

12 - Other antidepressants

Other antidepressants

© SPMM Course agonists, (e.g. buspirone) and bupropion (being a dopamine reuptake inhibitor) can reverse sexual dysfunction related to SSRI use. A nitric oxide-dependent second messenger (cGMP) mediates penile vasodilatation. cGMP is eventually broken down by phosphodiesterase type 5 enzyme. Sildenafil is an inhibitor of phosphodiesterase type 5, an action that enhances penile erection in patients with erectile dysfunction. Sildenafil (Viagra) has been tried successfully in the treatment of SSRI-induced erectile dysfunction. The side effects of sildenafil include headaches (most common), dizziness, blurred vision and a blue tinge to vision. Very rarely, persistent painful erection (priapism) can occur. Sildenafil must be avoided by patients with arrhythmias, unstable angina / uncontrolled hypertension.

Other antidepressants Venlafaxine: Sweating is more common than in SSRIs and is treated by terazosin. Significant numbers of patients receiving doses above 300mg/day experience an increase in diastolic blood pressure. This risk is not restricted to those with preexisting hypertension. Mydriasis and exacerbation of angle closure glaucoma are reported with venlafaxine; significant discontinuation reactions are reported due to the shorter half-life of venlafaxine - tapering gradually over 2-4 weeks is recommended. Duloxetine has side effects similar to venlafaxine, but fewer propensities to affect blood pressure. Trazodone is associated with priapism that can be serious if unattended. The first step in the emergency management of priapism is the intracavernosal injection of an alpha1 agonist such as metaraminol or epinephrine. The risk of priapism is greatest during the early phase of treatment. Nefazodone inhibits CYP3A4 and can cause serious hepatic damage and hence not used as often now. Though anticholinergic effects are predominantly absent, alpha1 antiadrenergic effects can produce pseudo-anticholinergic symptoms. Afterimage formation similar to the LSD related tracking phenomenon is reported in up to 12% patients on nefazodone. Both trazodone and nefazodone have a favourable profile for elderly and those with cardiac illness. Bupropion has a very different side-effect profile than the conventional antidepressants. It has no anticholinergic effects, does not cause sedation or weight gain and cause almost negligible sexual side effects compared to other classes of antidepressants. It does not cause orthostatic hypotension or cardiac side effects. It can exacerbate ADHD, eating disorders and tics in those with ADHD. It can enhance sexual activity unlike SSRIs; it increases the risk of seizures in a dose-dependent fashion. Headache, insomnia, dry mouth, tremor, and nausea are the most common side effects of bupropion. Severe anxiety or panic can be exacerbated by bupropion. Due to its effects on dopaminergic neurotransmission bupropion can cause

© SPMM Course psychotic symptoms as well as delirium. Bupropion can cause word-finding difficulties in some patients. Agranulocytosis is reported with mirtazapine use. Hence, signs of

infection need to be promptly followed. Bupropion can increase concentrations of haloperidol. Bupropion + MAOI can cause serotonin syndrome; 2-week washout period is recommended. CYP3A4 inhibitors such as erythromycin, itraconazole, nefazodone and grapefruit juice, increase bupropion plasma concentrations. Bupropion does not cause weight gain, sexual dysfunction, discontinuation symptoms, or significant sleep disturbance. It does not produce sedation. Mianserin and mirtazapine produce drowsiness during the first weeks of treatment but has a low propensity to produce orthostatic hypotension or cardiac effects. Increased weight gain and appetite are also noted while sexual side effects are minimal. 5-HT₃ blockade is associated with a reduction in nausea and vomiting; hence to treat depression associated with cancer chemotherapy, mirtazapine is a preferred option. Reboxetine is a noradrenaline reuptake inhibitor (NARI) with negligible serotonergic effects. It has a safe cardiovascular profile and can be used in the elderly. Atomoxetine belongs to the same group but not used as an antidepressant; it is used in ADHD. Reboxetine has a specific side-effect profile linked to the noradrenergic system. Urinary hesitancy has been observed in around 10% of male patients taking part in the clinical trials. Relief from this side effect could be achieved by using tamsulosin, a peripheral alpha₁-receptor blocker or doxazosin with a similar mechanism of action as tamsulosin. MAOIs such as phenelzine can induce orthostatic hypotension, pedal edema and insomnia. Apart from cheese reaction, MAOIs can also cause serotonin syndrome in combination with serotonergic agents. Tranylcypromine, and phenelzine to some extent can have stimulating effects leading to insomnia - hence the last dose is best given before 6 PM. Weight gain and sexual dysfunction are also reported. Cheese reaction: o MAOIs and tyramine (and other monoamine) rich foods interact to cause cheese reaction or tyramine reaction. o Tyramine has both direct and indirect (via vesicular release) sympathomimetic actions that develop 20 min to 1 h following ingestion of food. o It is characterized by nausea, apprehension, occasional chills, sweating, restlessness and hypotension with occipital headache, palpitations, and vomiting. o Sympathetic overdrive manifests as piloerection dilated pupils and fever. If severe cerebral hemorrhage and death can occur.

© SPM Course o In terms of the frequency and severity of the hypertensive crisis, the reversible MAOIs are safer. o Food materials to be avoided include any mature cheese such as Stilton, blue cheese, old cheddar and mozzarella. Fish, cured meats, sausage must be avoided together with mature poultry, wild game etc., liqueurs and concentrated yeast extract. o An MAOI-induced hypertensive crisis can be treated with alpha-adrenergic antagonists such as phentolamine or even chlorpromazine, which is immediately available in most psychiatric wards. This can lower blood pressure in few minutes.

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