DEALING WITH MOTIONS AND EMOTIONS: THE GASTROINTESTINAL SIDE EFFECTS OF PSYCHOTROPIC MEDICATIONS

Cristina Fragoeiro, Lília Monteiro, Bárbara Almeida, Carolina Machado, Pedro Moura Ferreira
Hospital Magalhães Lemos, Porto, Portugal

Illustration by Pete Gamlen

INTRODUCTION

We present the clinical case of a 64-year-old patient with a complex medical picture that includes pelvic floor dyssynergia with colonic inertia and clinically relevant anxious and depressive symptoms. Treatment of psychiatric symptoms has proven difficult, considering the gastrointestinal (GI) side effect profile of psychopharmaceuticals. We take this opportunity to reflect upon antidepressants (AD) currently available and their GI side effect profile.

CLINICAL CASE

A 64-year-old married woman with a history of major depressive episode in her 20s and later development of dysthymia in her 40s, presented to our Psychiatric outpatient clinic in 2015 for exacerbation of her clinical picture. She presented anxious and depressive symptoms, including anxiety, irritability, depressive mood, tearfulness, anhedonia, fatigue, social isolation, clinophilia, sleep maintenance insomnia and decrease in appetite, which had been developing over the previous 6 months. She had resorted to a few different private practitioners and was medicated at the time with alprazolam 1.5mg nocte, diazepam 5mg nocte, valerian extract 450mg t.i.d., as well as ethyl loflazepate S.O.S..

She presented an array of comorbidities: Menière’s disease (with the need of occasional corticosteroid treatment cycles), elastofibroma dorsi (removed in 2006), hiatal hernia with esophagitis (underwent fundoplication), *Helicobacter pylori* positive gastritis (did eradication), duodenal ulcer (healed), chronic anal fissure, with a long history of a tendency towards constipation. Medication included: betahistine, flunarizine, esomeprazole and senna extract.

Mirtazapine 15mg nocte was initiated and benzodiazepine adjustment was attempted. There was no subsequent improvement of the psychiatric clinical picture (nor aggravation of the GI one at the time), and the patient started abusing ethyl loflazepate to deal with her anxiety. Mirtazapine was suspended and paroxetine was initiated and escalated to 40mg, without benefit. She also did a trial with escitalopram (partial remission), agomelatine + escitalopram (side effects with agomelatine). Potentiation with antipsychotics was also attempted, but the patient described intolerance to side effects.

Along with her psychiatric symptoms, her overall health also declined: she had a relapse of elastofibroma which had invaded her pleura unilaterally and had occasional bouts of sciatica. Her GI symptoms also progressively worsened from 2016 onwards, with the need for laxatives and frequent intrusive measures to resolve constipation. She did various exams (upper GI endoscopy, colonoscopy, abdominal ultrasound, manometry, colonography by CT) which revealed pelvic floor dyssynergia (absence of relaxation of the puborectalis with increased anal pressure) and dolichocolon. Colleagues pointed towards iatrogenesis from psychiatric medication. Surgical intervention is now being considered.

She is currently on venlafaxine 75mg mane, clonazepam 0.5mg b.i.d., alprazolam 1mg nocte, along with regular psychology appointments. Despite slight improvement, she still reports significant psychiatric morbidity, which she attributes partially to her declining health.

ANTIDEPRESSANT GI SIDE EFFECTS

Neurotransmitters such as catecholamines and serotonin have roles not only in the central nervous system, but also on GI physiology, influencing blood flow, gut motility, nutrient absorption, the GI innate immune system, and the microbiome. Considering the action mechanisms of AD, these lead to a varying array of GI side effects. Some studies have associated specific GI pathology to AD.

	Xerostomia	Nausea, vomiting	Diarrhea	Constipation
Tricyclic antidepressants (TCAs)				
Clomipramine	+++	++	+	++
Selective serotonin reuptake inhibitors (SSRIs)				
Citalopram	++	++	+	
Escitalopram	+	++	+	+
Fluoxetine	+	++		
Fluvoxamine	+++	+++	+	++
Paroxetine	+++	++	++	++
Sertraline	++	++	++	+
Serotonin–norepinephrine reuptake inhibitors (SNRIs)				
Duloxetine	+++	++	+	++
Venlafaxine	+++	+++	+	+
Other classes				
Mirtazapine	+++	+		++
Trazodone	+++	++	+	+
Bupropion	+++	++		+
Agomelatine		+	+	+
Vortioxetine	+	++	+	+

+	0-10%
++	11-20%
+++	21-30%
++++	>30%
	Information not available

Dysphagia and gastroesophageal reflux disease (GERD): TCAs, by causing xerostomia (anticholinergic and antihistaminic effects) and inhibiting smooth muscle function, may contribute to dysphagia. Anticholinergic effects may also cause physiological impairment to the lower oesophageal sphincter resulting in or aggravating GERD.

GI bleeding: AD with serotonergic action deplete platelet serotonin, leading to a reduced ability to form clots and a subsequent increase in the risk of bleeding. SSRIs and, with limited evidence, mirtazapine and bupropion, are associated with a similar GI bleeding risk, mostly of the upper GI tract.

Microscopic colitis: May be iatrogenic - Nonsteroidal anti-inflammatory drug (NSAIDs) and SSRIs (particularly sertraline) most implicated.

CONCLUSIONS

Managing patients with medical comorbidities and polypharmacy is becoming a frequent occurrence in our daily practice. Greater awareness and understanding of AD-induced GI symptoms may limit unnecessary morbidity and diagnostic and treatment procedures.

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