Question and Answer Session Summary

PM&R's Role in Addressing Mood Disturbances and Pseudobulbar Affect (PBA) in Brain Injury
AAPMR Online Meeting
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Previously, on November 3, 2022, Richard D. Zorowitz, MD, Christine Greiss, DO, and Heidi Fusco, MD, gave presentations about mood disorders and disorders of affect in patients with traumatic brain injuries. In a second online question and answer session on November 30, 2022, they answered questions from participants and presented multiple choice poll questions on the material covered in the presentations.

Questions from participants

By what mechanisms would quinidine/dextromethorphan seem to work? How was it discovered?
Dr Griess answered that dextromethorphan reduces overall inflammation. It reduces NMDA activity by antagonizing the NMDA receptor and modulates dopamine activity and adrenergic activity. Although it is not a dopamine receptor agonist, it reduces calcium ion release into the cell which promotes dopamine production by reducing the apoptotic pathway.

Quinidine, a class III antiarrhythmic drug, is an inactive ingredient that inhibits cytochrome P450 enzymes in the liver. The effect reduces dextromethorphan breakdown to maintain a higher circulating concentration.

Have you used [dextromethorphan/quinidine] much and how long does it take to be effective?
Dr Griess said she has used dextromethorphan and quinidine. The medication is approved by the US Food and Drug Administration for the treatment of pseudobulbar affect.

Dr Griess recommended performing the Center for Neurologic Study-Liability Scale questionnaire at the initial appointment and at follow-up appointments to watch the trend in pseudobulbar symptoms. It should take 1-2 weeks for dextromethorphan/quinidine to begin antagonizing the NMDA receptor and then up to 90 days to see a full clinical effect.

Dr Zorowitz added that, like the other medications, the dosage should be titrated up starting with once per day for about one week and then increased to twice per day. Headache is a very common side effect.

Any experience with long-acting dextromethorphan alone versus quinidine/dextromethorphan?
Dr Zorowitz responded that quinidine is necessary for dextromethorphan to be effective. Dr Griess stated that she never prescribes it alone but has heard anecdotally from patients who could not get refills and took dextromethorphan alone. The dextromethorphan without quinidine was not as effective and caused headaches and nausea.

Any experience with [electroconvulsive therapy] for mood disorder with TBI [patients]? Any experience with transcranial stimulation for mood disorder in TBI? Any experience with EEG biofeedback (neurofeedback) for mood disorder in TBI [patients]?
Dr Zorowitz responded that he has had one patient with stroke and severe depression who had electroconvulsive therapy, and this therapy was successful. A psychiatrist would decide whether a patient is appropriate for these types of therapies. Currently, these treatments are not standard practice.

Dr Griess has seen patients with Parkinson disease and mood disorders who benefited from transcranial magnetic stimulation. There is ongoing research with transcranial magnetic stimulation in patients with Parkinson disease and patients with Parkinson disease who have TBI after falls. For patients with TBI and mood disorders, she has seen only one patient receive benefit from transcranial magnetic stimulation.

Dr Griess thought only certain therapists with expertise were willing to try biofeedback therapies.

Given how expensive [dextromethorphan]/quinidine is, can you give the [medications] separately as both are generic?
The panelists agreed that the medications must be given as a single pill. Dr Zorowitz responded that the amount of quinidine in the combined medication is only 10 mg compared with 200 mg, 300 mg, or 324 mg in tablets of quinidine alone.

Dr Fusco recommended looking at the savings programs and coupons on the company website. Contact your local dextromethorphan sales representative to see if you can get samples. She said she has started patients on samples which allowed for time to get the coupons. Panelists said having documentation, such as the Center for Neurologic Study-Liability Scale questionnaire results, is very helpful.

Any frustrations with having mental health professionals seeing patients with TBI? For example, your failed suicide patients that survive? In my area, once a [patient] has a TBI diagnosis, mental health cites the TBI as their problem and [does] not acknowledge any mood disorder issues.

Dr Fusco replied that, typically, outpatient rehabilitation programs or home visiting programs will not accept a patient who has attempted suicide until the patient is cleared by a psychiatrist and admitted into an outpatient psychiatric program. You will need to work with a social worker or a case worker to find a suitable program. They should not be released into the community without being cleared.

Dr Zorowitz said regular psychiatrists are often not equipped for managing patients with TBI who have had suicide attempts. A neuropsychiatrist should have the expertise, but there are not many neuropsychiatrists. It is especially difficult to find a psychiatrist to take patients with worker's compensation insurance. "Just trying to find a neuropsychiatrist to take worker's comp. is literally pulling teeth. It's a very, very tough problem," Dr Zorowitz said.

Finding an appropriate rehabilitation program for patients with TBI who also have many psychiatric problems is difficult. Dr Fusco described a patient who has TBI and neurobehavioral issues. Psychiatric programs rejected her because of her brain injury while outpatient rehabilitation programs rejected her because of the severity of her neurobehavioral problems. This patient from New York was finally accepted to the Brookhaven Hospital program in Oklahoma.

Dr Fusco said the Brain Injury Association of America has been helpful. There may be local advocacy groups in your area that can help with this frequent problem.

Are there any special diets regarding chromatograffin cells?
Dr Griess said to avoid processed foods and instead choose a low-inflammatory diet. The American Dietary Association advises nutritionists in rehabilitation programs about low-inflammatory diets. See the American Dietary Association website.

Poll questions

Poll question 1: A dysfunction in which of the following brain networks is believed to be associated with pseudobulbar affect?

A. Cerebellar network

B. Cortico-pontine network

C. Cerebral-pontine network

D. Cerebellar medullary network

The correct answer is B, the cortico-pontine network. The cerebral-pontine network is associated with other psychiatric disorders. The cerebellar network is associated with vestibular function.

Poll question 2: Which of the following is false regarding Post Traumatic Amnesia (PTA)?

A. Shorter durations of PTA are associated with a worse prognosis

B. PTA is characterized by the inability to consolidate new information, i.e., orientation, autobiographical data for peri- and post-injury period

C. PTA can be assessed using the GOAT and O-Log

D. People in PTA will have improved basic attention as compared to Posttraumatic confusional state

The correct answer is A. Being in PTA for less than 30 days is associated with an improved prognosis.

Poll question 3: A depression scale that is clinician-rated is:

A. Beck Depression Inventory

B. Patient Health Questionnaire-9 Item Scale (PHQ-9)

C. Neurobehavioral Functioning Inventory Depression Scale

D. Center for Epidemiological Scales for Depression (CES-D)

The correct answer is D. The Center for Epidemiological Scales for Depression (CES-D).
Respondents had difficulty with this question and all possible answers received votes.
Dr Zorowitz suggested participants review the rating scales because they are very useful.

Poll question 4: Which neurotransmitter pathway is responsible for regulating coordination?

A. Norepinephrine

B. Acetylcholine

C. Serotonin

D. Dopamine

The correct answer is D, dopamine.

Poll question 5: Which of the following is true regarding pharmacotherapy of neurobehavioral disorders after TBI?

A. A clinician's goal is to mask emotional distress for patients and decrease participation in rehabilitation

B. A clinician's goal is to minimize spontaneous recovery

C. A clinician's goal is to address neurotransmitter disturbances and compensate for disrupted neural circuitry with the minimal effective dose

D. A clinician should start at the maximal medication dose and concurrently treat side effects with additional medications

The correct answer is C, a clinician's goal is to address neurotransmitter disturbances and compensate for disrupted neural circuitry with the minimal effective dose. The clinician should try to help the patient with emotional distress and increase participation in rehabilitation. "The goal is always to get your patient to go to rehab," she said.

Poll question 6: A common co-morbidity of post-traumatic anxiety is:

A. Depression

B. Pseudobulbar affect

C. Borderline personality disorder

D. Psychosis

The correct answer is A, depression. Dr Zorowitz stated that depression and anxiety often "go hand in hand," and many medications can treat both.

Poll question 7: Which cellular precursors in the gut are responsible for the production of serotonin?

A. Lymphocytes

B. Megakaryocytes

C. Chromatograffin

D. Basophils

The correct answer is C, chromatograffin.

Dr Griess said that chromatograffin cells generate approximately 90% of the total body serotonin. In PTSD, chromatograffin cells increase serotonin production and turn over more rapidly. This increased gut serotonin production is why during a traumatic episode, we often have runny stools or watery diarrhea. Improved gut health can help with depression and anxiety in patients.

Poll question 8: What is the first line medication treatment for depression and anxiety in TBI?

A. Benzodiazepines

B. Haldol

C. SSRIs

D. Bupropion

The correct answer is C, SSRIs.