

Drug Safety for Tourette Syndrome (TS) and Obsessive- Compulsive Disorder (OCD)

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Objectives

- To review commonly used medications for TS and OCD
- To discuss potential adverse effects associated with the use of medications
- To discuss how to prospectively monitor medication safety and mitigate adverse effects



Behavioural Therapies

- First line treatments
 - OCD
 - Exposure and response prevention (ERP), cognitive therapy, mindfulness-based therapy
 - TS
 - Comprehensive Behavioural Intervention for Tics (CBIT), Habit Reversal Therapy (HRT)
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Selective Serotonin Re- Uptake Inhibitors (SSRIs)

- First line medical treatment for OCD
- Also commonly used for anxiety and depression
- Drugs in this class include
 - Fluoxetine/Prozac
 - Sertraline/Zoloft
 - Fluvoxamine/Luvox
 - Paroxetine/Paxil
 - Citalopram/Celexa
 - Escitalopram/Cipralex

SSRIs: How they work

- Increase levels of the serotonin in the brain
- Serotonin is a neurotransmitter – a chemical messenger between neurons (cells in the brain)
- Serotonin is increased by blocking the re-uptake of serotonin into neurons, making serotonin more available

SSRIs: Evidence to support use in OCD

- Randomized controlled trials have shown efficacy of SSRIs vs placebo for children, youth and adults with OCD
- Sertraline, fluvoxamine, fluoxetine, paroxetine, citalopram
- SSRIs are comparatively effective
- 40-70% of people with OCD will show an improvement with SSRIs; remission occurs in 25%
- 90% of people with OCD will show an improvement with out-patient CBT; remission occurs in 25%
- Residential intensive CBT – 50% asymptomatic at discharge

SSRIs: How they are used in OCD

- Start at low dose
- Slowly increase dose over a period of weeks based on response
- Effect on anxiety within 2-4 weeks
- Effect on OCD symptoms can take up to 12 weeks, may require upper end of dose range to obtain good response

SSRIs: Common side effects

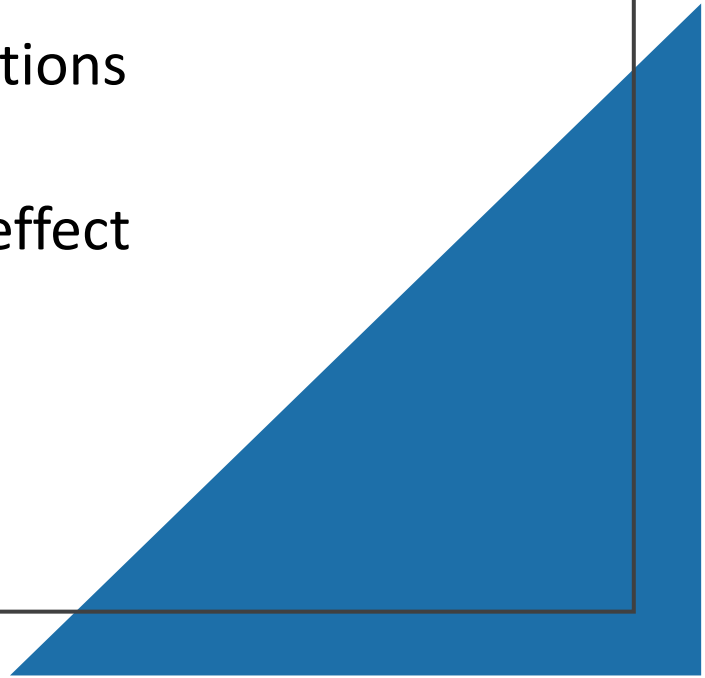
- Some small variations across SSRIs in frequency of different side effects
- Overall safe and well tolerated by most
- Most common
 - Nausea (20% vs 10% with placebo)
 - Headache (15%; not much different from placebo)
 - Insomnia (20-30% vs 10-20% with placebo)
- Other
 - Drowsiness
 - Dry mouth
 - Dizziness
- Sexual side effects (5-15%)
 - Reduced desire
 - Erectile dysfunction

SSRIs:
Uncommon
but
concerning
side effects

- Akathisia
 - Motor restlessness
- Suicidal thoughts
 - Black Box warning in youth
 - 4% vs 2% with placebo
- Serotonin syndrome
 - If combined with other drugs that affect serotonin
 - Anxiety, fever, sweating, confusion, tremor
- Abnormal heart rhythm
 - With high doses of citalopram (over 40 mg)

SSRIs: How to avoid side effects

- Taking medication with food may reduce nausea
- SSRIs can interact with other drugs – get all your medications from the same pharmacist
- Start at low dose and gradually increase dose based on effect
- Take medication consistently – don't skip doses



SSRIs: How to monitor safety

- Monitor weight and waist circumference
- In first few weeks
 - Suicidal thoughts
 - Motor restlessness



Discontinuing SSRIs

- Stopping treatment abruptly or missing several doses can cause a withdrawal-like syndrome
 - Anxiety
 - Nausea
 - Flu-like symptoms
 - Dizziness
- Dosage should be gradually lowered over period of weeks to months

What if SSRIs don't work or I can't take them?

- Clomipramine
 - Tricyclic antidepressant
 - May be more effective than SSRIs but has more side effects
- Venlafaxine
 - Serotonin norepinephrine reuptake inhibitor
- Adjunctive treatments
 - Medication added to SSRI
 - Antipsychotics – Risperidone, Aripiprazole
 - Topiramate
 - Memantine
 - Riluzole

Alpha Adrenergic Agonists

- Clonidine
- Guanfacine (Intuniv XR)
 - Similar drugs, but guanfacine is more selective than clonidine
- Stimulate alpha 2 receptors
- Inhibit release of norepinephrine from neurons
- Decreases stress response

Alpha Adrenergic Agonists: Evidence

- Evidence to support the use of clonidine and guanfacine for reduction of tics and ADHD symptoms
- More evidence in children than adults
- Evidence suggests may be more effective in children who have both tics and ADHD



Alpha Adrenergic Agonists: How they are used in TS

- Clonidine
 - Must be taken multiple times a day (3X ideal)
 - Start at low dose, slowly increase
 - Give higher dose at night
- Guanfacine
 - Long-acting (XR) form available – once daily dosing
- May take up to 12 weeks to see an improvement in tics

Alpha Adrenergic Agonists: Common Side Effects


Sedation/sleepiness

Stomachache

Low blood pressure

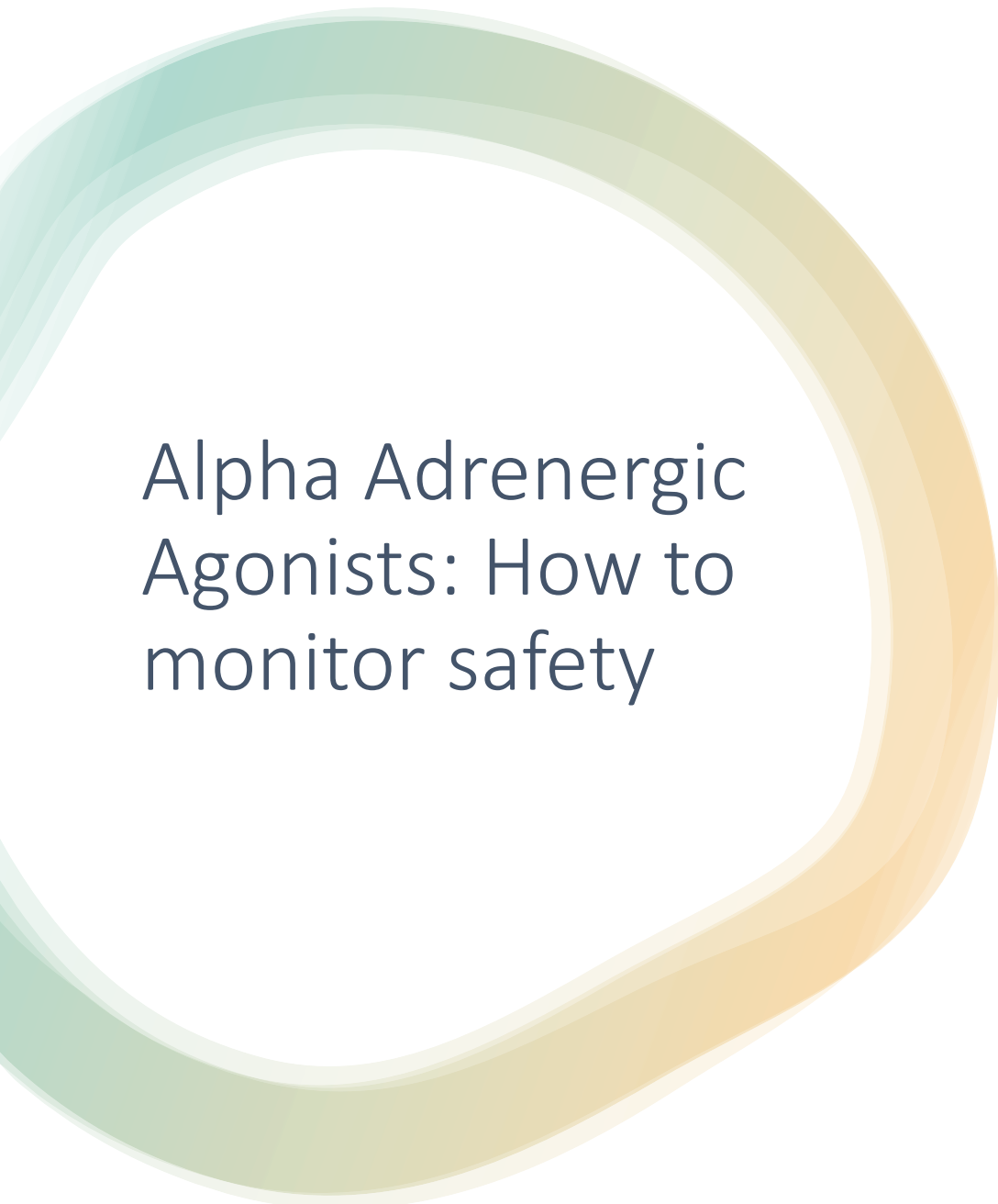
Low heart rate

Dizzy/lightheaded/fainting



Alpha Adrenergic Agonists: How to avoid side effects

- Start with night-time dosing to acclimate to sedative effect
- Stay well hydrated
- What to do if feeling lightheaded – lower position of head relative to body



Alpha Adrenergic Agonists: How to monitor safety

- Before starting and with each dose increase
 - Take blood pressure and heart rate in supine and standing positions
 - May need to avoid these medications if baseline blood pressure and heart rate are low
- Inquire about sedation and fainting

Alpha Adrenergic Agonists: How to discontinue

- Both clonidine and guanfacine must be gradually discontinued over a period of days to avoid re-bound hypertension




Antipsychotics

- Divided into
- First Generation Antipsychotics
 - Haloperidol, pimozide, fluphenazine
 - Block dopamine (D2) receptors
- Second Generation Antipsychotics
 - Risperidone, ziprasidone
 - Block dopamine (D2) and 5HT2 receptors
- Third Generation Antipsychotics
 - Partial dopamine agonists
 - Aripiprazole

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Antipsychotics: Evidence to support use in TS

- Antipsychotics are the most well studied type of medication for TS
 - Moderate to large effect sizes in both children and adults
 - Diminish tics within 2-3 weeks of reaching target dose
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Antipsychotics: How they are used in TS

- Used to diminish tics
- Can also help with aggression and irritability
- Used as an adjunctive treatment for OCD and depression (aripiprazole)
- Second and third generation antipsychotics used preferentially

Antipsychotics: Side effects

- Metabolic side effects
 - Weight gain, increase in body mass index (BMI)
 - Increase in waist circumference
 - Elevated cholesterol and triglycerides
 - Elevated blood sugar
 - Elevated liver enzymes
- Hormonal side effects
 - Elevated prolactin
 - Gynecomastia, galactorrhea, sexual side effects
- Neurological side effects
 - Drug-induced movement disorders

Antipsychotics: Drug-induced movement disorders

- More common with first generation antipsychotics and higher doses
- Acute dystonic reaction
- Akathisia
- Parkinsonism
- Tardive dyskinesia
- Tardive dystonia

Antipsychotics: How to avoid side effects

- Use the lowest effective dose
- Take medication consistently
- Diet
- Exercise

Antipsychotics: How to monitor safety

Prior to starting medication

- Height, weight, BMI, waist circumference, neurological examination
- Lab work for cholesterol, triglycerides, glucose, liver enzymes, prolactin

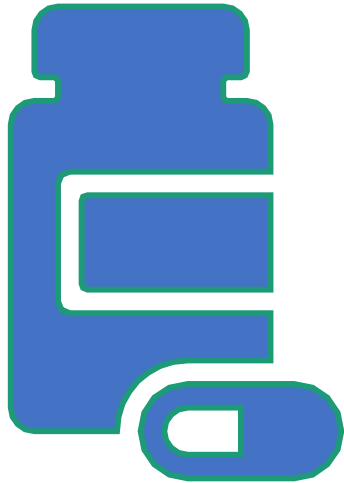
Physical exam at 1,2,3,6,9,12 months and yearly thereafter

Lab work at 3-6 months and yearly thereafter

Antipsychotics: What do I do if I have a side effect?

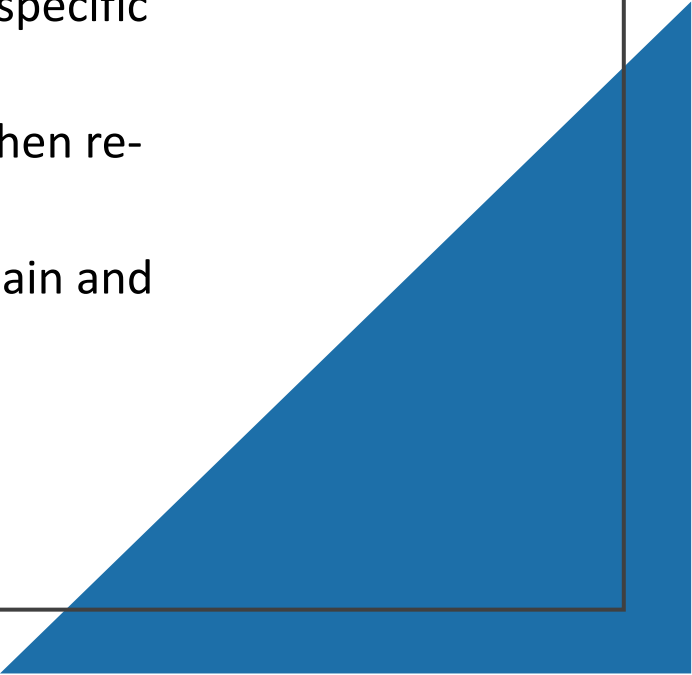
- Lower dosage or gradual withdrawal of medication
- Metabolic side effects
 - Weight gain is reversible
 - Metabolic laboratory abnormalities reversible with weight loss
- Hormonal side effects
 - Prolactin levels usually normalize within one year while taking the medication; will return to normal if discontinued
- Neurological side effects
 - Reversible, especially in younger people
 - In older people with long-term use, reversibility of adverse effects may take years

Topiramate



- Anticonvulsant medication
- Also used to prevent migraine headache and for tremor
- Can be helpful for tics
- Adverse effects
 - Sedation
 - Paresthesia
 - Weight loss
 - Kidney stones

Botulinum toxin injections

- Botox
 - Original use for neurological disorders
 - Works by weakening muscles it is injected into
 - Can be helpful for tics affecting specific muscle groups
 - Temporary – lasts 3-4 months, then re-injection required
 - Main side effects are injection pain and temporary muscle weakness
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Summary

- There are a number of medications that have demonstrated efficacy for TS and OCD
- While all medications can potentially cause adverse effects, they can be safely prescribed
- Proactive monitoring may improve detection of harmful effects and increase patient comfort with using medication

