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A BRAZILIAN CASE OF TREATMENT-RESISTANT GENERALIZED ANXIETY DISORDER SUCCESSFULLY TREATED WITH MONOAMINE OXIDASE INHIBITOR (MAOI)

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SUMMARY

In this brief report we present the case of a 53 year old man with a very debilitating Generalized Anxiety Disorder successfully treated with tranylcypromine. After several failed treatment attempts following international guidelines recommendations over the course of one year and a half, tranylcypromine was prescribed which led to effective and sustained remission of anxiety symptoms for this patient. We also briefly explore treatment options for resistant cases of generalized anxiety disorder, given the major negative impacts of untreated GAD in a person's daily functioning and quality of life.

Key words: *Generalized Anxiety Disorder - treatment resistance cases - monoamine oxidase inhibitors*

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CASE REPORT

Here we present a case of a 53 year old man Mr. M, with a 4-year history of debilitating anxiety symptoms, though free of comorbid psychiatric disorders, who was referred to our Anxiety Disorder Clinic. He reported excessive worrying, weight loss, insomnia, paresthesia in the left side of his body and inability to concentrate. He presented whilst on prescription of alprazolam 2mg, zolpidem 20mg and escitalopram 20 mg daily.

Following his first assessment, he was prescribed escitalopram 30 mg and clonazepam 4 mg daily. The treatment for 8 weeks with escitalopram 30 mg/day combined with clonazepam 4 mg/day did not lead to improvement in anxiety symptoms, and therefore, escitalopram was switched to venlafaxine. For the next 12 weeks, venlafaxine was gradually increased up to 300 mg/day, combined with clonazepam 4 mg/day, yet there was still no positive response to the treatment. Imipramine was then added, gradually increased up to 150 mg/day. After 3 months, significant clinical improvement was noted. Venlafaxine was then tapered off slowly due to side effects. After one year of sustained remission of anxiety symptoms, other medications were also gradually discontinued.

After three months without medications, he reported back to the clinic complaining of uncontrollable worrying along with other anxiety symptoms. Imipramine was re-initiated at 100 mg/day, but after one month, Mr. M reported back to the clinic, complaining of the worst anxiety he had ever experienced and deterioration in general functioning. Various rating scales showed considerable worsening with Beck Anxiety Inventory (BAI) score of 15, Beck Depression Inventory (BDI) score of 10, Generalized Anxiety Disorder (GAD-7) score of 11 and Clinical Global Impression – Severity of Disease (CGI-S) score of 7.

Tranylcypromine, a monoamine oxidase inhibitor (MAOI) was initiated at 30 mg/daily (progressively increase to 80 mg/daily), combined with quetiapine (which was progressively increased to 300 mg/daily), zolpidem 10 mg/daily, and with clonazepam 0.5 mg daily.

One month later, the patient experienced further increase in the anxiety symptoms (BAI: 14, BDI 19, GAD 7: 15, CGI- S: 6).

However, after 3 months of taking above medications, Mr. M experienced significant improvement of anxiety and general functioning. Rating scales at the time were: BAI: 2, BDI: 6, GAD-7: 9 and CGI-S: 3. Due to side effects, quetiapine and clonazepam were gradually discontinued, however, Tranylcypromine dose was maintained. The patient has remained stable with very few residual anxiety symptoms ever since. During his last consultation the rating scales were BDI: 3, GAD-7: 5, BAI: 1 and CGI-S: 2.

DISCUSSION

Generalized Anxiety Disorder (GAD) is the most common anxiety disorder which is more common in women and is often related to environmental stress. It presents with excessive and persistent anxiety that is not

restricted to a particular place, event or activities (i.e. it is "free floating"). This anxiety is usually accompanied by other nonspecific, variable, psychological and physical symptoms such as nervousness, restlessness, fidgeting, tension headaches, dizziness, epigastric discomfort and autonomic overactivity. (Stein & Sareen 2015). The prevalence of GAD varies considerably across different populations, however, in Brazil the lifetime prevalence has been estimated around 4.2% . In Brazilian primary care settings the prevalence of this disorder is around 37.6% (Gonçalves et al. 2014). As in many countries, most cases of GAD are managed at the primary care level. However, in treatment resistant cases, most guidelines, including NICE (NICE UK 2011) recommend referral to mental health specialists as it is reported in this case.

It is important to treat GAD effectively, given untreated GAD has a major impact on a person's daily functioning, quality of life and healthcare utilisation. It has also been found that longer duration of untreated GAD may be associated with worse clinical course and increased prevalence of concurrent psychiatric symptoms (Altamura et al. 2008).

Furthermore, treatment of GAD reduces risk of developing comorbid disorders, such as major depression (Goodwin & Gorman 2002), whilst it has also been found that GAD independently predicts increased risk of hypertension and coronary heart disease (Barger & Sydeman 2005).

For moderate to severe cases of GAD, medications for treatment include, SSRIs, SNRIs and Pregabalin (Bandelow et al. 2008). However, up to 40% of patients do not respond to first line agents (Stein & Sareen 2015). Second line options are Imipramine and Benzodiazepines. Benzodiazepines, despite their abuse potential, can be a good short term option in the first few weeks until onset of efficacy of antidepressant. There is also evidence supporting augmentation strategies with low dose antipsychotics as second line treatment (Katzman et al. 2014). However, in some rare cases as the herein reported, all the above strategies might still not be effective.

Although not included in guidelines, in such cases of treatment-resistant patients, MAOI might be a good option. There are studies indicating that MAOIs may be effective in the treatment of panic disorder and social anxiety disorder (Nardi et al. 2010, Williams et al. 2020), however, none demonstrate efficacy of MAOI in the treatment of GAD.

We hope that this case report and discussion highlights the importance of performing clinical trials for the use of MAOIs in treatment-resistant GAD patients, besides drawing attention to the clinical usefulness of MAOIs which these days are hardly utilized in clinical practice.

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Contribution of individual authors:

Clara Gitahy Falcão Faria conceived the idea of the paper, carried out literature search and wrote the paper.

Marcos Fidry helped to conceive the idea of the paper and reviewed the literature.

Mariana Costa do Cabo reviewed the literature.

Laiana Azevedo Quagliato reviewed the literature and contributed to the final draft.

Antonio Egidio Nardi reviewed the literature and contributed to the final draft.

Rashid Zaman reviewed the literature and wrote the final draft.

Rafael Freire helped to conceive the idea of the paper, reviewed the literature and contributed to the final draft.

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