Drugs And Dysphagia

Presented by:
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Section 2: Additional Medications Affecting the Central Nervous System
Medications Used to Treat Seizures
The number of anticonvulsants available for use has increased dramatically in the past few years. In addition to using these agents to prevent seizures, they are used in the treatment of neuropathic pain. Anticonvulsants work by affecting the central neurotransmitter GABA- (gamma- amino butyric acid) or by affecting the electrical discharge in the brain by affecting the transport of ions such as potassium and calcium into the brain cells. The increase in GABA, or the slowing of electrical discharge through alterations in these ions that results from anticonvulsants can slow the electrical discharges in the brain tissue and reduce the risk of seizures, but also can reduce cognition and cause depression of the central nervous system and contribute to dysphagia.
Anticonvulsants

- Examples include:
  - Phenytoin, Fosphenytoin (Dilantin, Cerebyx),
  - Valproic Acid (Depakote),
  - Carbamazepine (Tegretol),
  - Gabapentin (Neurontin),
  - Lamotrigine (Lamictal),
  - Levetiracetam (Keppra),
  - Oxcarbazepine (Trileptal)
  - Phenobarbital
  - Primidone,
  - Tiagabine (Gabitril),
  - Topiramate (Topamax)
  - Zonisamide (Zonigran).

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Anticonvulsants

- Side effects associated with Anticonvulsants that contribute to dysphagia:
- Sedation— inattention to eating, lack of coordination, decreased appetite
- GI upset
- Gingival hyperplasia
- Mucosal injury associated with hypersensitivity reactions
- (Stevens-Johnson syndrome or TEN toxic epidermal necrolysis)
Case #3: Dysphagia associated with Anticonvulsant Therapy

- P.R. is a 90 year old man who sustained a head injury from an automobile accident and is currently receiving Dilantin (Phenytoin ®) to prevent seizures.
- The physician rounding with the team is concerned that this medication is affecting the patient’s nutritional status, as he has lost 10 pounds in the last 3 weeks. He also has developed mucositis, sedation, and ataxia.
- He asks you whether the head injury has caused the patient’s dysphagia. What is your response? See additional information on the next slide!
Anticonvulsants

The summary table on the next slide lists the anticonvulsant medications, with corresponding starting and maximum dosing, along with side effects associated with each agent. The side effects are grouped into those that can contribute to dysphagia, and other important side effects that need to be considered in selecting an appropriate agent for a patient. The severity of the side effects are ranked from 0, which indicates little effect, to ++++, which indicates a high likelihood of encountering this side effect if this agent is used. Common side effects listed that contribute to dysphagia include sedation, ataxia, GI upset, xerostomia, mucositis. Rash indicates risk of developing a hypersensitivity rash (Stevens-Johnson syndrome) that can cause sloughing of the skin and mucous membranes. When selecting a medication for a patient, it is important not to select an agent that will worsen a problem that a patient already has- for example, a patient already on a sedating medication should avoid taking a medication that would increase his sedation.
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<th>Medication</th>
<th>Dose</th>
<th>Dysphagia Side Effects</th>
<th>CNS</th>
<th>Ataxia</th>
<th>GI</th>
<th>Xerostomia</th>
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Anticonvulsants

- Answer – Yes- the symptoms can be due to his injury, but Dilantin can also be causing these new symptoms!
- Looking at the chart, you can see that Dilantin can cause sedation, mucositis, and ataxia. Side effects can be much more pronounced in the older patient. In view of this patient’s symptoms, and the fact that the Dilantin is being used as a preventative rather than to treat actual seizures, it should be recommended to discontinue this medication.
- It is always best to use the minimum number of medications needed to minimize risk of drug interactions and side effects, especially in the older patient, as their ability to remove medications from the body through the kidney and liver is much slower than with younger patients. As a result, older patients like this 90 year old gentleman are at higher risk for adverse effects from medications!
Medications Used to Treat Anxiety and Sleep Disorders
Anti-anxiety medications are used for treatment of anxiety, used for treatment of panic disorders, obsessive compulsive disorders, and to enhance sleep for the insomniac. GABA and Dopamine are the brain’s two neurotransmitters that depress nerve function, and the antianxiety medications increase the effects of GABA, resulting in CNS depression, sedation, decreased cognition, decrease in motor coordination, and thus can contribute to dysphagia.
Antianxiety Medications

- Enhance effects of Neurotransmitter GABA, resulting in CNS depression.
- These agents can have anti-seizure effects, and the IV forms are used as sedation in surgical procedures.
- Avoid concurrent ETOH (drinking), as alcohol can greatly increase these depressive effects!
- Combining these with other CNS depressants will greatly enhance (potentiate) these effects, and can result in respiratory depression and oversedation.

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Benzodiazepines:
- Lorazepam (Ativan) (seizures and anxiety)
- Clonazepam (Klonopin)
- Diazepam (Valium) (seizures and anxiety)
- Estazolam (Prosom) (sleep)
- Temazepam (Restoril) (sleep)
- Alprazolam (Xanax)
- Flurazepam (Dalmane) (sleep)
- Midazolam (Versed) (IV for Procedures)
- Triazolam (Halcion) (sleep)

Non-Benzodiazepines:
- Buspirone (Buspar)
- Zaleplon (Sonata) (sleep)
- Zolpidem (Ambien) (sleep)
- Eszopiclone (Lunesta) (sleep)
Antianxiety and Sleep Medications

Dysphagia side effects include:
- Sedation, coordination disorders, decreased concentration resulting in inattention to meals and difficulty eating.
  - This is particularly true with agents having a long half-life such as Dalmane and Valium.

- Gastrointestinal side effects such as heartburn, nausea, vomiting, diarrhea and constipation

- Taste alterations, dry mouth.
  - For example, Xanax will result in taste loss.
Antianxiety Agents

- Chronic use of benzodiazepines:
  - “Chronic use of benzodiazepines can result in significant pharyngeal phase dysphagia, notably cricopharyngeal incoordination, hypopharyngeal incoordination and aspiration. The pharyngeal dysphagia may be diminished through cessation of the medication”.
  - Carl and Johnson, page 104
Case #4: Dysphagia with Antianxiety Medications

- A.Z., an 88 y/o F has significant symptoms of anxiety and insomnia since the death of her husband of 50 years two weeks ago.

- Her physician has prescribed Diazepam (Valium) 5mg three times daily for her anxiety, and Dalmane 15mg at bedtime for her insomnia.

- Her daughter calls, concerned with her mother’s inability to ambulate. She refuses to eat, stating her mouth is dry, and she has no interest in eating, feels like she is choking when she tries to swallow.
Case #4: Dysphagia with Antianxiety Medications

- She asks whether these new medications are causing these effects. What do you think?
- Please refer back to the slide on side effects of anti-anxiety medications.
Antianxiety Agents

- Answer – Yes, her mother’s symptoms are due to these two new medications!
- Because – both Valium and Dalmane have long half-lives, and also are converted to metabolites in the body that also cause sedation.

- Because of this, even one of these medications should not be used in the older patient, much less both of them together!
Antianxiety Agents

- It should be recommended to discontinue these medications, and use a low dose of a shorter acting antianxiety medication that does not have an active metabolite.

- A possible alternative regiment would be Restoril 7.5mg for sleep if needed, with Buspar 1mg twice daily if needed for anxiety.
Medications to Treat Bipolar Disorder (Manic Depressive illness)
Causes of Bipolar Disorder

- Bipolar disorder is the new term for manic-depressive illness, in which the patient cycles through periods of depression alternating with periods of euphoria and excessive energy often accompanied with actions dictated by poor judgment and grandiose ideas.
- These actions are related to alterations in the levels of the neurotransmitter norepinephrine, dopamine and serotonin.
Causes of bipolar disorder

- Stress often trigger the cycles.
- Medication therapy is the mainstay for bipolar disorder treatment, and is designed to treat the acute symptoms, and reduce the frequency of cycling from mania to depression.
- Anticonvulsants actions are also used to reduce the rapid cycling from mania to depression.
Medications Used to Treat Acute Mania Symptoms

- Acute treatment of mania:
  - Anti-anxiety and antipsychotic agents (to manage agitation)
  - Higher doses of lithium
  - Anticonvulsants valproic acid (Depakene®), or carbamazepine (Tegretol®)
  - Antipsychotic medication Seroquel®
Treatment of Bipolar Disorder

- Acute depression Symptoms Managed with:
  - higher doses of lithium (serum levels of 1.0-1.2 mEq/L)
  - or antidepressant of choice, buproprion (Wellbutrin®).

- Maintenance Medications to prevent Recurrence (Recycling):
  - lower doses of lithium
  - antidepressants
    - (Selective serotonin reuptake inhibitors (SSRI’s))
    - atypical antidepressants

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Bipolar Disorder - Lithium Use

- Lithium- dysphagia side effects include:
  - GI distress, xerostomia, tremors, neuromuscular weakness, ataxia, and sedation.
  - Xerostomia can cause difficulty in swallowing initiation.
  - Dysphagia can result from deglutitive inhibition on the esophageal striated or smooth muscle or from abnormal peristalsis on the smooth visceral muscle.
  - Sedation will impair mental abilities resulting in inattention to eating, decreased appetite and impaired motor coordination.
  - Lithium is a mainstay in the stabilization of a patient with acute mania and to reduce the frequency of recycling from mania to depression.
Bipolar Disorder- Lithium Side Effects

- Severe side effects include:
  - Toxicity (lithium levels >1.5 mEq/L):
    - lethargy, severe diarrhea, incoordination, delirium, ataxia, cardiac arrhythmias, hypotension, tinnitus, oral or facial tremor, and slurred speech.
  - Higher levels of 2.5-3.0 mEq/L:
    - myoclonic twitches, dysarthria, coarse tremors, confusion, dyskinesia, choreoathetoid movements, urinary and fecal incontinence can occur.
  - Levels > 3.0 mEq/L:
    - seizures, cardiogenic shock, peripheral vascular collapse, coma, and death can occur.
M.O. is a 45 y/o F with bipolar disorder maintained on Lithium and Zyprexa.

Her husband brings her into the clinic, worried about her inability to sleep, and unwillingness to eat.

She complains that her mouth is so dry she cannot taste anything, and she has a marked tremor, and difficulty swallowing.

She recently started Vasotec and a diuretic for newly diagnosed hypertension.

Her lithium level is elevated at 2.3mEq/L

What can be contributing to M.O’s dysphagia?

Case #5- Dysphagia with Lithium
Bipolar Disorder

- Answer – M.O.’s new diuretic has caused a drug interaction resulting in her symptoms
- Because Lithium is chemically related to sodium, and diuretics are designed to cause the body to loose sodium and water. When sodium is being removed, the lithium is being retained in the body as a substitute, resulting in increased lithium levels and resulting symptoms of toxicity.
- Another medication should be used to treat M.O.’s blood pressure, and the diuretic discontinued.
Medications Used to Treat Parkinson’s disease
Medications for Parkinson’s Disease

- Parkinson’s disease is associated with depletion of the neurotransmitter Dopamine and with dysfunction of the Extrapyramidal Motor System.
- Medications used to treat Parkinson’s Dx include:
  - Anticholinergic agents are used for mild tremor in early disease and include:
    - Benztropine (Cogentin)
    - Trihexyphenidyl (Artane)
  - These can cause dysphagia from dry mouth, confusion, decreased GI motility, sedation, ataxia
  - Enhanced dopamine levels will result in side effects similar to those encountered with the use of antipsychotics, and include extrapyramidal side effects which mimic the symptoms of the patient with Parkinson’s disease. Managing the symptoms of the disease, which are ever changing, and the dosing and side effects of these dopamine enhancers is a challenge to the physician.

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Medications for Parkinson’s Disease

- Other medications used enhance the effects of the dopamine left in the CNS and include:

- **Levodopa Enhancers:**
  - **Amantadine (Symmetrel)** –
    - Dysphagia side effects: nausea, confusion, dyskinesias, extrapyramidal symptoms (EPS), dry mouth, G.I. bleeding
  - **Levodopa, Sinemet (L-dopa with carbidopa)** –
    - Dysphagia side effects: abdominal pain, constipation, dry mouth, GI bleeding, xerostomia, changes in taste, dyskinesias, EPS, decreased attention span, mental status changes, impaired motor skills
    - Levodopa, Sinemet (L-dopa with carbidopa)
Medications for Parkinson’s Disease

- Direct Dopamine Receptor Agonists (act on dopamine receptors)
  - Bromocriptine (Parlodel)
  - Pramipexole (Mirapex)
  - Ropinirole (Requip)

- Dysphagia side effects: sedation, altered mental status, nausea, vomiting, constipation, G.I. bleeding, EPS, dyskinesia, dry mouth, anorexia
Medications for Parkinson’s Disease

- MAOI Inhibitors (work by preventing dopamine metabolism):
  - Selegiline (Eldepryl)
    - Dysphagia side effects:
      - xerostomia, nausea, peptic ulcers, confusion, EPS, dyskinesia

- COMT Inhibitors (Prevent metabolism of levodopa)
  - Entacapone (Comtan)
  - Tolcapone (Tasmar)
    - Dysphagia side effects:
      - EPS, dyskinesias, anorexia, nausea, vomiting, dizziness, hallucinations, xerostomia, G.I. bleeding, anorexia

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Case #6: Dysphagia Associated with Parkinson’s Medications

- R.S. is a 69 yoM with a 10 year history of Parkinson’s disease.

- His medications include:
  - Sinemet 25/100 sustained release given five times daily along with an immediate release dosage form prior to meals.
  - Phenytoin (Dilantin) 100mg three times daily for a seizure disorder.
  - Promethazine (Phenergan) 25mg every 4 hours prn nausea. (recently added)
R.S. is now admitted to the hospital with acute abdominal pain, confusion, dystonia, and symptoms of dysphagia.

Upon admission the SLP evaluation documented significant dyskinesia involving the mouth, mouth, and impaired esophageal swallow with aspiration.

Emergent administration of Benztropine (Cogentin) was administered with relief of the acute dystonia.

What is the most likely cause of dysphagia in R.S.?
Case #6-Parkinson’s medications

Answer—When a new side effect or new symptoms appear on a previously stable patient, always check to see what has changed recently. This approach is always recommended, and leads us to the culprit, the recently added Phenergan for nausea.

Because Phenergan blocks dopamine, and thus is reducing the effects of this patient’s Parkinson’s meds. A better approach to the new symptom of nausea is to see if his medication dose needed to be adjusted, rather than add another medication. The Phenergan should be discontinued, and careful history to determine the actual cause of the nausea is warranted, rather than just treating the symptom!
Medications Used to Treat Alzheimer’s disease
Medications for Alzheimer’s Disease

- Alzheimer’s Dx is characterized by a progressive decline in the levels of acetylcholine.
- Acetylcholine is the neurotransmitter associated with memory and cognition.

- There are four cornerstone agents to treat Alzheimer’s
  - Tacrine (Cognex)
  - Donepezil (Aricept)
  - Rivastigmine (Exelon)
  - Galantamine (Reminyl)
Medications for Alzheimer’s Disease

◦ These agents act by inhibiting the breakdown of acetylcholine.
◦ Cholinergic side effects:
  • nausea, vomiting, abdominal pain, diarrhea, dyspepsia, anorexia, ataxia, confusion, sedation, and tremor, can contribute to dysphagia.
◦ Other side effects: Insomnia, fatigue, muscle cramps
Memantine (Namenda) is a relatively new drug in America that influences memory, motor function, and perception.

It can be used dependently or in combination with the aforementioned medications for moderate to severe Alzheimer’s.

Dysphagia side effects:
- agitation, sedation, confusion, constipation, and diarrhea.
Case #7: Dysphagia associated with Alzheimer’s Medications

- B.W. is an 82 yoF with Alzheimer’s disease.
- Concurrent medical conditions/medications include diabetes, depression, hyperlipidemia, and mild renal insufficiency:
- Galantamine (Reminyl) 20 mg daily was recently initiated for her Alzheimer’s.
Case #7: Dysphagia associated with Alzheimer’s Medications

- Her daughter notes that recently her mom has been complaining of muscle pain, muscle weakness and fatigue. She has been taking Motrin IB over the counter to relieve the symptoms, without relief.

- In addition, her mom seems more confused than ever, with more difficulty sleeping at night, and nausea that has resulted in a decline in oral intake.

- She asks you if you think the new medication could be the wrong medication for her mom.
Case # 7 Alzheimer’s

Answer-

- Her mom’s new medication is almost certainly causing her new symptoms.
- Because her mom was started on the maximum dose of Reminyl, and her muscle pain may be a side effect of the medication. It is best to start low and go slow with medications in the older patient.
- In addition the self treatment with Motrin may be contributing to her mom’s confusion, as Motrin type products can frequently cause confusion in the elderly patient- even at the over the counter strength!
1. List dysphagia risk factors associated with lithium?
2. What neurotransmitters are deficient in Alzheimer’s disease?
3. How do medications for Alzheimer’s address the deficiency?
4. What are the dysphagia side effects with Parkinson’s medications?
Summary Topics for Discussion

- Answers:
  - 1. Extrapyramidal side effects, dry mouth, sedation.
  - 3. They preserve the remaining acetylcholine by interfering with its metabolism.
  - 4. Gastrointestinal side effects, changes in mental status, extrapyramidal side effects.
References

- The Peripheral Nervous System- http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/P/PNS.html
References

References


