

10 - Tricyclic agents

Tricyclic agents

© SPMM Course 4. Antidepressants - adverse effects Tricyclic agents Side effects of TCAs are related to anticholinergic, antihistaminic and antiadrenergic properties. Clomipramine is a more selective inhibitor of serotonergic reuptake selective; desipramine is the most noradrenergic selective of TCAs. Amoxapine, nortriptyline, desipramine, and maprotiline have the least anticholinergic activity; doxepin has the most antihistaminic activity. The TCAs are less likely to cause sexual dysfunction and insomnia than the SSRIs. Amitriptyline is associated with weight gain (antihistaminic effect - weight gain can also occur secondary to 5HTc antagonism in other antidepressants). TCAs may cause QT prolongation. Even at therapeutic doses, the TCAs cause tachycardia, flattened T waves, prolonged QT intervals, and depressed ST segment. TCAs are lethal in overdose, causing cardiac arrhythmias and anticholinergic delirium. This may occur 3-4 days after overdose due to the long half-life. No specific antidote available; needs lavage and QRS monitoring. Anticholinergic delirium is characterized by symptoms often described as 'Mad as a hatter, (confusion, disorientation, visual hallucinations), Hot as a hare (hyperpyrexia), Blind as a bat (loss of visual accommodation), Red as a beet (peripheral vasodilatation) and Dry as a bone (drying of mucous membranes)'. Amoxapine can cause hyperprolactinemia as it has dopamine antagonistic effects. SIADH and hyponatremia can occur with TCAs. Fine rapid tremor and dysarthria are sometimes reported with TCAs. Tricyclic agents such as amitriptyline and imipramine and the nontricyclic agents such as mianserin hydrochloride have been documented to precipitate an attack of angle closure glaucoma. TCA discontinuation: Can cause cholinergic rebound - best to reduce 25 to 50mg per 2-3 days. Discontinuation reaction may occur as early as 48 hours or as late as 2 weeks after discontinuation. Propantheline or reinstitution of withdrawn TCA can reduce cholinergic rebound symptoms.

© SPMM Course NMS vs. serotonin syndrome

NMS Serotonin syndrome Dopamine antagonism and suspected hypothalamic mediated sympathetic overdrive. Excess serotonin availability Onset subacute - days to weeks Sudden minutes to hours onset Resolves in 2 weeks - depending on t_{1/2} of offending drug Resolves as soon as excess serotonin is reduced - in 24 hours generally No myoclonus Myoclonus prominent Hypomania, not a feature Hypomania may be seen Reflexes normal or absent Hyperreflexia seen Rhabdomyolysis, resultant renal failure and acidosis occur commonly Muscle breakdown not common • Serotonin syndrome is a result of excessive serotonergic transmission in brain. Although no single mechanism appears to be responsible for all of the noted effects, most CNS symptoms are possibly mediated via 5HT_{2A} receptor stimulation. Mechanism of Serotonin Syndrome Mechanism of Serotonin Syndrome • It is characterized by diarrhea, myoclonus, diaphoresis, hyperactive reflexes, ataxia, hypomanic or labile mood, tremors and disorientation. • It may mimic

NMS or anticholinergic syndrome in those receiving psychotropics. Features of serotonin syndrome

Features of serotonin syndrome •Any serotonergic agent on overdose – including SSRI and TCA antidepressants, fenfluramine, LSD, ecstasy, anti-migraine (e.g. sumatriptan) drugs. •High risk with combinations of SSRI and MAOI or RIMA or SSRI themselves, or TCAs especially serotonergic, or SNRI, lithium or L-tryptophan. TCA and MAOI combinations. Tramadol, pethidine, meperidine can also cause serotonin syndrome on combination with the above agents. •Oxazolidinone antibacterial linezolid (which is a reversible non-selective MAOI), tetrabenazine (acts via dopamine and serotonin depletion at nerve endings), entacapone (COMT inhibitor) and selegiline are also implicated. Drugs with high risk of serotonin syndrome: Drugs with high risk of serotonin syndrome: •Withdraw the offending agent •Supportive care: correction of vital signs •Benzodiazepines •5HT_{2A} antagonists: cyproheptadine, atypical antipsychotics, chlorpromazine (? mirtazapine – controversial reports) •In severe cases neuromuscular paralysis and intubation may be required Treatment of Serotonin syndrome: Treatment of Serotonin syndrome:

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