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CASE REPORT

Chin Tremors Associated with Paroxetine in a Patient with Pancreatic Adenocarcinoma

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ABSTRACT

Context There have been many cases of medication-induced tremors. We report a patient who developed significant chin tremors after the administration of paroxetine. **Case report** A 68-year-old Vietnamese female with a past medical history including GIST and pancreatic cancer status post Whipple procedure and six months of adjuvant chemotherapy with gemcitabine presented with symptoms of anxiety for which she was treated with paroxetine. Within 2 weeks she developed chin tremors which resolved after paroxetine was discontinued. **Conclusions** To our knowledge, this is the first case report of a temporary chin tremor associated with paroxetine. The exact mechanism of this phenomenon is unclear. However, it has been suggested that movement disorders such as chin tremors may be related to elevated serotonin levels causing an inhibition of central dopamine.

INTRODUCTION

Mood disorders such as anxiety and depression are on the rise in this decade. According to the Centers for Disease Control and Prevention, about 30% of Americans will develop an anxiety disorder and about 17% will develop major depressive disorder [1]. Antidepressants were the third most common prescription drug taken by Americans of all ages in 2005-2008 [2]. It is the most common prescription drug taken by Americans between the ages of 18-44. The rate of antidepressant use in the United States among all ages has increased almost 400% from 1988-1994 through 2005-2008 [2]. It is evident that these numbers will continue to increase as more people are diagnosed with mood disorders. The World Health Organization has estimated that depression will rival heart disease as the second most prevalent cause of illness-induced disability by the year 2020 [3]. Mood disorders are especially significant in the population of patients with cancer. One meta-analysis of 94 interview-based studies showed that among patients with cancer, the pooled prevalence of Diagnostic and Statistical Manual of Mental Disorders-defined major depression was about 16% and the prevalence of anxiety disorders was about 10% [4]. Therefore, antidepressants and anti-anxiolytics are also being used in the cancer population. These medications rely on targeting the serotonin (5-HT) transporter. The selective serotonin reuptake inhibitors (SSRIs) account for about 80% of the antidepressants on the market [3]. The mechanism of action of SSRIs involves inhibiting 5-HT reuptake after it is released from the synapse, thereby prolonging the availability of serotonin in the synaptic gap. This allows repeated stimulation of the receptors of the recipient cell [3]. The success of SSRIs relies on the theory that major depressive disorder is a low serotonin state [5]. Other antidepressant drugs such as the serotonin and noradrenaline reuptake inhibitors (SNRIs) or the classic tricyclic antidepressant are used as well. However, SSRIs are better tolerated because of the absence of severe side effects compared with the tricyclic drugs [3]. However, SSRIs still have an extensive side effect profile. Since it is increasingly used among cancer patients it is imperative to be aware of its toxicities (Table 1).

We now describe a case of a patient who developed chin tremors within 2 weeks of treatment with

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Key words Anxiety; Depression; Pancreatic Neoplasms; Paroxetine; Tremor

Abbreviations 5-HT: serotonin; SNRI: serotonin and noradrenaline reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor

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Table 1. Adverse event frequency of major depressive disorders in placebo-controlled clinical trials of paroxetine (immediate-release). Adapted from Gibiino and Serretti, 2012 [6].

System	Side effect	Paroxetine
Autonomic	Sweating	11%
Gastrointestinal	Nausea	26%
	Decreased appetite	6%
Central nervous system	Somnolence	23%
	Dizziness	13%
	Insomnia	13%
	Tremor	8%
Uro-genital	Ejaculatory disturbance	13%
	Other male genital disorders	10%

paroxetine for anxiety. This report is clinically relevant as paroxetine remains one of the most commonly used SSRIs for treatment of anxiety and depression.

CASE REPORT

A 68-year-old Vietnamese female with a past medical history including GIST and pancreatic cancer status post Whipple procedure and six months of adjuvant chemotherapy with gemcitabine presented with symptoms of anxiety on cycle 1 day 15 of gemcitabine, which was December 21st, 2012. She reported difficulty sleeping which included waking up frequently through the night and therefore sleeping for two to three hours at a time. Prior to this, she would sleep about six hours straight through the night. She informed us that she was worried about her cancer. She was started on paroxetine 10 mg *po* once daily as well as lorazepam 1 mg *po* 1-2 tablets every six hours as needed. However, approximately 2 weeks after initiation of paroxetine, she developed a chin tremor. She noticed her chin and lower jaw were constantly shaking which resolved when she would sleep. She had no other tremors, headaches, dizziness, vision changes, slurred speech, confusion, lethargy, or any other neurologic complaints. On physical exam, she had a fine, constant tremor localized to the patient's entire chin and lower mandible with the axis being horizontal. The tremor decreased slightly when she smiled, puffed out her cheeks, spoke, or drank water. The tremor stopped when she clenched her teeth or opened her jaw wide. There were no focal motor or sensory deficits noted. Her cranial nerves were intact, deep tendon reflexes were symmetric in all extremities and her coordination was intact. There were no extremity tremors or rigidity seen on exam. Her vital signs were within normal limits. She does not have a history of essential tremors or Parkinson's disease and neither does her family. Her labs were significant for stable anemia and a low absolute neutrophil count of 1,400 cells/μL likely secondary to bone marrow suppression from chemotherapy. Electrolytes were significant for hyponatremia with Na of 133 mEq/L (reference range: 137-142 mEq/L) in the setting of decreased oral intake. Therefore, cycle 2 day 2 of gemcitabine was held and paroxetine was discontinued. She did continue taking lorazepam as needed for insomnia. However, the tremor persisted despite delaying gemcitabine. At this time, it was hypothesized that her symptoms could be secondary to early-Parkinsonism, somatization from anxiety, or a side effect of paroxetine. She was seen by a neuro-oncology specialist and was found to have no neurological deficits and it was suggested that her symptoms are likely related to paroxetine. Her WBC and absolute neutrophil count improved and she was given day eight of cycle two five days late and gemcitabine was no longer held. By week 7, patient reported her chin tremors had been decreasing in frequency to only once per week. By week 8, her symptoms had completely resolved and it has not recurred since. She was continued on lorazepam for anxiety with improvement in anxiety symptoms. Please refer to Table 2 for sequence of events.

DISCUSSION

Paroxetine, a widely used SSRI has many side effects that have been extensively studied in the medical literature. However, there is limited data regarding the relationship between chin tremors and paroxetine. To our knowledge, this is the first case report of chin tremors as a side effect of paroxetine. There are web reviews showing rare cases of patients experiencing chin tremors while taking paroxetine. Based on the Naranjo adverse drug reactions probability scale there is a probable adverse reaction of chin tremors secondary to the use of paroxetine (Table 3).

The exact pathophysiology of chin tremors due to paroxetine remains unclear. There have been several proposed mechanisms for similar movement disorders caused by paroxetine. There are case reports of paroxetine causing akathisia-like movement disorders such as bruxism. The mechanism behind these movement disorders was suggested to be secondary to elevated levels of

Table 2. Sequence of events following paroxetine initiation and development and resolution of chin tremors.

	Week	Chin tremor
Initiation of drug (Dec 21)	1 (Dec 21 to Dec 27)	No
	2 (Dec 28 to Jan 3)	Yes (Starting Jan 2)
Discontinued drug (Jan 7)	3 (Jan 4 to Jan 10)	Yes
	4 (Jan 11 to Jan 17)	Yes
	5 (Jan 18 to Jan 24)	Yes
	6 (Jan 25 to Jan 31)	Yes
	7 (Feb 1 to Feb 7)	Yes
	8 (Feb 8 to Feb 14)	No
	9 (Feb 15 to Feb21)	No

Table 3. Naranjo adverse drug reactions (ADR) probability scale.

1. Are there previous conclusive reports on this reaction?	*Yes (+1) No (0)* ***Do not know or not done (0)***
2. Did the adverse events appear after the suspected drug was given?	***Yes (+2)*** *No (-1) Do not know or not done (0)*
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?	***Yes (+1)*** *No (0) Do not know or not done (0)*
4. Did the adverse reaction appear when the drug was re-administered?	*Yes (+2) No (-1)* ***Do not know or not done (0)***
5. Are there alternative causes that could have caused the reaction?	*Yes (-1)* ***No (+2)*** *Do not know or not done (0)*
6. Did the reaction reappear when a placebo was given?	*Yes (-1) No (+1)* ***Do not know or not done (0)***
7. Was the drug detected in any body fluid in toxic concentrations?	*Yes (+1) No (0)* ***Do not know or not done (0)***
8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	*Yes (+1) No (0)* ***Do not know or not done (0)***
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	*Yes (+1) No (0)* ***Do not know or not done (0)***
10. Was the adverse event confirmed by any objective evidence?	*Yes (+1) No (0)* ***Do not know or not done (0)***
Scoring	• 9+ = Definite ADR • **5-8 = Probable ADR** • 1-4 = Possible ADR • 0 = Doubtful ADR

serotonin (5-HT) inhibiting central dopamine activity [7]. Paroxetine functions by inhibiting the pre-synaptic re-uptake of 5-HT resulting in elevated levels of 5-HT [8]. It has been hypothesized that elevated levels of 5-HT cause an increased serotonergic effect on the meso-cortical neurons from the ventral tegmental area leading to decreased dopamine levels. Since the meso-cortical tract is responsible for motor activity, a deficit of dopamine leads to movement disorders such akathisia-like jaw movements [7]. Other SSRIs such as citalopram have been reported to cause jaw tremors that were also suggested to be secondary to a decrease in central dopamine levels [9]. Further research is necessary to better delineate the relationship between jaw movement disorders and SSRIs so the appropriate symptomatic treatment can be determined.

The incidence of side effects of SSRIs is increasing with time as more patients are exposed to the drug. Therefore the side effect profile of SSRIs reported in clinical trials is not necessarily reflective of what patient's experience [10]. There may be many other unreported cases of chin/jaw tremors and other movement disorders secondary to SSRIs that are affecting patient's quality of life. Therefore, it is imperative that physicians treating depression or anxiety with SSRIs are aware of this side effect in order to prevent adverse outcomes. Our report is the first to establish the side effect of chin tremors in relation to paroxetine.

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References

1. National Center for Health Statistics (US). Health, United States, 2010: With Special Feature on Death and Dying. Hyattsville (MD): National Center for Health Statistics (US); 2011 Feb. PMID: 21634072

2. Pratt LA, Brody DJ, Gu Q. Antidepressant use in persons aged 12 and over: United States, 2005-2008. NCHS Data Brief. 2011 Oct; (76):1-8. PMID: 22617183

3. Celada P, Puig M, Amargós-Bosch M, Adell A, Artigas F. The therapeutic role of 5-HT1A and 5-HT2A receptors in depression. J Psychiatry Neurosci. 2004 Jul; 29(4):252-65. PMID: 15309042

4. Mitchell AJ, Chan M, Bhatti H, Halton M, Grassi L, Johansen C, Meader N. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. Lancet Oncol. 2011 Feb; 12(2):160-74. PMID: 21251875

5. Owens MJ, Nemeroff CB. Role of serotonin in the pathophysiology of depression: focus on the serotonin transporter. Clin Chem. 1994 Feb; 40(2):288-95. PMID: 7508830

6. Gibiino S, Serretti A. Paroxetine for the treatment of depression: a critical update. Expert Opin Pharmacother. 2012 Feb; 13(3):421-31. PMID: 22263916

7. Milanlioglu A. Paroxetine-induced severe sleep bruxism successfully treated with buspirone. Clinics (Sao Paulo). 2012; 67(2):191-2. PMID: 22358247

8. Foster RH, Goa KL. Paroxetine : a review of its pharmacology and therapeutic potential in the management of panic disorder. CNS Drugs. 1997 Aug; 8(2):163-88. PMID: 23338224

9. Tarlaci S. Citalopram-induced jaw tremor. Clin Neurol Neurosurg. 2004 Dec; 107(1):73-5. PMID: 15567557

10. Ferguson JM. SSRI Antidepressant Medications: Adverse Effects and Tolerability. Prim Care Companion J Clin Psychiatry. 2001 Feb; 3(1):22-27. PMID: 15014625