Clinical Resource Guide: Pseudobulbar Syndrome

OVERVIEW OF PSEUDOBULBAR AFFECT (PBA)

Pseudobulbar syndrome, also known as emotional lability, is a neurological condition characterized by uncontrollable episodes of emotional expression, such as laughing or crying, that are often exaggerated or inappropriate in context. This syndrome is typically associated with various underlying neurological disorders and can significantly impact a patient's quality of life. This can be especially distressing to patients and families in the hospice setting. The following guide has been created to help navigate management of pseudobulbar affect with the intent of reducing symptom burden and optimizing quality of life.

Pharmacist Corner Objectives	
1.	Define pseudobulbar affect and the impact on patients and families in the hospice
2.	Identify tools available to assist with diagnosing pseudobulbar syndrome and differentiating from other conditions commonly occurring in the hospice setting
3.	List the barriers to using Nuedexta and identify the alternative available if pharmacologic management determined to be necessary

CAUSES OF PSEUDOBULBAR AFFECT

Pseudobulbar syndrome can arise from various neurological conditions due to its association with disrupted neural pathways involved in emotional expression. The proposed mechanism underlying pseudobulbar syndrome involves the loss of inhibitory control over emotional centers in the brain, leading to inappropriate and uncontrollable emotional responses. Here are more specific details about potential causes and their mechanisms:

POTENTIAL CONTRIBUTORS TO PSEUDOBULBAR AFFECT	
Condition	**Overview**
Amyotrophic Lateral Sclerosis	In ALS, degeneration of neurons in the motor cortex and corticobulbar tracts leads to loss of inhibitory control over emotional centers
Multiple Sclerosis	MS is characterized by demyelination of nerve fibers, including those involved in the regulation of emotions. Demyelination disrupts the transmission of signals in the brain, thus resulting in disinhibition
Stroke	A stroke can damage specific regions in the brain responsible for emotional regulation, such as the frontal lobe and limbic system
Traumatic Brain Injury	TBI can lead to structural damage in the brain, affecting neural pathways responsible for emotional control

ASSESSMENT OF PSEUDOBULBAR AFFECT

Assessing pseudobulbar syndrome requires a comprehensive evaluation to distinguish it from other conditions with similar symptoms. If available, review of any or all the following can help guide decision making regarding symptom management.

CLINICAL ASSESSMENTS	
Clinical History	A detailed medical history, including information on neurological conditions, previous strokes and/or traumatic brain injuries.
Neurological Exam	Performed with the intent to identify signs of upper neuron dysfunction
Emotional Lability Observation	Observe and document episodes of emotional lability, including the frequency, triggers and intensity of episodes and assess appropriateness
Functional Assessment	Evaluate the impact of pseudobulbar syndrome on the patient's daily functioning, quality of life, and ability to communicate effectively
Differential Diagnosis	Rule out other potential causes of emotional symptoms, such as mood disorders, medication side effects or cognitive decline

NONPHARMACOLOGIC MANAGEMENT OF PSEUDOBULBAR AFFECT

Nonpharmacologic interventions have demonstrated effectiveness in managing pseudobulbar syndrome and improving patient emotional well-being. Without medication, the following techniques have proven valuable in reducing the frequency and severity of emotional episodes. These interventions aim to enhance emotional control and provide patients with the tools to cope with emotional lability, ultimately contributing to improvement of overall quality of life.

NONPHARMACOLOGIC TREATMENT STRATEGIES FOR PSEUDOPBULBAR AFFECT	
Intervention	**Brief Description**
Speech Therapy	Can help regain control over emotional expressions and improve communication
Supportive Counseling	Assists patients and families cope with the emotions of hospice diagnosis
Relaxation Techniques	Deep breathing and calming interventions can help reduce frequency and severity of outbursts

PHARMACOLOGIC MANAGEMENT OF PSEUDOBULBAR AFFECT

If pharmacologic intervention is thought to be necessary to manage pseudobulbar syndrome, one medication commonly prescribed for this purpose is Dextromethorphan/Quinidine, known by its brand name Nuedexta. Nuedexta is a combination medication with a proposed mechanism of action that targets the neural pathways involved in emotional expression.

PROPOSED NUEDEXTA MECHANISM OF ACTION	
Substance	**Activity**
Dextromethorphan (DM)	*NMDA receptor antagonist:* NMDA receptors play a crucial role in the regulation of glutamate, a neurotransmitter involved in neural communication. By blocking NMDA receptors, DM modulates glutamate signaling, reducing excessive excitability of neurons in the brain.
Quinidine	Enhances bioavailability of dextromethorphan by inhibit CYP2D6, which metabolizes dextromethorphan

Clinical Trials

The *STAR Pivotal Trial* studied the impact of Nuedexta on patients with MS or ALS presenting with PBA. The study found patients who used experienced a clinically and statistically significant decrease in emotional outburst episodes compared to placebo. However, it is worth noting that patients receiving placebo experienced a nearly 60% reduction in episodes at week 9, and was maintained at nearly 50% at week 12. Patients in the Nuedexta group experienced an 82% decrease in episodes at week 12.

The *PRISM II Trial* was an open-label trial designed to determine efficacy of Nuedexta in patients with PBA secondary to stroke, dementia or TBI. Across the treatment groups, patients started with about 12 episodes per week at baseline, 4 episodes by day 30, and 2 by day 90.

Barriers to Use

1. Cost: *> $700/month*
2. Administration: commercially available in capsule only
3. Side effects:
    a. Common side effects include dizziness (10%), diarrhea (13%), vomiting (5%)
    b. Routine assessment necessary to assess for efficacy and tolerability of medication

Alternative to Nuedexta Capsule

The two medications that combine to make Nuedexta, dextromethorphan and quinidine, are inexpensive and can be compounded into an oral suspension that decreases the cost of therapy and simplifies administration, especially in patients with difficulty swallowing tablets. The *dextromethorphan 20mg/quinidine 10mg oral suspension* is available to added as an orderable item, if needed, with just a quick call to our client support line.

SUMMARY

In summary, pseudobulbar syndrome is a neurological condition characterized by uncontrollable emotional expression, often linked to underlying neurological disorders. Assessment should involve a thorough evaluation of medical history and symptoms.

Nonpharmacologic interventions can significantly impact patient and family management of emotional outbursts. If medication is thought to be needed to improve quality of life, Nuedexta or the more cost-effective dextromethorphan/quinidine oral suspension are available to trial. Please reach out to our Clinical Pharmacy Team with any additional questions, issues, or concerns regarding management of pseudobulbar affect.

REFERENCES

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