



Case Studies

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Pharmacy Alternatives

Case Study #1

- 42 yr old African American female
- Admitted to group home 4 weeks ago
- Presents with symptoms of crying at mealtimes, physical aggression of hitting and spitting at staff and roommates, verbally threatening roommates, "angry" that needs to see psychiatrist because she misses opportunity to make money at workshop, hates group outdoor activities

Discussion

- Comments?
- Should she be seen at psych review?
- Behavior plan: what comments?
- If yes, what are the targeted behaviors?
- What class(es) of medications would be appropriate?

Case #1

- If at next psych review, same symptoms are seen, what would your next approach be?
- At third psych review?
- Subsequent psych reviews?

Case #1

- Monitoring?
- Dosage reduction plan?

Case #2

- 46 year old Caucasian male
- Diagnosis: MR, major affective disorder, autistic tendencies, anxiety disorder, OCD
- Maladaptive behaviors:
 - Striking top of his head
 - screaming while jumping up and down
 - Running through house and eloping
 - Verbalizations that appear odd
- Medications:
 - Anafranil 150mg at bedtime
 - Buspar 10mg bid
 - Ativan 2mg as needed per nurse's instruction

Comments

- Initial analysis?
- Behavior program?
- Targeted behaviors?
- Monitoring?

Case #3

- 58 year old Hispanic male
- Diagnosis: MR, Down Syndrome, hypothyroidism, depression
- Medications: MV, thyroxine 0.025mg, Prozac 10mg at bedtime
- Maladaptive behaviors:
 - Refuses to get on the bus for workshop
 - Wanders around group home and will not actively participate in outings
 - Urinates in corner of bedroom
 - Steals clothes from other housemates
 - Strips off clothing in public

Case #3

- Comments and approach?

Case #4

- 23 yr old African American female
- Diagnosis: hypertension, diabetes
- Medications: Atenolol 100mg in am, glyburide 10mg in am
- Maladaptive behaviors: picks at lint in carpet, talks to shoulder, slaps side of head and bangs head on table

Case #4

- Comments?

Case #4

- New symptom: tells staff devil made her pregnant and he talks to her in her room
- Psychiatrist starts her on Zyprexa 5mg twice daily
- Comment?
- Monitoring?

Anxiety



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Types

- Acute stress disorder
- Post-traumatic stress disorder
- Obsessive compulsive disorder
- Chronic generalized anxiety disorder
- Panic disorder
- Phobias

Symptoms

- Worrying
- Increased blood pressure
- Increased heart rate
- Sweating
- Dilated pupils
- Insomnia

What does this look like?

- Fidgeting, hand wringing
- Inability to sit still, pacing
- Facial expression of tension
- Stomach complaints
- Headache
- Skin picking

Barbiturates

- 30% of patients are non-responders
- Do not affect the core symptom of worry
- Cause a variety of adverse effects including disinhibition of the frontal lobe
- Potential for abuse, physical dependence and withdrawal, as well as high relapse rates when medication is withdrawn

Antianxiety medications

- Short acting barbiturates:
Xanax (alprazolam)
- Mid acting barbiturates:
Ativan (lorazepam)
- Long acting barbiturates:
Valium (diazepam)
Librium (chlordiazepoxide)
Klonopin (clonazepam)
Tranxene (chloazepate)

Pharmacology

- Short acting:
 - Peak plasma level in 1-2 hours, half life 12-15 hours
- Moderate acting:
 - Peak plasma level in 1-6 hours, half life 10-20 hours
- Long acting:
 - peak plasma in 1/2 to 2 hours, half life 20-50 hours

Side Effects

- Skeletal muscle relaxation
- Dizziness
- Drowsiness
- Amnesia
- Increase in falls

Monitoring Antianxiety Medications

- No blood levels are needed, rely on clinical signs and symptoms
- Evaluate degree of sedation keeping in mind an active life style of individuals
- Watch very carefully for potential falls
- Comment on side effects as they occur in writing, continue to evaluate and report troublesome side effects to clinician

Drug Interactions

- Additional sedating drugs including alcohol
- SSRIs like Prozac and Paxil may inhibit liver enzymes and prolong activity

Antidepressants

- Medication treatment of choice
- Drugs with primary effect on the serotonin system have become 1st line recommendations for the treatment of panic disorder, social phobia, OCD, and PTSD as well as generalized anxiety disorder
- Take longer to work than barbiturates

Antidepressants

- SSRIs like Prozac, Zoloft, Paxil, Celexa, Effexor, Serzone are probably more effective and easier to discontinue
- Tricyclics like Elavil and Tofranil may be useful for PTSD

Other agents

- Atarax (hydroxyzine)
- Buspar (buspirone)
- Catapres (clonidine)
- Inderal (propranolol)
- Tenormin (atenolol)
- Antipsychotics

Hydroxyzine (Atarax)

- Pharmacology: non benzodiazepine, sedating antihistamine, used for its side effect of sedation
- Usual dosage: 50-100mg every 6 hrs as needed
- Side effects: dry mouth, sedation, ataxia, slurred speech

Buspirone (Buspar)

- Pharmacology: binds to dopamine and serotonin receptors, anxiolytic
- Dosage: 20-30mg/day in 2-3 doses
- Drug interactions: all antidepressants
- Side effects: dizziness, drowsiness, nervousness, dry mouth, confusion

Antihypertensives

- Drugs: clonidine, atenolol, propranolol
- Pharmacology: acts as an antihypertensive, alpha 2 adrenergic blocking agents
- Dosage:
 - clonidine: 0.1-0.3mg twice daily
 - atenolol: 50-100mg/day
 - propranolol: 80-240mg twice daily (long acting product also available)
- Side effects: dry mouth, dizziness, sedation, fatigue, orthostatic hypotension

Antipsychotics

- Should be used as a last resort after attempt with other agents

Questions?





Treatment of Psychiatric Disorders

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Diseases

- Psychosis
- Schizophrenia
- Schizoaffective disorder

Antipsychotics

- Positive symptoms
 - Hostility
 - Excitability
 - Delusions
 - Suspiciousness/persecution
 - Hallucinatory behavior
 - Conceptual disorganization
 - Grandiosity

Antipsychotics

- Negative symptoms
 - Emotional withdrawal
 - Passive apathetic withdrawal
 - Difficulty in abstract thinking
 - Blunted affect
 - Lack of spontaneity/flow of conversation
 - Stereotyped thinking
 - Poor rapport

What does this look like?

- Bizarre behavior
- Talking to object or person that does not exist (watch appropriate mental age self talk or imaginary friend)
- Seeing things that do not exist
- Saying that God / devil is telling them to do something
- Feeling that you are poisoning them
- Suspicious of people

Pharmacology

- Dopamine Receptor Antagonists
 - Block dopamine receptors on post synaptic neurons
 - Effectively decrease the functional levels of dopamine
 - Most often used to treat psychotic patients whose psychosis is related to a hyperdopaminergic state

Antipsychotics

- Conventional agents (older drugs)
 - All were equally effective
 - Different subtypes of schizophrenics respond differently to different agents?
 - Agitated patients = more sedating
 - Withdrawn patients = less sedating drugs
 - Controlled trials failed to support

Antipsychotics

- Conventional agents
 - Differences confined to side effects, formulations available, cost
 - Examples:
 - Thorazine (chlorpromazine)
 - Mellaril (thioridazine)
 - Haldol (haloperidol)
 - Navane (thiothixene)
 - Stelazine (trifluoperazine)
 - Prolixen (luphenazine)

Typical Antipsychotics

- Absorbed erratically
- Very lipid soluble
- Highly protein bound
- Distributed throughout the tissues and concentrated in the brain

Side Effects of Typical Agents

- High, mid, low potency
- High potency = greater affinity for D2 receptor and greatest EPS
- Low potency = less EPS, more postural hypotension, sedation and anticholinergic effects

Atypical Antipsychotics

- Serotonin-dopamine antagonists, therefore broader coverage of symptoms
- Examples:
 - Clozaril (clozapine)
 - Risperdal (risperidol)
 - Seroquel (quetiapine)
 - Zyprexa (olanzapine)
 - Geodon (ziprasidone)
 - Abilify (aripiprazole)
 - Invega (paliperidone)

Atypical Antipsychotics

- Differ in having effects related to the ratios of dopamine and serotonin
- Antihistaminic - dry mouth sedation weight gain
- Muscarinic -dry mouth urinary retention constipation esophageal constriction
- Alpha adrenergic - heart block hypotension

Side Effect Considerations of Atypical Antipsychotics

- Sedation
- Orthostasis, esp upon arising
- EPS and TD
- Anticholinergic
- Gait disturbance
- Metabolic abnormalities
- Cerebrovascular adverse events: stroke, TIA
- QT prolongation

Clozapine (Clozaril)

- Primary importance: refractory patients
- Indications: schizophrenia, schizo-assoc. suicide risk reduction
- Dosage form: scored 25mg, 100mg tabs
- Dosage regimen: 1-3 times/day
- Dose: 150-300mg twice daily, max: 900mg/day
- Continue for 2 yrs, reassess and taper if possible

Clozapine

- Side effects:
 - Agranulocytosis
 - Sedation (high histamine blockade)
 - Orthostasis
 - Excessive drooling, increased sweating
 - Anticholinergic symptoms
 - Weight gain (high histamine blockade)
 - Hyperlipidemia, hypertension
 - Increased glucose levels
 - Lowers seizure threshold

Clozapine

- Interactions:
 - cigarette smoking
 - grapefruit juice

avoid carbamazepine (Tegretol), ciprofloxin (Cipro)

Risperidone (Risperdal)

- Indications: schizophrenia, psychiatric dementia, bipolar mania, autism
- Dosage form: 0.25mg, 0.5mg, 1mg, 2mg, 3mg and 4mg tab, liquid 5mg/5ml (not to be mixed w/cola or tea), quick dissolving tab, depot available (Consta)
- Dosage schedule: 1-3 times daily, most often 1/day at hs
- Dosage range: 0.25-16mg, most common in I/DD 1-4mg/day

Risperidone

Side effects:

- Few anticholinergic, watch constipation
- EPS low except at high (>6mg/day) dose
- Sedation
- Agitation, anxiety, insomnia
- Increased prolactin levels

Risperidone

- Weight gain: moderate
- Not associated with the same degree of hyperlipidemia, increased glucose levels as other agents
- Decreases seizure threshold
- Cerebral vascular accident-watch modifiable risk factors

Olanzapine (Zyprexa)

- Indications: psychosis, bipolar disorder
- Dosage schedule: 1 time/day
- Dosage range: 2.5-20mg/day, usual DD range 1.25-15mg/day
- Side effects:
 - Sedation, hypotension
 - Anticholinergic-highly
 - EPS much higher than others

Olanzapine

- Side effects (cont):
 - Headache, dizziness, insomnia, agitation
 - Weight gain!!!
 - Hyperlipidemia
 - Increased glucose levels, risk for diabetes mellitus
 - Lowers seizure threshold

Quetiapine (Seroquel)

- Indications: psychosis
- Dosage form: 25mg, 100mg, 200mg, 300mg tabs, liquid or fast dissolving NOT available
- Dosage schedule:1-4 times daily
- Dosage range:100-800mg/day, usual DD dose of 50-300mg/day
- Side effects:
 - orthostasis

Quetiapine

- Side effects (cont)
 - Moderate to high sedation
 - Weight gain
 - EPS/TD: low
 - Cataract formation: initial and every 6 month eye exam
 - Lowers seizure threshold
 - Histaminic-like side effects

Ziprasidone (Geodon)

- Dosage form: 20mg, 40mg, 60mg 80mg capsules, liquid or quick dissolve tabs NOT available, IM formulation is available
- Dosage schedule:1-2 times/day
- Dosage Range:20-160mg/day, usual DD dose is 20-80mg/day
- Side effects:
 - Nausea, dyspepsia, abdominal pain

Ziprasidone

- Side effects (cont):
 - Constipation
 - Insomnia or sedation
 - Prolongation of QT interval: baseline and routine EKG monitoring
 - Weight gain: low

Aripiprazole (Abilify)

- Indications: schizophrenia in adults as well as 13-17yr old, acute and maintenance bipolar disorder in adults as well as acute bipolar disorder in 10-17 yr old, adjunctive treatment for major depression in adults, acute agitation associated with schizophrenia in adults
- Dosage forms: 2mg, 5mg, 10mg, 15mg, 20mg, and 30mg tab, liquid, fast dissolving tab and depot formulation NOT available
- Dosage schedule: 1 time/day
- Dosage range: 2.5-30mg, usual I/DD dosage 10-15mg

Aripiprazole

- Side effects:
 - Sedation or activation
 - Hypotension
 - Lowers seizure threshold
 - Weight gain: low
- Drug interactions:
 - Decrease dose by $\frac{1}{2}$ if also using quinidine, ketoconazole, fluoxetine, or paroxetine
 - Double dose if using carbamazepine

Paliperidone

- Indication: schizophrenia
- Dosage: 6mg qam, may need 9 or 12 mg long acting formulation
- Side effects: sedation, prolactin increase, hypotension
- Drug interactions: QT prolongation drugs (Geodon)

Monitoring

- Many potential side effects
 - Evaluation of short term
 - Evaluation of long term (AIMS / DISCUS)
 - Evaluate and rank potential harmful vs troublesome
- Lab work:
 - Blood levels questionable and not needed
 - Metabolic effects (diabetes, hyperlipidemia, abdominal girth)

Questions?



Stimulants

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Stimulants

- Useful in the treatment of ADHD
- Alleviation of neurobehavioral symptoms of depression

Signs and Symptoms of ADHD

- Moderate to severe distractibility
- Short attention span
- Hyperactivity
- Emotional lability
- Impulsivity

What does this look like?

- Client difficulties at home in interpersonal relationships, attention to tasks and completion of chores
- Workshop production worsens or is poor
- Physically appears to be “wound up”, with difficulty relaxing, tense, bothersome and annoying physical activity
- Emotionally appears to be manic and irritable
- Depression many times accompanies this diagnosis

Medications

- Adderall (amphetamine and dextroamphetamine)
- Cylert (Pemoline)
- Ritalin (methylphenydate)

Amphetamine and dextroamphetamine

- Dosage in ADHD: 5-80mg/day in 1-2 doses
- Pharmacology: blocks reuptake and increases release of norepinephrine and dopamine, may activate the brain stem arousal system
- Side effects: HTN, aggressive behavior, strokes, Tourette's syndrome, growth suppression, nervousness, insomnia, headache, dizziness, loss of appetite, abdominal pain
- Adderall XR: dosage 20mg every morning

methylphenidate

- Concerta (18-72mg ER/day)
- Metadate CD (20-60mg ER/day)
- Metadate ER (10-20mg 1 to 2x/day)
- Methylin (5-15mg 2-3x/day)
- Methlin ER (10-20mg 1-2x/day)
- Ritalin (5-15mg 2-3x/day)
- Ritalin LA (20-40mg q am)
- Ritalin SR (20mg 1-2x/day)

Monitoring

- Blood levels not needed
- Evaluate side effects like weight loss. Insomnia and headache over time
- Watch individuals with cardiac symptoms especially carefully
- Report troublesome side effects to clinician

Antidepressants

- Antidepressants with stimulant properties also used
 - Welbutrin
 - Norpramin

Questions?



The Treatment of Depression

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Characteristics of Depression

- Five or more symptoms present nearly every day during same 2 week period:
 - A. Depressed mood
 - B. Markedly diminished interest or pleasure
 - C. Significant change in weight or appetite
 - D. Insomnia or hypersomnia
 - E. Fatigue or loss of energy
 - F. Feeling of worthlessness or excessive or inappropriate guilt

Characteristics of Depression

- Five or more symptoms
 - G. Decreased ability to think or concentrate, or inability to make decisions
 - H. Recurrent thought of death, or thoughts of suicide

Characteristics of Depression

- Symptoms cause clinically significant distress or impairment in social and/or occupational functioning
- Symptoms need to be evaluated as not to be due to substance abuse or medical conditions
- Symptoms should not be better attributed to normal bereavement patterns

What does this look like?

- In persons with I/DD, depressed mood may be described by others as irritable, grouchy, assaultive, self injurious behavior, spitting, yelling, swearing, property destruction or increase in ritualistic behaviors
- Facial expressions: sad, not able to show animation or smile
- Crying or if severe disease unable to cry

What does this look like?

- Neglect of personal appearance: untidy clothes, uncombed hair
- Body movements and voice: hesitant or delayed
- Poverty of speech: how long it takes and little comes out, sparse, long pauses
- Slowness of mental activity
- Anxious or agitated depression: restlessness, hand wringing, signs of tension such as scratching and picking at the skin

What does this look like?

- Pessimism
- Low self esteem
- Expecting the worst and negative expectations
- Self blame
- Difficulty in making decisions
- Body aches and pains
- Weakness and fatigue

What does this look like?

- Sleeping too much or too little
- Not wanting to eat
- Not wanting to be involved in activities or workshop
- Isolation
- Slowness of body functions such as salivation, bowel activity and menses
- Early wakening and feeling of exhaustion in the morning

Definitions

- Neurons
- Axon
- Dendrite
- Synapse
- Neurotransmitters
- Pre-synaptic
- Post-synaptic
- Synthesis
- Reuptake mechanism



Neurotransmitters

- Serotonin: problems with serotonin are associated with depressed mood, anxiety, insomnia, OCD, SAD, and violence
- Dopamine: Disruption in dopamine related to problems with attention, motivation, alertness, increased apathy, and difficulty in experiencing pleasure
- Norepinephrine: disorders in norepinephrine are associated with lack of energy, decreased alertness, and lethargy
- GABA: major calmativ neurotransmitter

Medications



Tricyclic Antidepressants

- The most widely used class of antidepressants prior to SSRI class
- More general effects on neurotransmitters, less refined
- Out of favor because overdose can be fatal
- May be prescribed when other classes have not worked

Tricyclic Side Effects

- Orthostatic hypotension (watch elderly)
- Weight gain
- Dry mouth
- Blurred vision
- Constipation
- Sweating
- Sexual dysfunction



Tricyclics

- | | |
|-----------------------------|-----------|
| • Anafranil (chlomipramine) | 75-300mg |
| • Ascendin (amoxapine) | 150-600mg |
| • Elavil (amitriptyline) | 75-300mg |
| • Ludiomil (maprotiline) | 75-225mg |
| • Norpramin (desipramine) | 75-300mg |
| • Pamelor (nortriptyline) | 50-150mg |
| • Sinequan (doxepin) | 150-300mg |
| • Surmontil (trimipramine) | 75-300mg |
| • Tofranil (imipramine) | 75-300mg |
| • Vivactil (protriptyline) | 15-60mg |

Selective Serotonin Reuptake Inhibitors (SSRIs)

- Came on the market in 1980s
- The most popular antidepressant
 - Side effects are less severe than older agents
 - Consequences of overdose are less severe
- Often first choice in antidepressant

SSRI Usage

- Major depressive disorder
- Dysthymia
- SAD
- Mixed depression and anxiety
- Anxiety related disorders
- Premenstrual syndrome
- Eating disorders
- Some types of chronic pain

SSRIs Pharmacology

- They “clog the pump” which normally tells first neuron to pump some of the released serotonin back into the cell as a measure of checks and balances
- Therefore increased amount of serotonin hangs out in the synapse available for usage
- Takes 1-4 weeks to become effective, 4-6 weeks before true evaluation of effectiveness
- No dosage or drug changes should take place sooner than 1 month

SSRIs Side Effects

- Increased anxiety
- Fatigue
- Upset stomach
- Insomnia
- Apathy
- Lack of sexual interest
- Inability to obtain orgasm

SSRIs Side Effects

- Dizziness
 - Sweating
 - Tremors
 - Dry mouth
 - Headache
 - Weight loss
 - Weight gain
- Side effects worse during the first couple of weeks and diminish with time

Monitoring Medications

- Seldom if ever are blood levels necessary or recommended
- Evaluation of effectiveness based on clinical picture
- Evaluate potential side effects and make specific comment(s) on whether they appear, to what extent, and precautions taken to counter side effects
- Discuss troublesome side effects with clinician

SSRI cautions

- Bipolar disease and increased activation of manic state
- Abrupt discontinuation: flu-like symptoms, vivid dreams and problems with sleep
- Black Box Warning for children and adolescents
- Avoid MAOIs

SSRIs

- Celexa (citalopram) usual dosage 10-60mg, may have fewer interactions with other drugs, and not particularly stimulating or sedating
- Lexapro (Escitalopram) usual dosage 10-20mg, chemically similar to Celexa, may work faster

SSRIs

- Luvox (fluoxetine) usual dosage 50-300mg, generally more sedating than the others, the first to be approved for OCD
- Paxil (paroxetine) usual dosage 20-60mg somewhat sedating, more drug interactions, weight gain, and more pronounced withdrawal symptoms
- Paxil CR usual dosage 12.5-62.5mg

SSRIs

- Prozac (fluoxetine) usual dosage 10-80mg, stimulating, may cause insomnia if taken late in the day, some report increase in anxiety, least withdrawal symptoms due to liver enzyme inhibition, but more drug interactions
- Zoloft (sertraline) usual dosage 50-200mg not as stimulating or sedating

Serotonin / Norepinephrine Reuptake Inhibitors (SNRIs)

- Cymbalta (duloxetine) usual dosage 30-120mg, although seldom effective >60mg, often used for pain
- Effexor (venlafaxine) usual dosage 75-375mg may have quicker action so good for severe depression, fewer drug interactions than most, may increase blood pressure in higher dosages
- Effexor XR as above

Serotonin-2 antagonists Reuptake Inhibitors (SARIs)

- Desyrel (trazadone) usual dosage 150-400mg sedating side effects, used mostly along with other antidepressants as a sleep aid
- Serzone (nafazodone) usual dosage 100-600mg may be sedating and help with anxiety
1 case liver failure resulting in death / transplant 250,000-300,000pt yrs, avoid if active liver disease

Noradrenergic / specific Serotonergic antidepressant (NaSSA)

- Enhances the release of norepinephrine and serotonin while blocking certain serotonin receptors
- Remeron (mirtazapine) usual dosage 15-45mg help when insomnia is a problem, may cause weight gain

Norepinephrine / Dopamine Reuptake Inhibitor (NDRI)

- Welbutrin (bupropion) usual dosage 150-450mg less likely to cause weight gain or sexual dysfunction, may initially increase anxiety, not for those with seizures
- Welbutrin SR (2 x daily dosing)
- Welbutrin XL (1 x daily dosing)

MAO Inhibitors

- First antidepressants marketed
- Discovered in the 1950's serendipitously by chemist looking for treatment for TB

MAO Pharmacology

- Monoamine: neurotransmitters
- Oxidase: enzyme that breaks down monoamines
- MAO inhibitors: destroy this enzyme
- Allow for increased amount of neurotransmitters
- Work on norepinephrine, dopamine and serotonin

MAO I side effects

- Dangerous sudden increase in blood pressure which may lead to death, cerebral hemorrhage
- Avoid tyramine, which also increases blood pressure
- Tyramine is a natural substance found in the body and food products, tyramine forms as proteins break down as they age

Foods with Tyramine

- Aged sausages
- Beer
- Red wine
- Avocados
- Aged cheese
- Smoked fish
- Soy products

Drug Interactions

- Other antidepressants
- Most drugs for colds and asthma
- Drugs for the treatment of diabetes
- Blood pressure medications
- Some pain killers

MAO Inhibitors

- Marplan (isocarboxazid) 10-40mg
- Nardil (phenelzine) 45-90mg
- Parnate (tranylcypromine) 30-60mg
- Emsam patch (selegiline transdermal) bypasses the GI tract, and at 6 and 9mg no dietary restrictions, but use tyramine free diet at 12 mg

Antipsychotics

- Abilify (aripiprazole) 5-10mg, start at 2mg and increase to 5mg then 10mg, then 15 or 20mg as needed
- Adjunctive treatment for major depressive disorder
- Has minimal tendency to cause weight gain, metabolic side effects, sedation or movement disorders
- Side effects and drug interactions: see atypical antipsychotics

Questions?





Hypnotics

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Sleep Disorders

- Primary Insomnia
- Primary Hypersomnia
- Narcolepsy
- Breathing related sleep disorder
- Circadian rhythm sleep disorder
- Nightmare disorder
- Sleep Terror disorder
- Sleepwalking

Medications

- Benadryl (diphenhydramine)
- Ambien and CR (zolpidem)
- Lunesta (eszopiclone)
- Rozerem (ramelteon)
- Sonata (zaleplon)
- Desyrel (trazadone)
- Melatonin

Medications

- Diphenhydramine
 - Pharmacology: antihistamine
 - Dose 25-50mg 30min prior to bedtime
 - Side effects: sedation, dizziness, hangover effect

Medications

- Ambien
 - Dose: 5-10mg at bedtime
 - Pharmacology: interacts with GABA-benzodiazepine receptors
 - No evidence of next day effects, half life 2 and 1/2 hours
 - Minor changes in REM sleep at usual doses
 - Side effects: headache, drowsiness, dizziness, aggressive behavior, sleep related behavior

Medications

- Lunesta
 - Dose: 2-3mg at bedtime
 - Pharmacology: GABA-benzodiazepine receptors
 - Peak plasma level in 1 hour, half life 6 hours
 - Extensively metabolized by CYP enzymes and metabolite has hypnotic activity
 - Unpleasant taste, dry mouth, dizziness, strange sleep behavior, insomnia, impaired memory, difficulty concentrating

Medications

- Rozerem
 - Dose: 8mg at bedtime, avoid high fat meal
 - Melatonin receptor agonist
 - Peak plasma levels in 1/2 to 1.5 hours
 - Half life: 1-2.6 hours
 - Side effects: headache, fatigue, dizziness, drowsiness, strange sleep complex

Medications

- Sonata
 - Dose: 5-10mg at bedtime, max. 20mg, avoid high fat meal
 - Pharmacology: GABA-benzodiazepine receptors
 - Decreases the time to get to sleep, does not increase sleep time or decrease awakenings
 - Peak plasma level 1 hour, half life 1 hour
 - Side effects: headaches, dizziness, nausea, strange sleep complex

Melatonin

- Over the counter product
- Naturally occurring hormone, increase in levels in lack of daylight
- Decreased amount in individuals with autistic spectrum?
- Dosage: 1-4 tablets
- Relaxes musculature to help one fall asleep

Sleep Disorders

- Avoid usage if at all possible
- Use only for short term (7-14 days)
- Use lowest dose possible
- Avoid abrupt withdrawal
- Remember they interrupt / hange normal REM sleep patterns

Monitoring Hypnotics

- No blood levels are needed
- Evaluate side effects and report as needed
- Use all other possible therapies prior to initiation of hypnotics
 - Investigate reason for lack of sleep (noise, roommate, GERD)
 - Quiet music, sound machine, warm bath, warm milk
 - Develop sleep patterns and hygiene

Questions?





Mood Stabilizers

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Mood Stabilizers

- Use of Anticonvulsant Medications
- Pharmacology: decrease electrical impulses as well as increase the amount of GABA
- Useful in the treatment of bipolar disorder or added in small doses to antidepressants to enhance their effects

Mood Disorders

- Bipolar I Disorder: one or more episodes of mania or mixed episodes and most often occurs alternating with major depressive disorder
- Bipolar II Disorder: one or more major depressive disorders occur with a minimum of one hypomanic episode
- Hypomania: similar features to a manic episode, but less severe

Mood Disorders

- Cyclothymic Disorder: a less severe disorder than Bipolar I disorder, but also has many similar features. Need to have at least 2 years in which the individual experiences repeated episodes of hypomania and multiple episodes of depression
- Mood disorder due to a general medical condition (hypothyroidism, heart disease, seizure disorder)

Mood Disorders

- Intermittent Explosive Disorder: discreet episodes of impulsive aggression that has the potential to produce serious assaults or property destruction. The aggression must exceed the usual or expected intensity or threat level of provocation or precipitating events, excluding other mental disorders or substance abuse

What does this look like?

- Physical aggression
- Verbal aggression and threats
- Swearing
- Angry facial features
- "flips a switch"

Characteristic Symptoms of Manic Phase of Bipolar Disease

- Abnormally and persistently elevated, irritable or expansive mood lasting >1 week
- Presence of 3 or more of the following:
 - A. Inflated self esteem
 - B. Decreased need for sleep
 - C. More talkative than usual or need to keep talking
 - D. Flight of ideas or racing thoughts

Characteristic Symptoms of Manic Phase of Bipolar Disease

- Three or more of the following (cont)
 - E. Distractibility
 - F. Increased goal oriented activity or psychomotor retardation
 - G. Excessive involvement in pleasurable activities with high potential for painful consequences

Characteristic Symptoms of Manic Phase of Bipolar Disease

- Mood disturbance is sufficiently severe to cause
 - Marked impairment in work or social functioning, usual social activities, or relationships with others
 - May cause need for hospitalization
 - May have psychotic features

Characteristic Symptoms of Manic Phase of Bipolar Disease

- Symptoms should be evaluated and determined to not be due directly to one or more of the following:
 - Substance abuse
 - Medical conditions eg. Mania due to antidepressant therapy or steroid usage

What does this look like?

- Speeding up of all processes:
 - Thinking
 - Ambition
 - Drive
 - Sex
 - Digestion

What does this look like?

- Little or no need for sleep
- Excessive talking
- “in your face”
- Can't relax
- Aggressive
- Sexual acting out

Characteristics of Depressive Phase of Bipolar Disease

- Five or more symptoms present nearly every day during same 2 week period:
 - A. Depressed mood
 - B. Markedly diminished interest or pleasure
 - C. Significant change in weight or appetite
 - D. Insomnia or hypersomnia
 - E. Fatigue or loss of energy
 - F. Feeling of worthlessness or excessive or inappropriate guilt

Characteristics of Depressive Phase of Bipolar Disease

- Five or more symptoms (cont)
 - G. Decreased ability to think or concentrate, or inability to make decisions
 - H. Recurrent thought of death, or thoughts of suicide

Characteristics of Depressive Phase of Bipolar Disease

- Symptoms cause clinically significant distress or impairment in social and/or occupational functioning
- Symptoms need to be evaluated as not to be due to substance abuse or medical conditions
- Symptoms should not be better attributed to normal bereavement patterns

Medications



Lithium

- 1950-1970's: alters the distribution and exchange of ions involved in the process of conduction of electrical impulses in the brain
- Toxicity especially with low sodium
- Salt (chloride, carbonate), non-sedating, prophylactic properties, inexpensive
- Weigh effectiveness vs. side effects

Lithium

- Therapeutic levels: 0.6 mEq/L-1.5 (2-3 300mg tabs of lithium carbonate/day), fine hand tremor, thirst, nausea, excessive sweating
- Toxic signs: diarrhea, vomiting, drowsiness, confusion, muscle weakness
- Levels>2.0: ataxia, tinnitus, kidney dysfunction
- Levels>3.0: coma, respiratory depression, death

Lithium

- Half life: 20-24 hours
- Slow release product: Lithobid
- May be better alternative with less potential for side effects

Classic Mood Stabilizers

- Lithium Carbonate Summary:
 - More effective for true Bipolar Type I disorder but may be helpful as adjunct
 - Need to periodically monitor levels, BUN, Cr, TSH and free T4
 - Concern for toxicity, Nephrogenic drug interactions
 - Need to consider med selection for other disorders (e.g. NSAIDS, diuretics, COX-2 inhibitors)

Depakene (Valproic Acid) and Depakote (Valproate)

- Pharmacokinetics
 - Depakote tablets lag in absorption (1hr on empty stomach, up to 8 hrs w/food)
 - Depakote tablets are coated to reduce possible GI side effects (Do not crush)
 - Depakene are liquid filled capsules, and appear to have more GI side effects (TID or QID)
 - Dosage strengths: 125, 250 and 500mg tablets

Mood Stabilizers (Divalproate)

- Very effective for mood stabilization (efficacy in both manic as well as depressive stages) and aggression
- Less medication interactions than Carbamazepine
- Need to monitor liver functions *and* platelet counts (especially in elderly)
- May require doses higher than antiepileptic doses for good control of impulsivity/aggression (blood levels of 100-150 mcg/ml)

Divalproex side effects

- Weight gain
- Brittle hair
- Easy bruisability (check platelets)
- Increase in liver function tests
- Sedation
- Dose related side effects: tremor and gait disturbance (back off on the dose)

Depakote sprinkles and ER formulation

- Sprinkles available in 125mg capsules that allow for smoother, extended release flow and more consistent blood levels
- Depakote ER formulated in 250 and 500mg tablets that allow for 1-2 times daily dosing minimizing side effects and allowing for a sustained release action

Mood Stabilizers

- Carbamazepine
 - Highly effective for aggression and agitation, less so mood stabilization
 - Inducer of hepatic enzymes and may cause havoc with blood levels of other meds
 - Need to monitor for liver functions and CBC for marrow suppression
 - Optimal treatment may be with higher doses (levels of 10-12)

Carbatrol and Tegretol XR

- Carbatrol
 - 200mg and 300mg sustained release capsule
- Tegretol XR
 - 100, 200, and 400mg sustained release tablets
- Advantages of both
 - Ease of dosing (bid)
 - Smoother blood level
 - Less potential side effects

Newer Antiepileptic Medications

- Oxcarbazepine (Trileptal)
- Topiramate (Topamax)
- Gabapentin (Neurontin)
- Lamotrigine (Lamictal)
- Tiagapine (Gabatril)
- Levetiracetam (Keppra)

Lamotrigine (Lamictal)

- Pharmacokinetics:
 - Highly affected by concomitant use of other antiseizure medications, so initial dose must be low, start slow, and titrate over several MONTHS.
 - Initial dose if on divalproex and enzyme inducers is 25mg qod.
 - If not on divalproex, but on enzyme inducer, use 50mg/day.
 - » Inducers: carbamazepine, phenobarbital, phenytoin

Lamotrigine (Lamictal)

- More than 95% metabolized, many metabolites, some active
- Dosage form: 25, 100, 150, 200mg tabs; 2.5 and 25mg chewable tabs

Lamotrigine

- Maintenance dose of 100-150mg/day if on divalproex,
- otherwise, 300-500mg/day dosed bid
- Half-life:
 - Ave 25hrs (monotherapy)
 - Ave 14hrs (inducers)
 - Ave 27hrs (inducers & VPA)
 - Ave 70 hrs (VPA)

Lamotrigine

- Steady state: 3-15 days
- Side effects:
 - CNS: drowsiness, diplopia, dizziness, ataxia
 - Rash
- Drug interactions:
 - carbamazepine and phenytoin decrease half-life
 - divalproex prolongs half-life

Monitoring

- Differentiate dose related vs idiosyncratic side effect if possible
- Monitor and report side effects as they occur
- Lab work:
 - Drug blood levels very helpful, usually every 1-3 months
 - Liver function testing
 - Additional lab work as needed (platelet count)

Questions?

