



PHARMACOLOGY

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Number

1

Subject

Bipolar disorder

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Price:

Bipolar disorder

Bipolar disorder

- BP-I: Mania with or without Depression
- BP-II: Depression and hypomania

Mood Stabilizers

- Lithium
- Anticonvulsants
 - Valproic Acid [Depakote]
 - Carbamazepine [Tegretol]
 - New Anticonvulsants (?):
 - Lamotrigine [Lamictal]
 - Topiramate [Topamax]
 - Gabapentin [Neurontin]
- Antipsychotics
 - Classic (Haloperidol)
 - Novel (Clozapine, Olanzapine)

Lithium Pharmacodynamics

- **No psychotropic effect on non-Bipolars**
- **Affects nerve membranes, multiple receptor systems and intracellular 2nd messenger impulse transduction systems.**
- **Interacts with serotonin**
- **Potential to regulate CNS gene expression, stabilizing neurons associated multiple gene expression change.**

Lithium Side Effects and Toxicity

- Relate to plasma concentration levels, so constant monitoring is key
- Higher concentrations (1.0 mEq/L and up produce bothersome effects, higher than 2 mEq/L can be serious or fatal
- Symptoms can be neurological, gastrointestinal, enlarged thyroid, rash, weight gain, memory difficulty, **kidney disfunction**, cardiovascular
- Not advised to take during pregnancy, affects fetal heart development

If Lithium Doesn't Work

- 40% of Bipolars are resistant to lithium or side effects hinder its effectiveness
- Therefore, we must consider alternative agents for treatment

Valproic Acid (Depakote)

- **An anti-epileptic, it is the most widely used anti-manic drug**
- **Augments the post-synaptic action of GABA at its receptors (increasing synthesis and release)**
- **Best for rapid-cycling and acute-mania**
- **Therapeutic blood levels: 50-100 Mg/L**
- **Side effects include GI upset, sedation, lethargy, tremor, metabolic liver changes and possible loss of hair**

Lamotrigine

- Reported effective with Bipolar, Borderline Personality, Schizoaffective, Post-Traumatic Stress Disorders
- Inhibits neuronal excitability and modifies synaptic plasticity
- Side Effects may include dizziness, tremor, headache, nausea, and rash??????

Atypical Anti-psychotics

- Clozapine, Risperidone, and Olanzapine, Aripiprazole
- Risperidone seems more anti-depressant than anti-psychotic
- Clozapine is effective, yet not readily used due to potential serious side effects
- Olanzapine is approved for short-term use in acute mania
- Aripiprazole is effective for the treatment of acute manic episodes of bipolar disorder in adults

CNS Stimulants

- Defination

“Stimulants are a substance which tends to increase behavioral activity when administered”

Psychomotor stimulants cause: Excitement, Euphoria, Decrease feeling of fatigue & Increase motor activity

Methylxanthines (caffeine, theophylline),
nicotine,
cocaine,
amphetamine,
modafinil,
methylphenidate.

- Signs and symptoms:
- 1- Elevate Mood
- 2- Increase Motor Activity
- 3- Increase Alertness
- 4- Decrease need for Sleep
- In case of overdose lead to convulsion and death.

Therapeutic Indications

- **Obesity (anorectic agents).**
- **Attention Deficit Hyperactivity Disorder (ADHD); lack the ability to be involved in any one activity for longer than a few minutes.**
- **Narcolepsy: It is a relatively rare sleep disorder, that is characterized by uncontrollable bouts of sleepiness during the day.**

Contraindications

- patients with anorexia, insomnia, asthenia, psychopathic personality, a history of homicidal or suicidal tendencies

Amphetamine

- **MOAs :**

- Block the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space.

- **- Clinical use:**

1. Narcolepsy.
2. Attention-deficit hyperactivity disorder

Adverse effects

Cardiovascular: Hypertension (7% to 22%, pediatric)

- **Endocrine metabolic: Weight loss (4% to 9%, pediatric; 11%, adults)**
- **Gastrointestinal: Abdominal pain (11% to 14%, pediatrics), Loss of appetite (22% to 36%), Xerostomia (35%)**
- **Neurologic: Headache (26%), Insomnia (12% to 17%, pediatric; 27%, adults)**
- **Psychiatric: Feeling nervous (6%)**

Methylphenidate

- It has CNS stimulant properties similar to those of amphetamine and may also lead to abuse, although its addictive potential is controversial.
- It is taken daily by 4-6 million children in the USA for ADHD.
- Methylphenidate is a more potent dopamine transport inhibitor than cocaine, thus making more dopamine available.
- It has less potential for abuse than cocaine, because it enters the brain much more slowly than cocaine and, does not increase dopamine levels as rapidly.

Adverse Effects

Adverse reactions: GIT effects are the most common; abdominal pain and nausea.

In seizure patients, methylphenidate seems to increase the seizure frequency, especially if the patient is taking antidepressants. ●

Nicotine

- is the active ingredient in tobacco. Used in smoking cessation therapy, Nicotine remains important, because:

- Actions of Nicotine:

Low dose: ganglionic depolarization

High dose: ganglionic blockade

Actions of Nicotine

- I. CNS: Low dose: euphoria, arousal, relaxation, improves attention, learning, problem solving and reaction time.

High dose: CNS paralysis, severe hypotension (medullary paralysis)

- II. Peripheral effects: Stimulation of sympathetic ganglia and adrenal medulla → ↑ BP and HR (harmful in HTN patients)
- Stimulation of parasympathetic ganglia → ↑ motor activity of the bowel. At higher doses, BP falls & activating ceases in both GIT and bladder.

Adverse effects

- CNS; irritability and tremors
- Intestinal cramps, diarrhea
- ↑HR & BP
- Withdrawal syndrome: nicotine is addictive substance, physical dependence on nicotine physical dependence on nicotine develops rapidly and can be severe.

Quitting

- irritability, anxiety, depression, impatience, trouble sleeping, restlessness, hunger or weight gain, and difficulty concentrating.
- Bupropion: can reduce the craving for cigarettes.
- Transdermal patch and chewing gum containing nicotine.

Varenicline

Chantix and Champix