

## HIGH DOSES ALPRAZOLAM INDUCED AMENORRHOEA AND GALACTORRHOEA

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### SUMMARY

*Alprazolam belongs in the group of anxiolytics, medicaments used for reducing anxiety. As most other drugs, it can cause various adverse events, including hormonal disturbances and imbalance. Prolactin elevation is one such hormonal adverse event that can lead to galactorrhoea, or abnormal milk discharge from the breast and amenorrhoea. In this case report we will present the case of a female patient that developed galactorrhoea while treated with alprazolam, after all physical factors that can also cause these symptoms were excluded.*

**Key words:** alprazolam – amenorrhoea - galactorrhoea

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### INTRODUCTION

Alprazolam belongs in the group of anxiolytics, medicaments used for reducing anxiety. As most other drugs, it can cause various adverse events, including hormonal disturbances and imbalance (Sevy et al. 1994, Zemishlany et al. 1991).

Prolactin elevation is one such hormonal adverse event that can lead to galactorrhoea.

Galactorrhoea is abnormal milk discharge from the breast and it most commonly occurs due to excessive prolactin production by a benign tumour of the pituitary gland called a prolactinoma, but it can also be caused by several hormonal diseases (Vrhovac et al. 2003). Variety of medicaments can also increase prolactin levels and subsequently cause amenorrhoea and galactorrhoea (Molitch 2005). Of all psychopharmacs, antipsychotics are one of the major culprits for causing galactorrhoea. Even though practically every medicament from that group was reported to cause these side effects, sulpiride and risperidone are the most common (Fric et al. 2003, Bostwick et al. 2009, Sethi et al. 2010, Raza et al. 2010, Peitl et al. 2010a, Peitl et al. 2010b, Kovács et al. 2006).

### CASE REPORT

We will present the case of a 35 year old female patient, unmarried and without children. Family history reveals that her father died because of colon cancer and that her mother is undergoing psychotherapy. She also has a younger sister who is physically and psychically healthy.

Medical history: suffered from common childhood illnesses. HPV infection diagnosed year and a half before seeking psychiatric help. The patient had her first menstruation when she was 13 years old, last one was few days before contacting her psychiatrist. Five years ago stopped using oral contraceptives.

Habits: smokes cigarettes from when she was 14 years old, one pack of cigarettes per day and sometimes drinks alcohol. During the July of 2010 she was late with her period, did not have menstrual bleeding for two months and believed she was pregnant. However, when showering she discovered that her breasts discharge milk.

### Course of psychiatric treatment

First time that she sought psychiatric help was three years ago, after her father died and she was feeling sad and dysfunctional. At that time she was treated with sulpiride and bromazepam, without any side effects and adverse events. One year later, her general practitioner prescribed her alprazolam 0.25 milligrams tablets which she took occasionally, without any apparent change in her functioning. At the beginning of last year (2010) she began having work related problems, along with mood deterioration, constant fear and frequent waking. She also verbalized somatic symptoms, like palpitations, arrhythmias, gastric discomfort and felt like “I was breathing in only half the air as I usually do”. General practitioner then introduced sertraline into treatment but the patient discontinued it after only two weeks, as she felt that alprazolam was helping her more than sertraline. She then began self-medicating herself with increased doses of alprazolam, combining 3 milligrams of alprazolam XR and 5 to 6 milligrams of regular alprazolam daily. During September of 2010 she again sought psychiatric help, after discovering that she did not have regular menstrual bleeding for two months and that her breasts discharge milk.

Endocrinologist, gynecologist and cardiologist examined her and all tests were satisfactory except prolactin values at 987 mU/L. CT scan of the brain (pituitary gland) did not show any abnormal findings.

During September of 2010, alprazolam was gradually discontinued with gradual introduction of

quetiapine and fluvoxamine. Galactorrhoea ceased in November and regular menstrual cycle was restored in December of 2010. Prolactin values decreased to 376 mU/L. Psychological state of the patient improved.

## DISCUSSION

While hyperprolactinemia was reported in several case reports (Sevy et al. 1994, Zemishlany et al. 1991) and amenorrhoea in at least one (Bondolfi et al. 1997) during the treatment with alprazolam, galactorrhoea has not previously been reported.

Clinical exams and laboratory test that were performed excluded possible somatic causes of galactorrhoea and amenorrhoea. Also, it is very important to mention that the patient did not use any other medication while using alprazolam. That makes it considerably easier to attribute already mentioned side effects to the effects of higher doses of alprazolam.

Why did then alprazolam cause galactorrhoea and amenorrhoea in our patient? Especially if we consider that quite a big number of people treated with alprazolam use it in doses higher than optimal, or even abuse it, and still do not develop these side effects? We believe that this is just one more proof that every person is unique and responds differently to same medication through complex interplay of different pharmacogenetic factors. (Francetić et al. 2007, Daudén-Tello 2006).

## CONCLUSION

Some sort of an organic substrate that could have caused increased levels of prolactin and consequently amenorrhoea and galactorrhoea was ruled out through thorough clinical examination and laboratory tests. Therefore appearance of amenorrhoea and galactorrhoea can be attributed to higher doses of alprazolam, even more though because gradual discontinuation of alprazolam lowered prolactin levels and restored regular menstrual cycle, without galactorrhoea.

## REFERENCES

1. Bondolfi G, Rubin C, Bryois C, Eap CB: Galactorrhoea induced by a pharmacodynamic interaction between citalopram, alprazolam and tramadol: a case report. *Therapie*, 1997; 52:76-7.
2. Bostwick JR, Guthrie SK, Ellingrod VL: Antipsychotic-induced hyperprolactinemia. *Pharmacotherapy*, 2009; 29:64-73.
3. Daudén-Tello E: Pharmacogenetics I. Concept, history, objectives and areas of study. *Actas Dermosifiliogr*, 2006; 97:623-9.
4. Francetić I, Vitezić D: *Osnove kliničke farmakologije*. Zagreb: Medicinska naklada, 2007.
5. Fric M, Laux G: Plasma prolactin level and incidence of adverse endocrinologic effects during therapy with atypical neuroleptics. *Psychiatr Prax*, 2003;30(Suppl 2):S97-101.
6. Kovács L, Kovács G: Endocrine side effects among psychiatric patients treated with antipsychotics. *Neuropsychopharmacol Hung*, 2006; 8:61-6.
7. Molitch ME: Medication-induced hyperprolactinemia. *Mayo Clin Proc*, 2005; 80:1050-7.
8. Peitl MV, Peitl V, Grahovac T, Pavlović E: Galactorrhea - side effect of risperidone in combination with depakine chrono in a patient with bipolar disorder. *Psychiatr Danub*, 2010a; 22:125-7.
9. Peitl MV, Pavlović E, Peitl A, Peitl V: Amenorrhoea - consequence of combined treatment with sulpiride and risperidone in a patient suffering from schizophrenia. *Psychiatr Danub*, 2010b; 22:123-4.
10. Raza S, Haq F: Ziprasidone-induced galactorrhea in an adolescent female: a case report. *Prim Care Companion J Clin Psychiatry*, 2010;12.
11. Sethi S, Sharma M, Malik A: Dose-dependent galactorrhea with quetiapine. *Indian J Psychiatry*, 2010; 52:371-2.
12. Sevy S, Brown SL, Wetzler S, Kotler M, Molcho A, Plutchik R, van Praag HM: Effects of alprazolam on increases in hormonal and anxiety levels induced by meta-chlorophenylpiperazine. *Psychiatry Res*, 1994;53:219-29.
13. Vrhovac B, Francetić I, Jakšić B, Labar B, Vucelić B: *Interna medicina*. Zagreb: Naklada Ljevak, 2003.
14. Zemishlany Z, McQueeney R, Gabriel SM, Davidson M: Neuroendocrine and monoaminergic responses to acute administration of alprazolam in normal subjects. *Neuropsychobiology*, 1991; 23:124-8.

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