

SYMPTOMS OF AGITATED DEPRESSION AND/OR AKATHISIA

Marija Vučić Peitl¹, Joško Prološčić¹, Sandra Blažević-Zelić¹,
Ivona Škarpa-Usmiani¹ & Vjekoslav Peitl²

¹Psychiatric Clinic of University Hospital Centre Rijeka, Croatia

²Psychiatric Clinic of University Hospital Centre Sestre Milosrdnice, Zagreb, Croatia

SUMMARY

Akathisia is a syndrome characterized by the unpleasant sensation of “inner” restlessness that manifests itself in the inability of sitting still or not moving. Many types of medicaments can cause akathisia as an adverse event of their use and they include: antipsychotics, antidepressants, antiemetics, antihistamines, and psychoactive substances.

We will present the case of a 50 year old patient, treated on two occasions for psychotic depression. During the second hospitalization it is possible that antipsychotic treatment combined with an antidepressant caused akathisia or there were symptoms of agitated depression and akathisia present at the same time, which is very difficult to determine in everyday clinical practice.

We can conclude that in this case, as in many others, akathisia as a possible adverse effect of psychopharmacs was very hard to identify. Therefore, it is necessary to have akathisia in mind when using certain medicaments, especially when combining several that use the same enzymatic system and consequently raise levels of at least one of them.

Key words: agitated depression - akathisia

* * * * *

INTRODUCTION

Severe or agitated depression is characterized by strong psychomotor agitation combined with suicidal ideas and a number of “somatic” symptoms (WHO 1994). Along with those, more common symptoms of depression are also present, as: lowered mood, loss of appetite, sleep disturbances and feelings of guilt and worthlessness. Sometimes it is very hard to differentiate between psychomotor agitation and akathisia, which is characterized by the unpleasant sensation of “inner” restlessness that manifests itself in the inability of sitting still or not moving (Brüne M 2002, Mohr et al. 2002). The manifestations of akathisia are varied and may range from subtle (often confused with anxiety) to lethal, in the form of suicide (Hamilton et al. 1992).

Akathisia can also be caused, although to a far lesser extent, by Parkinson disease, similar syndromes and possibly other neurological illnesses (Szabadi 1996). Healy and associates described features of akathisia as: tension, insomnia, sense of unease, motor restlessness, anxiety and panic (Healy et al. 2006), all of which can also be symptoms of agitated depression (Maj et al. 2006). Healy, Herxheimer and Menkes noticed that akathisia is sometimes wrongly recognized in antidepressant clinical trials as “agitation, emotional instability and excessive hypokinesia” (Healy et al. 2006).

CASE REPORT

We present the case of a 50 year old patient on the brink of divorce, which is the main cause of his depressive disorder. He was stationary treated on two occasions for psychotic depression. When admitted for

the second time it was due to worsening of his psychical condition. He stated to be tense, with a feeling of strong inner restlessness and not being able to settle down. Furthermore, he was occupied with marital problems and by the intense fear of that something bad will happen, along with negative anticipation of his future and troubles sleeping. The patient negated drinking alcohol and stated that he regularly took his medicaments prescribed as therapy: antidepressant, antipsychotic, anxiolytic and hypnotic.

Psychical examination showed that the patient is fully conscious, orientated in all relations, with contact relatively easily established although maintained with assistance. Furthermore, he was intrapsychically tensioned, anxious, of lowered mood and affect. His thought process was normal, while in thought content we explored depressive ideas. Also, the patient denied any sort of delusions and hallucinations, as well as suicidal ideas, although he was hypobulic and with decreased volition-drive dynamisms.

Performed diagnostic procedures:

- Laboratory results: ALT 63-41 and γ GT 149-80, on both occasions they were increased compared to normal.
- Thyroid hormones: normal.
- EEG: non-specific dysrhythmic trace.
- CT of the brain: without significant changes of the brain parenchyma.
- Psychological assessment: mnemonic functioning below the age expected level, very easily distracted, with impaired ability of retaining and reproducing logical, mechanical-numerical and visual material. Sensomotoric functioning is dominated with signs of psychoticism. Personality plain shows an evident shift towards psychosis with elevated dimensions of

depression and paranoia and abundant somatic symptomatology. Emotionally labile, dependent in interpersonal relations, prone to manipulation. Disturbed testing of reality.

- Ophthalmological findings: normal.
- Neurological findings: No rigidity, no cog-wheel phenomenon, no tremor, Romberg testing normal and cranial nerves normal. Diagnosis: It is probably a case of acute iatrogenic parkinsonism and I recommend a follow up and neurological control exam in six months time. Therapy: nothing.

Course of treatment

Typical antipsychotics haloperidol and promazine were administered during the first six days of hospitalization due to intense psychomotor restlessness and insomnia, combined with the increased dose of atypical antipsychotic olanzapine. Along with supportive treatment when needed, in the form of benzodiazepines, a hypnotic and an anticholinergic. Patient verbalized anxiety, unrest, had difficulties sleeping and became rigid, stiff and sluggish. Therefore on the seventh day haloperidol was discontinued and fluvoxamine (Fevarin) was introduced into treatment. Fluvoxamine was slowly titrated up to 300 mg across 19 days of treatment. Despite of using relatively high doses of fluvoxamine and olanzapine, patients' psychical state remained unchanged, with intense psychomotor restlessness, anxiety, constant movements, pacing and not being able to stay still and rest, along with depressed mood and latent suicidality. Due to already stated psychical state, olanzapine was changed to quetiapine, while fluvoxamine remained at 300 mg. Furthermore, mood stabilizer valproate (Depakine chrono) was introduced into treatment because of patients' low frustration tolerance, along with an anxiolytic and a hypnotic. Quetiapine was titrated up to 400 mg per day, with valproate at 900 mg per day. These changes in treatment led to significant improvement of patients' psychical state: his sleep improved, psychomotor restlessness and anxiety significantly diminished, mood improved, suicidal ideas ceased and with that he fulfilled the criteria for demission from psychiatric care.

DISCUSSION

Selective-serotonin reuptake inhibitors, both as monotherapy and in combination with typical antipsychotics, have been associated with extrapyramidal effects (Gill et al. 1997, Leo 1996, Koliscak et al. 2009). Olanzapine, on the other hand, in therapeutic doses rarely causes akathisia (Vena et al. 2006, Kane et al. 2009, Makkos et al. 2006). However, it is a substantiated fact that fluvoxamine increases serum levels of olanzapine and that could have caused symptoms of akathisia to emerge, which were not recognized as such in this case. Therefore, it is plausible

that serum levels of olanzapine in this patient were higher than 20 milligrams daily.

In the case of combination with antipsychotics, possible mechanisms include decreased clearance of antipsychotic via inhibition of cytochrome P450 2D6, or a synergistic increase in the release of norepinephrine and dopamine (Gossen et al. 2002, Zhang et al. 2000).

One of the questions that still remain - Was increasing the daily dose of olanzapine to 20 milligrams, along with fluvoxamine at 300 milligrams, which led to significant deterioration of patients' psychical state, the factor which maybe led to the development of akathisia? Especially as introduction of an antipsychotic with better anxiolytic and sedative effects improved patients' psychical state and relieved already mentioned symptoms.

CONCLUSION

This case report illustrates that akathisia as a psychopharmac side effect is very hard to recognize in everyday clinical practice. It needs to be stressed that one should always consider akathisia when treating patients with certain psychopharmacs, especially when combining several that use the same enzymatic system and consequently raise serum levels of at least one of them.

REFERENCES

1. Brüne M: *Ladislav Haskovec and 100 Years of Akathisia. Am J Psychiatry*, 2002;159:727.
2. Gill HS, DeVane CL, Risch SC: *Extrapyramidal symptoms associated with cyclic antidepressant treatment: a review of the literature and consolidating hypotheses. J Clin Psychopharmacol*, 1997;17:377-89.
3. Gossen D, de Suray JM, Vandenhende F, Onkelinx C, Gangji D: *Influence of fluoxetine on olanzapine pharmacokinetics. AAPS PharmSci*, 2002;4:E11.
4. Hamilton MS, Opler LA: *Akathisia, suicidality, and fluoxetine. J Clin Psychiatry*, 1992;53:401-6.
5. Healy D, Herxheimer A, Menkes DB: *Antidepressants and violence: problems at the interface of medicine and law. PLoS Med*, 2006;3:e372.
6. Kane JM, Fleischhacker WW, Hansen L, Perlis R, Pikalov A, Assunção-Talbott S: *Akathisia: an updated review focusing on second-generation antipsychotics. J Clin Psychiatry*, 2009;70:627-43.
7. Koliscak LP, Makela EH: *Selective serotonin reuptake inhibitor-induced akathisia. J Am Pharm Assoc*, 2009;49:28-36.
8. Leo RJ: *Movement disorders associated with the serotonin selective reuptake inhibitors. J Clin Psychiatry*, 1996; 57:449-54.
9. Maj M, Pirozzi R, Magliano L, Fiorillo A, Bartoli L: *Agitated "unipolar" major depression: prevalence, phenomenology, and outcome. J Clin Psychiatry*, 2006; 67:712-9.
10. Makkos Z, Csonka A: *Akathisia in the course of olanzapine treatment. Neuropsychopharmacol Hung*, 2006;8:215-7.

11. Mohr P, Volavka J: *Ladislav Haskovec and akathisia: 100th anniversary. Br J Psychiatry*, 2002; 181:537.
12. Szabadi E: *Akathisia-or not sitting. Br Med J (Clin Res Ed)*, 1986; 292(6527):1034-1035.
13. Vena J, Dufel S, Paige T: *Acute olanzapine-induced akathisia and dystonia in a patient discontinued from fluoxetine. The journal of emergency medicine*, 2006; 30:311-317.
14. WHO: *International statistical classification of diseases and related health problems. Zagreb: Medicinska naklada*, 1994.
15. Zhang W, Perry KW, Wong DT, Potts BD, Bao J, Tollefson GD, Bymaster FP: *Synergistic effects of olanzapine and other antipsychotic agents in combination with fluoxetine on norepinephrine and dopamine release in rat prefrontal cortex. Neuropsychopharmacology*, 2000; 23:250–62.

Correspondence:

Marija Vučić Peitl
Psychiatric Clinic of University Hospital Centre Rijeka
Cambierieva 17/7, 51000 Rijeka, Croatia
E-mail: marijapvp@gmail.com