Propranolol Abuse: A Case Report on the Harmful Consequence of Over-the-Counter Medications

Sir,

Substance use disorders are frequently comorbid with anxiety disorders, which can be explained by the self-medication model.[1] The self-medication model, and the substance-induced model 1. General population epidemiological studies provide strong evidence of the frequency of the association for the most used substances: tobacco, alcohol, cannabis, and to a lesser extent sedatives, opiates, and cocaine. For substances that are less commonly used in the general population, the frequency of the co-occurrence can more precisely be studied in clinical samples. We provide the most recent literature results on the association of SUDs and anxiety, and evidence for one explicative model or the other when available. For substances with sedative properties (alcohol, benzodiazepines, cannabis, opioids The treatment modalities for anxiety disorders include psychotherapy and pharmacotherapy, with a better evidence for the combination treatment.[2] Though the mainstay of pharmacotherapy of anxiety disorders involve monoaminergic psychotropics, anxiolytics such as beta-blockers and benzodiazepines are also prescribed and procured over the counter (OTC). respectively.[3] There is a dearth of evidence regarding the abuse of beta-blockers and its consequences, probably because they are not considered as drugs with abuse potential. Hence, we report a case of propranolol abuse in a patient with generalized anxiety disorder.

Case Report

Mr S, a 60-year-old male who had recently retired from his job, consulted the psychiatric outpatient department. He had been diagnosed with generalized anxiety disorder 20 years ago when he had presented with excessive worries about day-to-day activities along with physical symptoms of anxiety such as tremors, palpitations, choking sensation, restlessness, and sweating. He had been treated with Tab. Imipramine 50 mg/day, Tab. Sertraline 100 mg/day, Tab. Propranolol 40 mg/day, and Tab. Alprazolam 0.25 mg/day, with which he had improvement in cognitive symptoms of anxiety such as excessive worries, but the physical symptoms had persisted for the past 20 years. No history of any substance use was reported.

Mr S had been on follow-up for the initial one year, after which he had been self-medicating with the above psychotropics in varying doses, procuring them OTC for the past 19 years, without any discontinuation. He had been taking sertraline and imipramine as prescribed but consuming higher doses of Tab. Propranolol at 280–320 mg/day and Tab. Alprazolam at 0.5–1 mg/day. He would alter the dosage of propranolol and alprazolam based on his assumption about the potential of the day's job to provoke anxiety, such as a change in workload or schedule as well as a change in the usual routine, such as traveling, or attending or organizing family events.

During a recent medical checkup, he was diagnosed with systemic hypertension and type-2 diabetes and was started on Tab. Olmesartan 20 mg/day and a combination of Tab. Glimepiride 2 mg and Tab. Metformin 500 mg twice daily. Prior to the current psychiatric evaluation, he had retired from his job and had cut down the dose of propranolol and alprazolam because his workload had reduced drastically and as he was apprehensive about continuing the psychotropics along with the new antihypertensive and antidiabetics. Following the reduction in the dosage of the anxiolytics, he experienced a worsening of tremors, palpitations, restlessness, choking sensation, and decreased sleep and was increasingly irritable towards the family members when they prevented him from consuming higher doses of propranolol and alprazolam. No history of nausea, vomiting, agitation, headache, or seizures suggestive of benzodiazepine withdrawal was noted.

On examination, he was found to have excessive perspiration and tremors, with an elevated heart rate of 120 beats/min and blood pressure of 180/110 mmHg. Systemic examination was found to be normal. Baseline investigations such as blood sugar, lipid profile, renal profile, and hemogram were within normal limits except for elevated HbA1C of 7.8% (normal range 4%–6%). Though electrocardiogram revealed sinus tachycardia, echocardiogram and an exercise stress test on the treadmill, for the evaluation of propranolol-withdrawal-related adverse cardiac events, were uneventful. Elevated blood pressure was controlled by an optimization of the antihypertensive regimen to Tab. Prazosin 10 mg/day, Tab. Olmesartan 40 mg/day, and Tab. Cilnidipine 10 mg/day.

The patient was changed over to sustained-release formulation of propranolol 80 mg/ day and Tab. Clonazepam 2 mg/day, with which he had an improvement in the sleep and the physical symptoms of anxiety. Over the following four weeks, Tab. Sertraline was increased to 150 mg/day, whereas Tab. Alprazolam and Tab. Imipramine were tapered and stopped, with the monitoring of anxiety symptoms and sleep. Concurrent nonpharmacological interventions, such as regular deep breathing exercises (15–20 minutes/day for four weeks), regular brisk walking (30 minutes/day for five days in a week for four weeks) and education on sleep hygiene, were provided. The patient has been on regular follow-up and is currently on Tab. Sertraline 150 mg/day and a tapering regimen of Tab. Propranolol 40 mg/day, whereas Tab. Clonazepam was tapered to 0.25 mg/day based on the benzodiazepine dependence tapering schedule along with the continuation of antihypertensive and antidiabetic medications. Informed written consent was obtained from the patient and his legally accepted representative.

Discussion

In patients with anxiety disorders, apart from the prescription of specific anti-anxiety drugs, various adjunctive agents help in early and enhanced symptom control. The adjunctive agents commonly used are benzodiazepines and sympatholytic agents. The existent literature cautions about the abusive use of anxiolytics such as benzodiazepines. This case study adds to the literature about the abuse of propranolol as OTC medication and the clinical factors leading to such abuse.

As highlighted in the present case scenario, the mainstay of management of anxiety disorders in resource-limited settings is pharmacological, despite the global literature supporting better efficacy for combination therapies.Though recent guidelines shun the use of beta-blockers and benzodiazepines in the management of anxiety, their conventional use by psychiatrists and medical personnel do continue.[4]

In our patient, the first use and regular use of propranolol were associated with the onset and gradual worsening of anxiety symptoms, respectively. Withdrawal from higher doses of propranolol is associated with rebound symptoms of anxiety, elevated blood pressure, and adverse cardiac events, as in this patient who required multiple antihypertensive medications.[5] However, the treating team considered different possibilities for the somatic anxiety symptoms: poor glycemic control/hypoglycemia, hypertensive crisis, benzodiazepine withdrawal, and propranolol withdrawal.

The treating team implicated psychotropic-withdrawal anxiety and ruled out diabetes mellitus and hypertension as causes because the onset of somatic anxiety symptoms was clearly preceded by the self-reduction in the doses of psychotropics (propranolol and alprazolam), whereas the oral hypoglycemic agents and antihypertensive drugs were taken without any dose modifications by the patient. Literature reveals that concurrent presentations of anxiety and hypertensive crisis can be precipitated by withdrawal of propranolol or alprazolam.[6] Due to the inherent overlap in causative roles for both propranolol and benzodiazepine in withdrawal anxiety, the treating team posited combined propranolol and benzodiazepine withdrawal. However, the absence of clinical signs specific to benzodiazepine withdrawal, such as nausea or vomiting, agitation, altered mental status, headache, or seizures suggested that propranolol could have played a greater role than alprazolam in precipitating withdrawal symptoms in this patient.

However, the complex interplay between anxiety and medical disorders (diabetes mellitus and hypertension) could underlie the propranolol abuse in our patient. The regular self-administration of increased doses of propranolol over the years could have been triggered and maintained by autonomic hyperactive states due to recurrent hypoglycemia and uncontrolled hypertension. Further, two other properties of propranolol, a non-vasodilatory beta-blocker, could have contributed to the worsening of the diabetic status: the "inherent metabolic side effects" (such as the worsening of glucose tolerance, insulin resistance, and dyslipidemia) and the "property to mask the self-recognition of hypoglycemic states" leading to poor glycemic control.[7]

Anxiety and depression have been found to have a predictive role in OTC medication procurement in the elderly population.[8] The abuse of propranolol has been previously reported in an individual with social anxiety where doses of up to 320 mg/day were used.[9] The intake of propranolol in social anxiety is usually situation-triggered. However, the use of propranolol at an increased frequency to control incessant anxiety, as noted in our patient, could have contributed to the progression of the use to an abuse. In addition, the clinical profile of this individual, with prominent physical symptoms of anxiety, has been known to be associated with an orientation towards pharmacotherapy and OTC preparations rather than psychotherapy.[10]

We conclude that a combination treatment of pharmacotherapy and psychotherapy, along with psychoeducation about the illness course and medications, would help in better management of anxiety disorders. Review visits should preferably entail evaluation for OTC medications and abuse in such patients. Identifying the risk factors such as old age, predominant physical symptoms of anxiety, and depressive symptomatology would prove beneficial in the prevention of anxiolytic abuse.

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Diagnostic and Therapeutic Implications of Borderline Personality Disorder on Topical Steroid Dependence: A Case Report

Sir,

Topical steroids (TSs) are used to treat various inflammatory dermatological disorders. Increasing use of TS is being reported due to prescription by non-dermatologist doctors and increasing over-the-counter (OTC) purchase.[1] Personality attributes such as negative emotionality, neuroticism, and impulsivity, characteristic of borderline personality disorder (BPD) also predispose to substance abuse.[2] Substance use disorders are prevalent in up to 80% of those with BPD, with high novelty-seeking and poor coping strategies as risk factors.[3] We report a young adult female with topical steroid dependence (TSD), concurrent mood disorder, and BPD traits, to describe the role of maladaptive personality traits in the clinical presentation of TSD and the need for integrated psychobiological management in such patients.

Case Report

Miss S, a 23-year-old unmarried female, presented to the emergency services with acute onset (two weeks) of irritability, episodes of aggression, persistent low mood with frequent crying spells, decreased interaction with her family members, diminished interest in her usual activities, disturbed biological functions, and an episode of deliberate self-harm (DSH). The above symptoms were precipitated by interpersonal conflict. Her pre-morbid history was characterized by stormy affective changes, sensitivity to rejections in interpersonal contexts, impulsivity in social relationships, disturbances in self-image, and recurrent threats for self-harm, suggestive of BPD. Her past history revealed that over a period of three years, she had experienced two episodes of moderate depression, precipitated by interpersonal and family conflicts, with the last episode one year back. The past history was negative for mania, hypomania, and mixed episodes. Apart from hypothyroidism, for which she was on irregular treatment, there were no other medical co-morbidities. There was no history of oral/parenteral substance use. There was a history of alcohol dependence in her father and paternal and maternal grandfathers, as well as suicide in her mother, who passed away when the patient was aged five.

Mental status examination revealed mood swings, tearfulness, agitation, and demanding behavior. Hamilton Depression Rating Scale (HDRS) score was 10, indicative of mild severity. International Personality Disorder Examination (IPDE) ICD-10 revealed emotional instability, impulsivity, interpersonal sensitivity, and self-harm tendencies typical of the emotionally unstable type of BPD. Physical examination revealed pale facies, fatty hump on the nape of the neck, and thin skin with bruise-like lesions of prominent veins all over the body.

The forensic expert ruled out the likelihood of assault and bruises, due to the absence of typical progressive color changes and the presence of itching. The dermatologist opined that the pruritic reddish skin lesions are typical of TS abuse. A further detailed inquiry revealed OTC purchase and self-administration of skin-whitening creams for the past four years, which comprised of high-potency TSs (mometasone 0.1% and clobetasol propionate 0.05 %). While the first use was prescription-based, the subsequent usage was perpetuated by herself when she perceived that the cream improved her skin texture; this also led her to progressively apply the cream more frequently and in increasing amounts suggestive of craving. Any reduction in the usage of the creams would cause her itching, redness, and local swelling, as in the current presentation when she had stopped applying the cream after hospitalization. The absence of persistent preoccupation and associated checking and reassurance-seeking behaviors ruled out the possibility of body dysmorphic disorder.

Her blood biochemistry was normal. The panel revealed low basal serum cortisol (fasting, 8 AM) of 1.01 µg/dL (normal range: 7–28 µg/dL) and a normal serum adreno-corticotropic hormone level (fasting, 8 AM) of 5.70 pg/mL (normal range: 5–50 pg/mL) with a normal thyroid profile. The endocrinologist opined that the paradoxical low levels of serum cortisol with cushingoid features could be due to the sudden stoppage of steroid application leading to the hypothalamo-pituitary-adrenal (HPA) axis suppression.

She was diagnosed with recurrent depressive disorder, current episode moderate depression without somatic syndrome, BPD, TSD with withdrawal features, and iatrogenic ACTH-independent Cushing's syndrome due to TSs.

She was started on cap. fluoxetine (20 mg/day) and tab. olanzapine (10 mg/day) for her depressive symptoms, along with individual psychotherapy (focusing on building positive coping skills, emotional resilience, anger management, and relapse prevention strategies) and family interventions (psychoeducation about illness, personality attributes, and need for positive support system). Oral prednisolone was given with a tapering regimen for the acute steroid withdrawal (started at 5 mg/day for a week and tapered to 2.5 mg/day for another week and stopped), and the skin changes were topically treated with emollients. Physical features of Cushing syndrome gradually resolved. Improvement was noted in depressive symptoms (HDRS after four weeks = 5), craving for TSs, and impulsivity traits and had