Review of All Medications at least **annually**

- assess allergies, current medications including over-the-counter and herbal supplements
- surgeries, hospitalizations

Specific Antidepressants

Selective Serotonin Reuptake Inhibitors (SSRIs)

e.g. citalopram, escitalopram, fluoxetine, fluvoxamine, sertraline

Bleeding Risk

- Identify whether concomitant medications may affect clotting.
- SSRIs may potentiate the hypoprothrombinemic effects by inhibiting serotonin uptake by platelets.
- Monitor for signs of bleeding.

Fasting Blood Glucose

Use of SSRIs was associated with lower insulin secretion in nondiabetic participants and an increased risk of insulin dependence in type 2 diabetics in older adults. However, additional studies are required to confirm our results. [4]

ECG if indicated

SSRIs may in combination with some medication lead to QT interval prolongation.

Tricyclic antidepressants (TCAs)

e.g. amitriptyline, desipramine, imipramine, nortriptyline, protriptyline

Electrocardiogram (ECG)

- TCAs can cause arrhythmias, and heart block in patients with pre-existing conduction disorders.
- Evaluate patients for cardiac risk factors such as a personal history of heart disease or syncope, a family history of sudden death under the age of 40, or congenital long QT syndrome. Avoid TCAs if recent MI, history of ventricular arrhythmia or other conduction defects.
- Baseline ECG if cardiac risk factors are present or patient is older than 50 and a follow up ECG if the patient has symptoms associated with QT interval prolongation such as syncope

Plasma levels

- drug interactions that can greatly elevate plasma levels

Thyroid Function at least **annually**

Tricyclic antidepressant drugs complex with iodine and thyroid peroxidase and deactivate them, induce deiodinase activity and interfere with the hypothalamo-pituitary-thyroid (HPT) axis by decreasing TSH response to TRH. [5]

Liver Function Tests

Fasting Blood Glucose

Lipid Panel

- total cholesterol, LDL, triglycerides and HDL at baseline and as clinically indicated

The unfavourable effect of weight gain promoting antidepressants (e.g., tricyclics, mirtazapine) on serum lipid parameters (i.e., triglycerides and low-density lipoprotein cholesterol) is a consistent finding. Weight-neutral antidepressants (e.g., bupropion, venlafaxine, duloxetine), however, are less likely to disrupt the lipid milieu. [4]

Mirtazapine

Lipid Panel

- total cholesterol, LDL, triglycerides and HDL at baseline and as clinically indicated
- Mirtazapine is extensively metabolized in the liver. [6]

Fasting Blood Glucose

Weight

The antidepressant therapy with mirtazapine seems to be associated with a significant increase in body weight, body fat mass, and leptin concentration. In contrast to other psychotropic medications inducing weight gain, such as some second-generation antipsychotics, mirtazapine treatment is unlikely to influence the glucose homeostasis. [7]

(The risk of QT/QTc prolongation with the majority of newer non-SSRI antidepressants at therapeutic doses seems low. [7])

Venlafaxine

(e.g. Efexor®)

Blood Pressure

- Venlafaxine has been associated with elevated blood pressure, especially at high doses (300-375mg/day). Although there are studies that cannot reproduce this observation. [12]

(The risk of QT/QTc prolongation with the majority of newer non-SSRI antidepressants at therapeutic doses seems to be low. [12])

Bupropion

Screen for history of seizures

- Bupropion is known to reduce seizure thresholds, with a seizure rate of about 1 in 1000 subjects treated. [9]
- Bupropion is contraindicated if there is a pre-existing seizure disorder. It should be avoided in those at higher risk for seizures, including those undergoing abrupt discontinuation of alcohol or benzodiazepines/sedatives, those with eating disorders including anorexia or bulimia, head trauma or brain tumours.

Blood pressure

- Assess blood pressure before initiating treatment with Wellbutrin XL, and monitor periodically during treatment [10]

Nefazodone

Liver Function Tests

Nefazodone belongs to a group of antidepressants with a higher risk of hepatotoxicity. [2] [3]

- Do not initiate treatment if active liver disease and use caution with elevated baseline serum transaminases. Advise patients to be alert for signs of liver dysfunction such as jaundice, GI complaints as nefazodone has potential for hepatic injury.
- If AST or ALT levels increase to three times the upper normal limit, withdraw the drug and do not restart.

MAO Inhibitors

e.g. phenelzine, tranylcypromine, moclobemide, selegiline

Hepatic function (at least the irreversible non-selective MAO inhibitors: phenelzine, tranylcypromine, etc)

Renal function (at least the irreversible non-selective MAO inhibitors: phenelzine, tranylcypromine, etc)

Assess diet (to avoid the tyramine reaction)

(The selective monoamine oxidase-B inhibitor selegiline and the selective and reversible inhibitor of monoamine oxidase-A (RIMA) seem to have a much lower or no risk of causing a hypertensive crisis [13])

- avoid tyramine containing foods and caffeine during treatment and for 2 weeks after discontinuing
- (combinations may cause severe headaches, increased blood pressure or irregular heartbeat. Tyramine-containing foods to avoid include aged cheeses, aged/processed meats and pickled fish, beer, ale, wine, sherry, hard liquor, liquors, avocados, bananas, figs, raisins, soy sauce, miso soup, yeast/protein extracts, bean curd, or over-ripe fruit. Also, avoid caffeine including tea, coffee, chocolate or cola)

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