

MEDICATIONS FOR ADHD

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Attention Deficit/Hyperactivity Disorder in Adults

Attention Deficit Hyperactivity Disorder (ADHD) was once considered a childhood disorder; however, it has become clear that it also affects a significant number of adults. As symptoms delineate throughout the life of a patient, it is important to optimize treatment strategies. Additionally, adults with ADHD often have comorbid disorders which may be more obvious than the ADHD symptoms and thus delay the correct diagnosis of ADHD.

According to Kessler (2006), 50% of adults ADHD patients have a comorbid anxiety disorder; 40% have a comorbid mood disorder; 35 – 50% have a historical or present substance use disorder. Additionally, Stahl (2009) has stated that non-medicated ADHD patients have a higher tendency to be obese than their normal counterparts. He postulates that likely this is due to poor impulse control and inability to differentiate between multiple stimuli.

Neuropsychological and imaging studies have shown that ADHD is associated with alterations in the prefrontal cortex (PFC) and its connections to striatum and cerebellum (cortical-striatal-thalamic-cortical [CSTC] loops). Inefficient information processing in particular brain areas that are a part of the CSTC loop can hypothetically lead to different symptoms of ADHD: Malfunctioning of the dorsal anterior cingulate cortex (ACC) results in problems with selective attention and emotional regulation; impairments in the dorsolateral prefrontal cortex (DLPFC) may result in problems with sustained attention, cognitive flexibility, planning, and problem solving; impairments in the prefrontal motor cortex leads to symptoms of hyperactivity; impairments in orbital frontal cortex (OFC) may lead to impulsivity, compulsivity, as well as problems with sensory integration and emotional regulation.

Neurotransmitters important to executive functioning include dopamine (DA), norepinephrine (NE), histamine (HA), and acetylcholine (ACh). Therefore, medications to alleviate symptoms associated with ADHD will target these neurotransmitters.

Stahl (2009) recommends the following treatment protocol for adults with ADHD. The non-stimulants such as atomoxetine (Strattera), guanfacine ER (Intuniv), bupropion (Wellbutrin), and perhaps modafinil (Provigil) are a preferred first choice of treatment, followed by slow-dose, extended-release stimulants or prodrugs. Immediate-release stimulants and noradrenergic antidepressants are second-line options, whereas atypical antipsychotics are adjunctive options, used particularly with co-morbid conditions and/or issues of impulse control.

First Line Treatment Non-Stimulants

- **atomoxetine (Strattera):** NE reuptake inhibitor
 - This is not thought to have abuse potential.
 - Use with caution in patients who may have bipolar disorder. It can destabilize latent or undiagnosed bipolar disorder.
 - Also used for treatment-resistant depression.
 - May be useful in treatment of chronic pain.
 - This medication can cause HTN and increased heart rate. Monitor in individuals with HTN.
 - Not likely to exacerbate tics.
 - May cause sedation, fatigue, decreased appetite.
- **modafinil (Provigil):** MOA is unknown but hypothetically acts as an inhibitor of DA transporter
 - Modafinil is listed as a “wake-promoting” agent but has shown effectiveness in treating some cases of ADHD.
 - Less abuse potential than stimulants.
- **guanfacine ER (Intuniv):** Alpha 2a agonist
 - Guanfacine is listed as a hypertensive but has shown effectiveness in treating ADHD, motor tics, and Tourette’s syndrome
 - May be used as monotherapy or in combination with stimulants for treatment of ODD.
 - There is no known abuse potential.
 - Immediate release guanfacine (Tenex) has also shown benefits for ADHD.
- **bupropion (Wellbutrin, Wellbutrin SR, Wellbutrin XL, Zyban;):** NE and DA reuptake inhibitor
 - Primarily used for MDD, SAD, Bipolar depression.
 - Also used in smoking cessation.
 - May exacerbate tics.
 - Used to treat the sexual dysfunction common with SSRIs.
 - Less likely to induce hypomania than other antidepressants.
 - Monitor for HTN.

First Line Treatment Stimulants (long-acting stimulants)

Note: There are contraindications for all stimulants. Do not use stimulants if there is a history of stimulant abuse, cardiac arrhythmia or other significant cardiac problems, extreme anxiety or agitation, HTN, or paranoia.

Note: Common side effects for stimulants include: insomnia, headache, exacerbation of tics, nervousness, irritability, dizziness, anorexia and weight loss. Most stimulants cause sexual dysfunction long-term but can also improve sexual function short-term. Dangerous side effects include psychosis, seizures, palpitations, tachycardia, hypertension, activation of mania.

Stimulants are also used for treating narcolepsy and treatment-resistant depression.

Some patients respond better to methylphenidate than amphetamines and vice versa.

- **lisdexamfetamine (Vyvance)** : prodrug; blocks NE and DA reuptake
 - Less abuse potential than other stimulants. Because it is a prodrug, inhalation produces no euphoria. However, it can be abused orally
 - Also used for treating narcolepsy and treatment-resistant depression.
- **d-amphetamine spansules (Dexedrine Spansules)**: NE & DA reuptake inhibitor
- **dl-amphetamine salts – XR (Adderall XR)**: NE & DA reuptake inhibitor
- **OROS-methylphenidate (Concerta)** NE and DA reuptake inhibitor
 - May be preferable for those who work longer days or need to concentrate in the evenings.
- **LA – methylphenidate (Ritalin LA, Metadate, CD)** NE and DA reuptake inhibitor
 - May be preferable to Concerta for those who lose their appetite for dinner or have insomnia with Concerta.
- **d-methylphenidate- XR (Focalin XR)**: NE and DA reuptake inhibitor
- **Transdermal methylphenidate (Daytrana)**: NE and DA reuptake inhibitor
 - Transdermal formulation may confer lower abuse potential than oral formulations.
 - Transdermal formulation may enhance adherence to treatment due to slower onset.

Second Line Stimulants (short-acting stimulants)

- **methylphenidate (Ritalin, Methylin)**: NE and DA reuptake inhibitor
- **d-methylphenidate (Focalin)**: NE and DA reuptake inhibitor
- **d-amphetamine (Dexadrine)**: NE & DA reuptake inhibitor
- **dl- mixed amphetamine salts (Adderall)**: NE and DA reuptake inhibitor

Second Line Non-Stimulants

- **mirtazapine (Remeron)**: Alpha2 agonist; NaSSA (noradrenaline serotonergic agent); dual serotonin and norepinephrine agent
 - Mirtazapine is also approved for MDD, panic disorder, GAD, and PTSD.
 - Sedation can be problematic. It is usually taken before bedtime.
 - Adding alpha2 antagonism to agents that block serotonin and/or norepinephrine reuptake may be synergistic for severe depression.
 - Adding mirtazapine to venlafaxine or SSRIs may reverse drug-induced anxiety and insomnia.
 - Weight gain can occur. If it has not been demonstrated by week 6, it is unlikely to be significant.

Adjunctive Medications

The following adjunctive medications are atypical antipsychotics. They are primarily used for the impulsivity and behavioral disturbances that accompany ADHD.

- **paliperidone (Invega):** Serotonin-DA agonist
 - Also approved for treatment of bipolar disorder and schizophrenia.
 - May accelerate osteoporosis
 - Monitor for metabolic syndrome
- **quetiapine (Seroquel)** 5HT & DA agonist
 - Also used for severe treatment-resistant anxiety and depression
 - Most commonly used as hypnotic
 - Approved for treatment of bipolar disorder and schizophrenia
 - Has shown some efficacy in treating PTSD, including symptoms of sleep disturbance and anxiety.
 - Monitor for metabolic syndrome.
- **risperidone (Risperdal):** 5HT & DA agonist
 - Also approved for treatment of bipolar disorder and schizophrenia.
 - Monitor for metabolic syndrome.
 - May accelerate osteoporosis.
- **ziprazadone (Geodon):** 5HT & DA agonist
 - Also approved for treatment of bipolar disorder and schizophrenia.
 - Monitor for metabolic syndrome. Some indication that ziprazadone has fewer metabolic side effects than other atypicals.
- **olanzapine (Zyprexa):** DA partial agonist
 - Also approved as adjunctive treatment for depression.
 - Associated with less weight gain than other atypicals.
 - Monitor for metabolic syndrome
- **aripiprazole (Abilify):** DA partial agonist
 - Also approved for treatment of bipolar disorder and schizophrenia
 - Monitor for metabolic syndrome

NOTE: Always check drug profiles for side effects and DDIs before recommending any medication.

References:

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