MEDICATION MANAGEMENT OF BRAIN INJURED PATIENTS

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Dr. Collins has no financial or non-financial conflicts of interest related to this activity.

Non-FDA approved products and indications will be discussed during this presentation.
OBJECTIVES

- Describe the obstacles for standardizing medication treatments in brain injured patients.
- Identify at least 3 neurotransmitter targets for pharmacotherapy.
- Discuss factors that should be considered in choosing medication treatment in a brain injured patient.
- List 2 medications that should be used with caution in a brain injured patient.
Spot 10 differences
OBSTACLES TO DEVELOPING STANDARD OF CARE

Differences among patient population

- Individual injury
  - Neuroanatomy
  - Neurophysiology
  - Neurochemistry
- Individual pre-morbid function
- Individual post-injury sequela
OBSTACLES TO DEVELOPING STANDARD OF CARE

- Variable responses to medications
  - Some patients benefit
  - Some patients get worse
  - Some patients more sensitive
  - Some patients resistant or need extreme doses

- Compliance issues
  - Memory
  - Adverse effects and interactions

- Measuring cognition and behavior
  - Patient may test well, but function poorly
  - Patient may test poorly, but function well

- Variations in biochemistry balance

CRAIG NEUROREHABILITATION & RESEARCH HOSPITAL
OBSTACLES TO DEVELOPING STANDARD OF CARE

<table>
<thead>
<tr>
<th>Standards</th>
<th>Guidelines</th>
<th>Options</th>
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<tbody>
<tr>
<td>Based on at least 1, well-designed class I study with adequate sample OR overwhelming class II evidence</td>
<td>Based on well-designed class II studies</td>
<td>Based on class II or class III studies with additional grounds to support a recommendation</td>
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*Lack of evidence ≠ lack of efficacy*
NEUROCHEMICAL APPROACH TO TREATMENT
NEUROCHEMICAL APPROACH TO TREATMENT

Serotonin
- Memory
- Emotion
- Sleep/wake

Side effects
- Nausea
- Sexual side effects

Selective serotonin reuptake inhibitors (SSRIs)
- Sertraline (Zoloft®)
- Citalopram (Celexa®)

Serotonin/norepinephrine reuptake inhibitors (SNRIs)
- Duloxetine (Cymbalta®)
- Venlafaxine (Effexor®)

Tricyclic antidepressants (TCAs)
- Amitriptyline (Elavil®)
- Nortriptyline (Pamelor®)
**NEUROCHEMICAL APPROACH TO TREATMENT**

**Dopamine**
- Voluntary movement
- Motivation/initiation
- Memory

**Side effects**
- Nausea
- Headache
- Impulsivity

**Parkinson’s disease medications**
(↑dopamine)
- Bromocriptine (Parlodel®)
- Levodopa/carbidopa (Sinemet®)

**NMDA antagonists**
(↑dopamine/↓glutamate)
- Amantadine (Symmetrel®)
- Memantine (Namenda®)

**Atypical antipsychotics**
(↑serotonin/dopamine)
- Risperidone (Risperdal®)
- Aripiprazole (Abilify®)
- Quetiapine (Seroquel®)
NEUROCHEMICAL APPROACH TO TREATMENT

Norepinephrine
- Arousal
- Attention
- Improve cognitive function

Side effects
- Agitation
- Insomnia
- Decrease appetite

Stimulants (↑ norepinephrine/dopamine)
- Methylphenidate (Ritalin®)
- Dextroamphetamine (Dexedrine®)
- Atomoxetine (Strattera®)

β-blockers (↓ norepinephrine)
- Propranolol (Inderal®)
NEUROCHEMICAL APPROACH TO TREATMENT

Acetylcholine

- Memory
- Improve fatigue

Side effects
- Nausea
- Insomnia
- Impulsivity

Acetylcholinesterase inhibitors (↑ acetylcholine)

- Donepezil (Aricept®)
- Galantamine (Razadyne®)
- Rivastigmine (Exelon®)
NEUROCHEMICAL APPROACH TO TREATMENT

**Glutamate**
- Excitatory transmitter
- Overstimulation → cell death
- Affects cognition

**Side effects**
- Headache
- Insomnia

**NMDA antagonists**
(↑dopamine/↓glutamate)
- Amantadine (Symmetrel®)
- Memantine (Namenda®)
- Dextromethorphan (Neudexta®)
APPROACH TO TREATMENT

Medication considerations
- Age
- Comorbidities
- Drug interactions
- Sensitivities
- Adherence
- Costs

Control environment

Remove medication contributors

Consider medication treatment
PATIENT CASE

- MF is a 58 year old male who sustained a traumatic brain injury (TBI) due to a un-helmeted motorcycle accident approximately 2 months ago. Toxicology screen was positive for alcohol, marijuana, and cocaine.

- Past medical history is significant for asthma, hypertension, 20 pack year smoker.

- His course has been complicated by bilateral deep vein thrombosis (DVTs), occurrence of seizure, urinary retention, need for enteral feeding, and significant shoulder pain.
PATIENT CASE

Today’s presentation

- Patient is agitated, un-oriented with reports of striking nursing staff and verbal outbursts that are un-intelligible.
- His blood pressures are labile.
- He is holding his head and moaning.
- Nursing reports poor sleep.
MEDICATION TREATMENT TARGETS

Post Traumatic Headache
Hyper arousal/ aggression
Sleep
Cognition/Memory
Aphasia
POST TRAUMATIC HEADACHE

• Occurring in 25-78 % of individuals with mild TBI
• More frequent in individuals with mild versus moderate of severe TBI
• Exacerbated by very mild physical or mental exertion
• Can be episodic or continuous

Presentation Types
• Migraine headache
• Tension headache
• Medication overuse headache

POST TRAUMATIC HEADACHE
ABORTIVE TREATMENT OPTIONS

Patient considerations
- Consider scheduled dosing
- Caution for medication overuse
- Avoid sedating or activating agents
- Assess bleeding risk

Acetaminophen ± combinations
- APAP/caffeine/ibuprofen

Anti-emetics
- Prochlorperazine
- Promethazine

NSAIDS
- Ibuprofen
- Ketorolac

Serotonin receptor agonists
- Sumatriptan
- Rizatriptan

Calcitonin gene-related protein (CGRP) inhibitors
- Ubrogepant
- Rimegepant
POST TRAUMATIC HEADACHE PROPHYLAXIS OPTIONS

Initiate headache prophylaxis if:

- migraine occurs >1/week or if tension headache occurs >3/week
- is disabling despite aggressive interventions
- affecting ADLs
HYPER-AROUSAL

Agitation/Aggression
- Common during post-traumatic amnesia
- Affects safety and adherence to treatment
- Most common in the acute phase, but can persist long term

Storming - dysautonomia
- Tachycardia
- Dystonia
- Diaphoresis
- Hypertension
HYPER-AROUSAL

Atypical antipsychotics
- Aripiprazole
- Risperidone
- Quetiapine

SSRIs (↓)
- Citalopram
- Sertraline

NMDA antagonists (↑dopamine/↓glutamate)
- Amantadine
- Memantine

β-blockers (↓ norepinephrine)
- Propranolol

Patient Considerations
- Prioritize safety
- Consider PMH of HTN
- Monitor closely for side effects
Sleep disorders include
- Hyper somnolence
- Sleep related breathing disorders

Prevalent and persistent
- Present in 30-70% of patients with a history of brain injury
- Higher in the acute phase
- Usually decreases after a few years
SLEEP

Patient Considerations
- Urinary retention
- Seizure history
- Goal is short term treatment

- Trazodone
- Melatonin
- Orexin inhibitors
- SSRIs
- "Z" meds (zolpidem)

Others: histamine, orexin, melatonin

Serotonin
COGNITION/MEMORY

- 40-60% of patients 1-3 months following TBI
- Correlates with injury severity
- Prolonged
- Removing or decreasing medications may be considered a "therapeutic event"

VA/DOD 2016; BHATNAGER 2016; ARCINIEGAS 2002
COGNITION/MEMORY

Patient Considerations
- Avoid stimulants
- Monitor for side effects
- Set expectations for benefit

Stimulants (↑ norepinephrine)
- Methylphenidate
- Dextroamphetamine
- Atomoxetine

NMDA antagonists (↑dopamine/↓glutamate)
- Amantadine
- Memantine

Acetylcholinesterase inhibitors
- Donepezil

BHATNAGER 2016; MANKTELOW 2017
“Drug therapy might improve recovery from loss of language (aphasia) after stroke, but no drug has yet been proven to do more good than harm.”

J Greener, Cochrane Stroke Group, Division of Clinical Neurosciences. 2010
APHASIA

TCAs

SSRIs

NMDA antagonists

Stimulants

Dopamine agonists

Acetylcholinesterase inhibitors

Patient considerations
- Consider medication if useful for other comorbidities
MEDICATIONS TO USE WITH CAUTION

Benzodiazepines
- Common for insomnia and agitation
- Exacerbate confusion ("benzodiazepine psychosis")
- Impair memory
- Abuse potential
- Stopping the medication may be the “therapeutic event”

Typical antipsychotics (1st generation)
- Block dopamine
- May interfere with cognitive recovery
- Sedation->confusion-> aggression
PATIENT CASE

Treatment plan

- Initiate one intervention at a time
- Start low, go slow
- Monitor for response and side effects
- Trial lower doses with improvement or when stable
- Re-evaluate often