Case report

Impact of antipsychotic agents in bone mineral density of schizophrenic patients

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INTRODUCTION

The use of antipsychotics has been pointed as factor for osteopenia/osteoporosis or reduced bone mineral density (BMD) in schizophrenic patients, due to increased prolactin blood levels caused by drugs.[1-6] The treatment using antipsychotics results in the blockade of D2 dopamine receptors and subsequent hyperprolactinemia.[3] Increased prolactin blood levels suppress the reproductive endocrine system, due to the reduction in synthesis of sexual hormones. Hyperprolactinemia is associated with the suppression of secretion of gonadotropin-releasing hormone (GnRH) and luteinizing hormone (LH) of the hypothalamus, compromising the pituitary response to GnRH.[3] High prolactin levels have inhibitory effects on the release of GnRH hypothalamic impulses and lead to the inhibition of positive feedback effects in estradiol levels over LH secretion. The primary mechanism of bone loss is a result of the hypogonadism that occurs in a subset in men and women with hyperprolactinemia.[7] Although the mechanisms and most visible effects of hyperprolactinemia are known, such as secondary amenorrhea and reduced libido, little attention has been drawn to these patients in relation to the identification of the impact of antipsychotics on another important parameter of health, which is the BMD of that population.[3,8]

CASE REPORT

Woman, 53 years old, Caucasian, body mass index 23.87 kg/m^2 (eutrophic), nonsmoker, diagnosed with undifferentiated schizophrenia (International Classification of Diseases, Vol. 10, or ICD-10) with onset at 23 years of age. She has been taking antipsychotics for 30 years, including haloperidol (mean dose of 10 mg) and sulpiride (mean dose of 1,200 mg), besides biperiden (mean dose of 2 mg). She started taking lithium in 2001 (mean dose of 600 mg), maintaining the other drugs. She has been taking clozapine 100 mg for 18 months. She became menopausal at 47 years of age. According to a survey on the hospital's medical records on 09/12/97, there was a register of 264 ng/dl and thyroid stimulating hormone (TSH) of 2.47 μIU/mL; on 08/27/99, follicle stimulating hormone (FSH) of 96.1 miliIU/mL, LH of 37.4 miliIU/mL and estradiol of 31.0 pg/mL. In 2002, the

patient presented hypothyroidism due to lithium and, after suspension, she became euthyroid. Bone densitometry was requested after hyperprolactinemia caused by antipsychotics and consequent deleterious effect on the bone due to hypogonadism. The results showed osteopenia of the spine and total proximal femur, according to criteria defined by the World Health Organization (table 1).

Table 1 - Bone mineral density of this case report

Region/Conclusion*	**Bone mineral density**	**T Score**
Spine	0.828 g/cm^2	-2.14
Osteopenia		
Femur	0.781 g/cm^2	-1.32
Osteopenia		
Femoral cervix	0.749 g/cm^2	-0.90
Normal		
Greater trochanter	0.550 g/cm^2	-1.52
Osteopenia		
Ward's triangle	0.597 g/cm^2	-1.17
Osteopenia		

* Criteria established by the World Health Organization (1994) for lumbar spine, femoral cervix and middle third of the radius: BMD up to -1 (T score): normal; BMD between -1 and -2.5 (T score): osteopenia; BMD ≤ -2.5 (T score): osteoporosis; and BMD ≤ -2.5 (T score) associated with fragility fracture: established osteoporosis.

DISCUSSION

The literature warns about the need of drawing more attention to psychiatric patients, since antipsychotics seem to induce hyperprolactinemia, increasing the potential to develop osteoporosis.[1,3,4] Researches have shown an increase in prolactin in about 60% of patients taking

typical antipsychotics,[4,6] and there is evidence of the increase in mean prolactin levels of approximately three times above the normal limit in both genders. However, other studies suggest that atypical may be safer than typical neuroleptics in terms of BMD reduction[2] and seem to reduce the effect caused by the prolactin hormone.[6] Antipsychotics are not recognized by the World Health Organization, neither by the Royal College of Physicians as risk factor for osteoporosis, and there are still no epidemiological studies to investigate the prevalence of BMD reduction in schizophrenic patients. Therefore, further studies are recommended.[3]

Osteoporosis can be expected in female patients who developed amenorrhea after hyperprolactinemia secondary to antipsychotics, although there are no plausible mechanisms in men.[5] In male patients, it is suggested that hyperprolactinemia results in hypogonadism and bone loss.[1] Many other factors that were not assessed in this study induce reduction in BMD: smoking, inadequate diet, sedentary lifestyle, gender, race, among others. According to the guidelines for osteoporosis recommended by the Brazilian Ministry of Health, proper investigation of clinical history and physical examination with active search of the diagnosis in risk patients should be performed, as well as preventive treatment of osteoporosis.[9] Therefore, we warn the professionals who work with those patients about the need of investigating, in clinical practice, presence of amenorrhea, sexual disorders, infertility and increased blood prolactin levels, since osteoporosis is a chronic comorbid condition that has a great impact on public health.

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ABSTRACT

Studies have shown a high risk of osteoporosis in schizophrenic patients. Some studies have demonstrated that typical neuroleptics and risperidone may induce osteoporosis or reduce bone mineral density. This can be due to the fact that prolonged use of those drugs induces hyperprolactinemia to levels above normal in both genders, and reduces the levels of estrogen and testosterone, thus increasing the risk of osteopenia/osteoporosis. We report on a case of osteopenia in a 53-year-old female patient using antipsychotics for 30 years. We comment on the recommended procedures to detect osteopenia and on the existing guidelines for its management.

Keywords: *Case report, schizophrenia, bone mineral density, antipsychotics.*

Title: *Impact of antipsychotic agents in bone mineral density of schizophrenic patients*

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