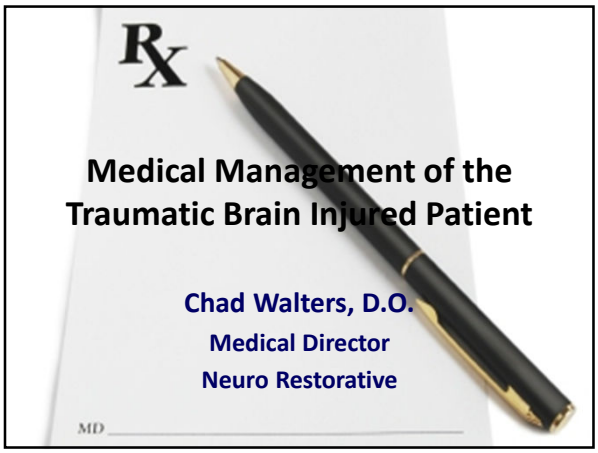

Medical Management of the Traumatic Brain Injured Patient

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Outline

- **Common Medical Problems**
  - Post-traumatic Seizures/Epilepsy
  - Spasticity
  - Depression/Anxiety
  - Agitation/Aggression
  - Sleep disorders
  - Attention deficits
- **Medications and side effects for each**

Medication Management Philosophy

- Start low and go slow
- Change one medication at a time
  - Adding/stopping medications
  - Changing doses
- Look for medications that can be eliminated before adding others
- Give adequate time for therapeutic effect
- Educate patients and families on reasonable outcomes, targeted effects, side effects
- Treat the "Why" and not the "What"

Post-traumatic Seizures

- **Post-traumatic Seizures**
  - Immediate: first 24 hours
  - Early: 1 – 7 days
  - Late: after 7 days
- **Post-traumatic Epilepsy**
  - Two or more late onset seizures separated by at least 24 hours that is not attributable to other causes (Infections, Electrolytes, Medications)

Post-traumatic Seizures

- Generalized
  - Bilateral hemisphere involvement
  - Also known as "Grand Mal"
  - Nearly all involve loss of consciousness (LOC)
- Partial
  - Unilateral involvement
  - Complex or Simple
    - Complex: (+) LOC
    - Simple: (-) LOC
  - **Most common form found in TBI**

Post-traumatic Seizures

- Generalizations
  - 80% of seizures will develop in first 2 years
  - Neuro-imaging is NOT helpful in predicting PTS
  - EEG is NOT helpful in predicting PTS
    - False positives and negatives are common

Post-traumatic Seizures

- Treatment
  - Only treat late-onset seizures
  - Tegretol, Depakote, Lamictal, Topamax, Vimpat, Trileptal, Keppra
  - Duration is physician dependent
    - 1st seizure: 18 months
      - Limit potentially cognitive sedating meds as much as possible
    - 2nd Seizure: 2 years
    - 3rd seizure: lifetime
- Seizures lasting greater than 5 minutes have a high risk of developing status epilepticus

Post-traumatic Seizures

- Medications
  - Tegretol (Carbemazepine)
  - Depakote (Valproic Acid)
  - Lamictal (Lamotrigine)
  - Topamax (Topiramate)
  - Keppra (Levetiracetam)
  - Vimpat (Lacosamide)
  - Trileptal (Oxcarbazepine)
  - Zonegran (Zonisamide)

Post-traumatic Seizures

- Mechanism of Action
  - Stabilizes cell membranes to decrease frequency of spontaneous firing
- Common Side effects
  - Lethargy
  - Confusion
  - Dizziness/Gait unsteadiness
  - Weight gain
  - Hepatotoxicity
  - Pancytopenia

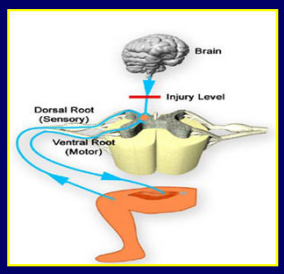
Post-traumatic Seizures

- Monitoring levels
  - Can get levels on any anti-seizure medication to assure therapeutic range
  - CBC, CMP and drug levels every 3 months
- Toxicity effects
  - Marked lethargy/somnolence
  - Hallucinations/Paranoid delusions
  - Fever

Spasticity

- Definition: Velocity dependent increase in muscle tone with resistance to stretch
- Occurs due to deficiency or absent of descending inhibitory pathways
  - Gamma Amino Butyric Acid (GABA) is the primary inhibitory neurotransmitter that turns off the spinal reflex

Spasticity



Spasticity

- Treatments
  - PT/OT for stretching, splinting/casting and modalities (heat, ice, ultrasound, E-Stim)
  - Oral Medications
    - Baclofen, Dantrium, Zanaflex
  - Injections
    - Botulinum toxin, Phenol
  - Invasive treatments
    - Intrathecal Baclofen pump
    - Tendon lengthening procedures

Spasticity

- Medications (cont.)
  - **Dantrium (Dantrolene Sodium)**
    - **50-100mg BID or TID**
    - Inhibits muscle activity at the muscle itself (only agent that works at the muscle level). Inhibits Calcium release from the sarcoplasmic reticulum.
    - Side effects: **Hepatotoxicity**, weakness, lethargy
    - Monitoring: CBC, CMP every 3 months

Spasticity

- Medications
  - **Baclofen**
    - **5-20mg TID**
    - enhances effect of GABA in the CNS in effort to "turn off" the spinal reflex pathway
    - Side effects: weakness, lethargy, confusion, dizziness, respiratory distress
    - Withdrawal: increase muscle tone, itching (without presence of a rash), hallucinations (usually visual), seizures, fever, death
    - Oral or Intra-thecal preparations

Spasticity

- Medications (cont.)
  - **Zanaflex (Tizanidine)**
    - **2-8mg TID**
    - Inhibits descending excitatory pathways both at the brain and spinal cord levels
    - Usually used as an adjunct to other medications
    - Side effects: **hypotension**, **sedation**, fatigue, dizziness, hepatotoxicity

Spasticity

- Injectible treatments
  - Botulinum toxin (Botox, Myobloc, Dysport)
    - Inhibit the release of Acetylcholine into the synapse to prevent muscle contraction
    - Best if localization measures are used
      - EMG, Electrical stimulation, Ultrasound
    - Side effects: Muscle irritation, localized pain, fever, nausea, dysphagia (if used close to the neck)
    - FDA approved for upper extremity spasticity and cervical dystonia only

Depression

- Definition: psychological disorder that presents as a depressed mood, lost of interest or pleasure, feelings of guilt or low self-worth
  - Not just feeling "sad"
- Patients often claim to feel "lost in the world"
- Pathophysiology
  - deficiency in serotonin, norepinephrine and/or dopamine in the Central Nervous System

Depression

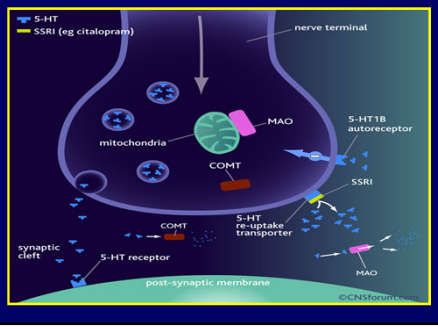
- Medications should be used in conjunction with psychotherapy and counseling
- Medication classes
  - SSRI
  - SNRI
  - TCA
  - "Novel"

Depression

- **SSRI's**
  - Selectively inhibits the reuptake of **Serotonin** in the synapse making it more available to the post-synaptic membrane

Depression

SSRI Mechanism of Action



Depression

- **SSRI's** (cont.)
  - **Zoloft** (Sertraline) 50-150mg daily
  - **Paxil** (Paroxetine) 20-50mg daily
  - **Celexa** (Citalopram) 10-40mg daily
  - **Lexapro** (Escitalopram) 10-20mg daily
  - **Prozac** (Fluoxetine) 20-80mg daily
  - Luvox (Fluvoxamine) 50-150mg twice daily

Depression

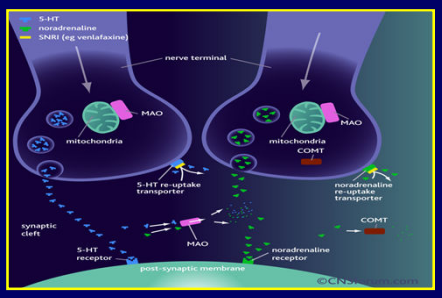
- **SSRI's** (cont.)
  - Side effects: Nausea, Vomiting, Diarrhea, Dry mouth, sedation (esp with Paxil), delayed ejaculation, decreased libido, serotonin syndrome (especially when used with other SSRI's)
  - Must give 3-4 weeks trial before changing dose or switching medications

Depression

- **SNRI's**
  - Inhibits the reuptake of **Serotonin** and **Norepinephrine** in the nerve synapse

Depression

SNRI Mechanism of Action



Depression

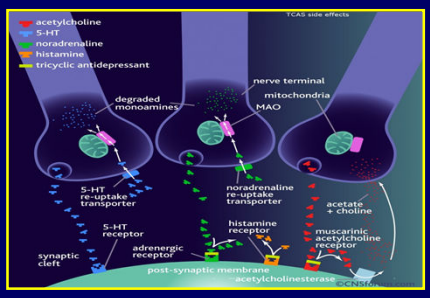
- **SNRI's** (cont.)
  - **Cymbalta** (Duloxetine) 30-60mg daily
  - **Effexor** (Venlafaxine) 37.5-75mg BID or TID
  - **Pristiq** (Desvenlafaxine) 50mg daily
  - Side effects: Insomnia, nausea, vomiting, diarrhea, seizures, HTN, heart arrythmias, anxiety, agitation/aggression

Depression

- **TCA's** (Tricyclic/Tetracyclic Antidepressants)
  - Inhibits re-uptake of **Norepinephrine**, **Serotonin** and **Histamine** at the synapse.
  - Anticholinergic effects which limit use in TBI population and is cause for most common side effects

Depression

TCA Mechanism of Action



Depression

- **TCA's** (Tricyclic/Tetracyclic Antidepressants)
  - **Elavil** (Amitriptyline) 50-150mg qhs
  - **Pamelor** (Nortriptyline) 50-150mg qhs
  - **Anafranil** (Clomipramine) 50-250mg qhs

Depression

- **TCA's** (Tricyclic/Tetracyclic Antidepressants)
  - **Side effects**: Memory loss, attention and concentration deficits, sedation, confusion, delerium, hypotension, urine retention, constipation
  - Used mostly in TBI population for sleep disorders, not depression

Depression

- "Novel" Group
  - **Wellbutrin** (Buproprion) 50-150mg BID
    - Inhibits reuptake of serotonin, norepinephrine and dopamine at nerve synapse
    - Useful for depression and attention/concentration deficits
    - Side effects: anxiety, insomnia, seizures, hallucinations
  - **Remeron** (Mirtazapine) 15-30mg qhs
    - Used mostly for sleep disorders and poor appetite
  - **Trazodone**
    - Used predominately for sleep disorders

Anxiety

- Definition: psychological disorder presenting as feelings of fear, uneasiness and/or restlessness
  - Situational or Generalized
- Commonly accompanies depression as a clinical syndrome

Anxiety

- **Situational**
  - Panic disorder usually triggered by an external stimulus
  - Crowded areas such as malls, grocery stores, events, etc…
  - Includes social phobias, OCD and PTSD
- **Generalized**
  - Constant feeling of tension, uneasiness, fear

Anxiety

- **Generalized**
  - SSRI's
    - Paxil 10-40mg daily
    - Celexa 10-40mg daily
    - Lexapro 10-20mg daily
    - Zoloft 50-150mg daily
  - Beta-blockers
    - Propranolol 20-60mg BID or TID - scheduled

Anxiety

- **Situational**
  - Anxiolytics
    - Short Acting (half-life 8-10 hours)
      - **Xanax** (Alprazolam) 0.25-1mg TID prn
      - **Serax** (Oxazepam) 10-30mg TID
    - Medium acting (half-life 10-14 hours)
      - **Ativan** (Lorazepam) 2-6mg/day divided BID or TID prn
      - **Estazolam** 1-2mg qhs prn

Anxiety

- **Situational**
  - Anxiolytics (cont.)
    - Long Acting (half-life 20-40 hours)
      - **Klonopin** (Clonazepam) 0.5-5mg TID
      - **Valium** (Diazepam) 2-10mg BID to TID
      - **Dalmane** (Flurazepam) 10-30mg qhs
    - Non-Benzodiazepine
      - **Vistaril** (Hydroxyzine) 25-50mg TID
      - **Inderal** (Propranolol) 10-30mg TID
  - Used mostly on an as needed basis

Anxiety

- **Side effects**
  - Benzodiazepines (all classes)
    - Lethargy, Drowsiness, Dizziness, Confusion, Delerium, Ataxia, Potential for abuse/addiction, Respiratory depression
  - Vistaril
    - Dry mouth, dizziness, lethargy, drowsiness
  - Inderal
    - Drowsiness, hypotension, bradycardia, depression

Agitation

- A psychological state manifested by verbal and/or physical aggression or rage
- Usually caused by an external trigger, but not always
- **Must identify what is causing the agitation in order to treat it effectively**
  - **Commonly not mood instability but rather an underlying anxiety disorder, sleep disorder, depression or frustration**
- Physiologically is a state of sympathetic overdrive and/or excessive dopamine
- Treatments are aimed at controlling these physiologic changes

Agitation

- **Treatments**
  - Mood Stabilizers
    - Depakote 250-1500mg BID
    - Tegretol 100-400mg BID
  - Atypical Antipsychotics
    - Risperdal 1-3mg BID
    - Seroquel 50-200mg BID
    - Zyprexa 5-20mg at night
    - Geodon 20-80mg BID

Agitation

- **Treatments**
  - Typical Antipsychotics
    - Haldol
    - Thorazine
    - Compazine
  - These agents should NEVER be used for maintenance therapy in brain injury patients
  - Evidence of delayed and incomplete cognitve recovery
  - Tardive Dyskinesia

Agitation

- **Treatments**
  - Maintenance therapy (cont.)
    - Beta-blockers
      - Propranolol 20-60mg BID or TID
    - Anxiolytics
      - Hydroxyzine 50-100mg TID
      - Clonazepam 1-3mg BID
    - Antidepressants
      - SSRI's
    - Neurostimulants
      - Ritalin, Adderall, Concerta, Strattera

Sleep disorders

- Difficulty with initiation, maintenance or both
  - Recommendation: 6-8 hours/night uninteruppted
- Must take a thorough history in order to treat sleep problems effectively
  - Night time routines
  - Caffeine intake
  - Napping during the day
  - Headaches
  - Awakening due to other medical problems
    - Pain, Urination, muscle spasms

Sleep disorders

- Treatment
  - First line is environmental changes
    - "Settling down" period at night
    - Relative dark environment with little/no noises
    - No caffeine after 7pm
  - If headaches are associated, may need to get a sleep study
    - Spouse/significant other reports patient snores excessively
  - Treat any underlying medical problem that is contributing

Sleep disorders

- Treatment
  - Initiation only problem
    - Brain can't "shut down" at night
    - Once patient can get to sleep they can stay asleep for 6-8 hours
      - **Melatonin**
        - » 3-6mg at night about an hour prior to wanting to go to sleep
      - **Trazodone**
        - » 50-150mg at night

Sleep disorders

- **Treatment**
  - Maintenance or Combined problem
    - Patients have difficulty with getting to sleep and staying asleep….OR….can get to sleep fine, but have trouble staying asleep
    - Awaken 5-7 times per night
    - Again….must treat any underlying medical cause

Sleep disorders

- **Treatment**
  - Maintenance or Combined problem
    - Medications
      - Restoril (Temazepam) 15-30mg at night
      - Ambien 5-10mg at night

Sleep disorders

- Side effects
  - **Melatonin**: nightmares, sleepwalking, headaches
  - **Trazodone**: headaches, dizziness, nausea, vomiting, dry mouth
  - **Restoril**: drowsiness, fatigue, "hangover" effect, dizziness
  - **Ambien**: sleepwalking, night terrors, hallucinations, dizziness, lethargy, "hangover" effect

Attention Deficits

- Inability to maintain focus and concentration on visual or auditory tasks
- Common with Frontal and/or Temporal lobe injuries
- Physiologically is a deficiency in the dopaminergic and/or noradrenergic pathways
- Can be associated with or without a hyperactivity component
- Again, a thorough history needs to be taken before any agent should be started
  - Heart disease (personal or family), seizures, sleep disorders, psychosis

Attention Deficits

- Clinical presentations
  - Poor memory
  - Agitation
  - Frustration
  - Irritability
  - Tangential speech
  - Restlessness (hyperactive)

Attention deficits

- **Treatment**
  - Neurostimulants
    - **Ritalin** – blocks the re-uptake and increases the release of Norepinephrine (and some Dopamine) at the synaptic terminal
      - 5-20mg every morning and noon
      - Side effects: Agitation, hallucinations, mania, hypertension, tachycardia, anorexia. Anxiety, insomnia
    - **Adderall** – same as Ritalin but with less Dopamine effects
      - 10-20mg every morning and noon
      - Side effects: Same as Ritalin

Attention deficits

- **Treatment**
  - Dopaminergics
    - **Amantadine**: Increases the release of dopamine from the pre-synaptic membrane
      - 100-200mg every morning and noon (should not be taken after 3pm)
      - Side effects: Hallucinations, Seizures, Irritability, Anxiety, Insomnia
    - **Bromocryptine**: Blocks the re-uptake of dopamine from the synapse
      - 2.5-10mg every morning and noon (should not be taken after 3 pm)
      - Side effects: Same as Amantadine

Attention deficits

- Treatment (cont.)
  - Concerta, Strattera and Vyvanse have not been well studied in TBI population and should be used if others have failed or side effects observed
  - Antidepressants
    - Wellbutrin 50-150mg BID

Summary

- Start low and go slow
- Change one thing at a time if possible
- Knowing side effect profiles and goals of treatment are vital
- Education is important
- Treat problems, not symptoms