Letters to the Editor

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A CASE OF PARANOID SCHIZOPHRENIA AND SEVERE ANTIPSYCHOTIC-INDUCED PARKINSON'S DISORDER TREATED WITH A COMBINATION OF OLANZAPINE AND LURASIDONE

Dear Editor:

Schizophrenia is a chronic neuropsychiatric disorder that affects approximately one percent of the population worldwide.[1] Since the introduction of the first-generation of antipsychotics in the 1950s, the pharmacological approach has become the most widely accepted therapeutic modality for the treatment of schizophrenia.[2] The advances in neurosciences and drug development broadened the armamentarium available to clinicians. Today, there are 20 antipsychotic medications approved by the United States Food and Drug Administration (FDA) for the treatment of schizophrenia. Lurasidone is a novel psychotropic agent with D_2 receptor and 5-HT_{2A} antagonistic properties. It also has a very high affinity to 5-HT_7 receptor and moderate partial agonist effects at the 5-HT_{1A} and moderately potent antagonist effects at $alpha_{2C}$ receptor.[3]

Case report. A 41-year-old Caucasian man with history of schizophrenia, paranoid type, and neuroleptic-induced parkinsonism presented for the initial psychiatric evaluation per recommendations of his neurologist accompanied by his mother. During the past 20 years, the patient had nine admissions to psychiatric hospitals and was treated with a wide range of first- and second-generation antipsychotics. For the first 10 years, haloperidol was the most effective. Trials of ziprasidone and aripiprazole resulted in severe parkinsonism; clozapine and quetiapine caused severe cases of priapism, which required surgical intervention. Without antipsychotic medications, he had increasing hallucinations and paranoia, with only minimal improvement in his mobility. Anticholinergics were minimally effective and caused dry mouth and cognitive impairment.

During the initial psychiatric examination, the patient presented on a combination of olanzapine 5mg and zolpidem 10mg (at bedtime), risperidone 0.5mg, cyclobenzaprine 10mg, benztropine 1mg (twice daily), lorazepam 1mg (three times daily), and amphetamine and dextroamphetamine 10mg (once daily). He appeared at his biological age, pleasant, and cooperative. His face was moderately masked; an intermittent tremor in his chin and resting tremor in his arms and legs bilaterally was noted. He had difficulties ambulating due to stiffness and muscle rigidity, his posture was stooped, and his gait was unsteady and wide; he required assistance to get in and out of the chair. Due to severe dysarthria and drooling, his speech was decreased in rate, tone, and volume. His language skills remained adequate. His mood was euthymic and affect was flat. His thought process was logical, organized, and goal-directed; his thought content was negative for suicidal and homicidal ideations, delusional beliefs, and paranoid ideations. He reported auditory hallucinations, but no visual and tactile hallucinations. He displayed no major cognitive symptoms. His overall insight and social judgment were considered as fair. In addition to transient symptoms of psychosis and parkinsonism, he reported mild irritability and tachycardia. The patient reported no difficulties falling asleep.

After weighing the risks and benefits, zolpidem, stimulants, and risperidone were discontinued, and a trial of lurasidone 40mg at bedtime was initiated. During the next 12 months, the patient and his mother independently reported that the patient was able once again to feed and dress himself. He began using his computer and walked with his care provider to a local library. He had less difficulties in articulation and pronunciation. The overall spasticity decreased and tremor in upper extremities subsided. He regained some motor strength in his lower extremities and was able to ambulate faster. His gait improved as well.

Discussion. The wide range of adverse effects and extensive similarities in side-effect profiles between first- and second-generation antipsychotics continues to present practitioners, patients, and their families with formable challenges. In many instances, combining psychotropic medications is a common therapeutic approach.[4] Therefore, in our view, despite the polypharmacy discussed above, the presented case further highlights the unmet therapeutic needs in developing a new generation of antipsychotics with improved safety profile across the range.[5]

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POSTTRAUMATIC STRESS DISORDER EXACERBATION WITH CHOLINESTERASE INHIBITOR IN A PATIENT WITH DEMENTIA

Dear Editor:

We report a case of posttraumatic stress disorder (PTSD) exacerbation with donezepil, a cholinesterase inhibitor.

Case report. An 80-year-old Korean War veteran with combat trauma-related PTSD presented with progressive memory loss. He was diagnosed with PTSD 18 years ago. His symptoms included distressing and intrusive recollection of events and images from the Korean War and avoidance of any reminders of the war. He experiences hyperarousal and nightmares up to five times a month. He presented again to the outpatient clinic with complaints of progressive memory loss, word finding difficulties, getting lost while driving, and occasionally forgetting to turn the stove off. He scored 18 out of 30 on a Montreal Cognitive Assessment. He lost points prominently on delayed recall, abstraction, and concentration. A subsequent neuropsychological testing was consistent with a diagnosis of mixed dementia. He was started on a donezepil 5mg every morning. Within 2 weeks of starting the cholinesterase inhibitor, he experienced an exacerbation of PTSD symptoms, with increased intrusive thoughts, worsening of anxiety, and nightmares every night. Donezepil was subsequently discontinued and PTSD symptoms reverted back to their baseline in seven days.

Discussion. PTSD has a life-time prevalence of eight percent.[1] It is a chronic illness afflicting patients across the life span including late life. PTSD increases the risk of dementia by two-fold.[2] Donezepil is a reversible cholinesterase inhibitor, and acts via increasing acetylcholine concentration in the brain. Cholinesterase inhibitors have been used in the treatment of dementia, delirium, traumatic brain injury, schizophrenia, and bipolar disorder.[3] A Pubmed search reveals a contrasting effects of cholinesterase inhibitors on PTSD symptoms. Two cases report emergence of PTSD symptoms related to prior war trauma in patients with cognitive dysfunction without any prior PTSD diagnosis, with cholinesterase inhibitors.[4,5] The onset of PTSD symptoms in both these patients was attributed to a dose increase of donezepil from 5mg to 10mg. Another case series of four patients without cognitive dysfunction reported improvement in nightmares with donezepil.[6] However, in our case, existing PTSD symptoms worsened with donezepil 5mg initiation.

The role of cholinergic pathways in anxiety disorders is not clear. Anxiety related to dementia improves with cholinesterase inhibitors. However, the mechanism of PTSD exacerbation with cholinesterase inhibitors is not known. Chronic PTSD is associated with smaller hippocampal volume.[7] Hippocampus plays a key role in integrating memory elements from primary sensory and secondary association areas.[7] It is possible that cholinergic stimulation might have an inadvertent activation of the circuits encoding for the suppressed traumatic experiences making them prominent. Cholinergic projections promote both wakefulness and REM sleep, and modulating these pathways possibly impacts nightmares.

We recommend close monitoring of patients for any exacerbation of PTSD-related symptoms when started on cholinesterase inhibitors.

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THE DEMOGRAPHICS OF PAIN CATASTROPHIZING IN A PRIMARY CARE SAMPLE

Dear Editor:

The Pain Catastrophizing Scale (PCS),[1] which assesses catastrophic thoughts and feelings about pain, is well represented in the empirical literature. For example, the PCS has been studied in relationship to cross-cultural validation;[2–4] various medical conditions, such as low-back pain,[5] whiplash,[6] chronic pain in incarcerated women,[7] vaginismus,[8] cancer,[9] and postoperative pain;[10] and various psychological investigations including family relationships,[11] positive personal attributes,[12] attachment dynamics,[13] anxiety,[14] and major depressive disorder.[15] In addition, the PCS has been used to explore demographic differences in specific types of patient samples (e.g., samples defined by a singular pain syndrome). In these studies, gender,[16–18] age,[19] and ethnicity[20,21] have tended to demonstrate demographic variations (i.e., higher in women in 2 of 3 studies; no age differences; higher in African-Americans). However, we were unable to locate a single study using the PCS to determine the demographic profile of pain catastrophizing in a primary care sample—the focus of the present study.

Potential participants were men and women, ages 18 years or older, who were being seen at an outpatient internal medicine clinic for nonemergent medical care. The clinic is staffed predominantly by residents in the department of internal medicine, and is located in a mid-sized mid-western United States city. We excluded individuals with compromising medical (e.g., debilitating pain), intellectual (e.g., mental retardation), cognitive (e.g., dementia), or psychiatric symptoms (e.g., psychotic) of a severity to preclude the candidate's ability to successfully complete a survey (n=13). This exclusion process was informal and undertaken by the recruiter as patients registered for clinical service.

Whereas 349 individuals were approached, 244 agreed to participate, for a participation rate of 70 percent. As for the 105 individuals who did not participate, 68 refused outright, 13 appeared too distressed, 21 appeared too burdened (e.g., struggling with children), and 21 reported not wanting to commit the time. Of the 244 individuals who agreed to participate, 239 completed the Pain Catastrophizing Scale. Of these 239 respondents, 62.3 percent were women and 37.7 percent were men, ranging in age from 21 to 80 years (mean [M]= 45.74, standard deviation [SD] = 15.12). Most participants were White (76.2%); however, 20.5 percent of participants were African-American, 0.8 percent Asian, 1.7 percent Hispanic, and 0.8 percent "Other." With regard to educational attainment, all but 2.1 percent had at least graduated high school, whereas 24.3 percent had earned at least a bachelors degree.

During clinic hours, one of the authors (D.A.W.) positioned himself in the lobby of the clinic, approached consecutive incoming patients following registration, and informally assessed exclusion criteria. With potential candidates, the recruiter reviewed the focus of the project (i.e., a study examining pain) and then invited each to participate. Each participant was asked to complete a six-page anonymous survey, which took about 10 minutes. Surveys were completed onsite in the lobby, before appointments with providers. Participants were asked to place completed surveys into sealed envelopes and then into a collection box in the lobby of the clinic. Completion of the survey was considered implied consent, which was explained to participants on the cover page to the survey.

In addition to demographic variables, we assessed the catastrophizing of pain using the PCS.[1] The PCS is a 13-item self-report measure that assesses catastrophic thoughts and feelings about pain. This measure has a 5-point Likert-style response scale (0=not at all to 4=all the time) and the scoring range is 0 to 52, with higher scores indicating higher levels of catastrophic thoughts and feelings about pain. The PCS has three underlying factors or dimensions of pain catastrophizing: rumination (items 8, 9, 10 and 11), magnification (items 6, 7 and 13) and helplessness (items 1, 2, 3, 4, 5 and 12). With regard to validity, the PCS has been validated in both clinical and nonclinical populations.[1,22–24] In the current study, Cronbach's alpha was 0.98 for the 13-item measure, 0.97 for the rumination subscale, 0.88 for the magnification subscale, and 0.96 for the helplessness subscale. In the current study, each of the three subscales of the PCS were very highly correlated with each other (all three correlations were 0.93) and with the total score (correlations ranged from 0.97–0.98), so only the total PCS score was considered further.

As for the demographic patterns associated with pain catastrophizing, scores on the PCS were statistically significantly correlated with both age (r= -0.30, $p<0.001$) and level of education (r= -0.22, $p<0.98$), yet age and education were not statistically significantly correlated (r= 0.003, $p<0.98$). Mean scores on the PCS did not differ significantly between men (M=11.73, SD=12.83) and women (M=14.11, SD=13.27), $F(1,237)=1.83$, $p<0.19$. With regard to race/ethnicity, the only two groups large enough for comparison were White and African-American. Mean scores on the PCS did not differ significantly between White (M=13.73, SD=13.05) and African-American (M=11.67, SD=14.06) respondents, $F(1,229)=0.98$, $p<0.35$.

In contrast to most previous studies using the PCS, we did not find any gender or racial/ethnic differences with regard to pain catastrophizing. However, also in contrast to previous studies, we found that age and education were related to PCS scores. To place findings into a general perspective, it appears that demographic findings with the PCS may be sample-dependent. However, additional research is needed to confirm that primary care samples demonstrate the preceding patterns.

This study has a number of potential limitations. These include the self-report nature of all data; small sample size; and indigent nature of the clinic, which may affect the ability to generalize findings to other types of clinics. However, this is one of the few studies, if only study, to examine pain catastrophizing with the PCS in a general primary care sample, and demographic findings demonstrate some contrasting results in comparison with other studies.

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