

Nieves Basterreche<sup>1, 2</sup>  
Mercedes Zumárraga<sup>3</sup>  
Aurora Arrue<sup>3</sup>  
Olga Olivas<sup>1</sup>  
Wendy Dávila<sup>4</sup>

# Aripiprazole reverses Paliperidone-induced Hyperprolactinemia

<sup>1</sup>Short Stay Unit  
Hospital de Zamudio. Red de Salud Mental de Bizkaia  
<sup>2</sup>Psychiatry Department  
Facultad de Medicina  
Universidad del País Vasco

<sup>3</sup>Neurochemical Research Department  
Hospital de Zamudio  
Red de Salud Mental de Bizkaia  
<sup>4</sup>Avances Médicos SA

Hyperprolactinemia is a common side effect of antipsychotic treatments. Existing alternatives to resolve this problem include decreasing the antipsychotic dose or switching to a different antipsychotic agent. Nevertheless, said modifications can sometimes lead to decompensation of the patient. We report a clinical case of a female patient in whom the combined treatment of 5 mg/day of aripiprazole (5 mg/day) reversed paliperidone-induced hyperprolactinemia within four weeks.

**Key words:** Hyperprolactinemia, Paliperidone, Aripiprazole

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## Aripiprazol como corrector de la hiperprolactinemia causada por paliperidona

La hiperprolactinemia es un efecto secundario frecuente provocado por los fármacos antipsicóticos. Una opción para resolver este problema es disminuir las dosis o cambiar de antipsicótico, pero en ocasiones se produce la descompensación del paciente. Comentamos el caso de una paciente en la que la combinación con 5 mg/día de aripiprazol resolvió en 4 semanas la hiperprolactinemia producida por la paliperidona.

**Palabras clave:** Hiperprolactinemia, Paliperidona, Aripiprazol

## INTRODUCTION

Hyperprolactinemia is a frequent antipsychotic drug caused side effect. A total of 42-47% of men and 48-93% of premenopausal women diagnosed of schizophrenia who take conventional antipsychotic drugs have hyperprolactinemia.<sup>1</sup> Among the atypical antipsychotics, those producing a greater increase in the levels of this hormone in blood are amisulpiride, risperidone and its metabolite paliperidone.<sup>2</sup>

Prolactin is a sexual hormone segregated by the adenohypophysis into the bloodstream that stimulates the production of milk in the mammary glands and the synthesis of progesterone in the corpora lutea.<sup>3</sup> Antipsychotic drugs exert a type D2 dopaminergic receptor blockade of the adenohypophyseal lactotroph cells. This is how the inhibition that causes dopamine in the synthesis of prolactin is suppressed.

The symptoms that may be provoked by hyperprolactinemia are: menstrual irregularities, sexual dysfunctions, infertility, gynecomastia and galactorrhea, among others.<sup>5</sup> Furthermore, when this situation is maintained over time, as occurs with the long-term treatments of psychotic patients, serious problems may appear. These problems may be defects in bone mineralization,<sup>6</sup> depression of immunity,<sup>7</sup> increased risk of suffering neoplasms such as breast cancer<sup>8</sup> and endometrial cancer,<sup>9</sup> for example, as well as an increase in platelet activation.<sup>10</sup>

In spite of their severity, these side effects are frequently underdiagnosed because the physician does not systematically look for them, does not observe them visually and the patient feels ashamed to mention some of the spontaneously.

## A CASE REPORT

A 30-year old woman diagnosed of paranoid type schizophrenic disorder of 10 years evolution. She had no

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Correspondence:  
Nieves Basterreche  
Hospital de Zamudio  
Arteaga Auzoa 45  
48170 Zamudio. Bizkaia  
Spain  
Phone: 944006500  
Fax: 944006527  
E-mail: nieves.basterrechezaguire@osakidetza.net

medical-surgical background of interest. She has never required psychiatric hospitalization and has been maintained with outpatient treatment. Among the clinical symptoms, cenesthopathic sensory perception, delusional contents of self-referential type and of harm, and phenomena of theft, thought insertion and diffusion stand out. The negative symptomatology was not very apparent but the patient had clear awareness of deficit, complaining of apathy, abulia and alogia. She strictly complies with the medical visits, treatments prescribed and does not consume toxics.

She was psychologically stabilized with paliperidone 12 mg/day and lorazepam 3 mg/day. In one of the follow-up visits, she reported the presence of amenorrhea of 3 months evolution, so that measurement of prolactin in blood was requested. The test showed 141 ng/mL (reference values 3-30 ng/mL). At first, we decreased the paliperidone dose to 9 mg/day, but she suffered an exacerbation of the positive psychotic symptoms. After, we decided to reestablish the initial doses of this antipsychotic drug and we added 5 mg/day of aripiprazole. We chose the option of maintaining the paliperidone and adding aripiprazole at a minimum dose because the latter drug had been previously used with this patient at a dose of 15 mg/day and had to be withdrawn due to appearance of acathisia. Four weeks after the establishment of treatment with 5 mg/day of aripiprazole, prolactin level in blood was 37 ng/mL.

## DISCUSSION

The degree of elevation of serum prolactin levels is related with the type of antipsychotic, doses used, gender and age of the patient, among other factors. Within the group of antipsychotic drugs, those causing this effect most frequently are the conventional neuroleptics, amisulpiride, risperidone and its metabolite paliperidone.<sup>2</sup> In turn, the dose-dependent effect is more frequent in women and among them in the young age.<sup>3</sup> Our patient fulfilled several risk factors associated to the appearance of hyperprolactinemia: being a woman, being young and being treated with paliperidone.

In spite of that mentioned above, in our setting, risperidone and its metabolite paliperidone are drugs used due to their great efficacy. They are monoaminergic antagonists that possess high affinity for the D2 dopaminergic receptors, also binding to another type of receptor.<sup>11</sup> The increase in the prolactin levels in blood is produced after a few hours of initiating acute treatment with these drugs. However, once the treatment is interrupted, the levels of this hormone may remain high for a prolonged period of time.<sup>12</sup>

There are several strategies to attempt to correct the increase of prolactin levels, such as decreasing the antipsychotic doses or switching the antipsychotic, or adding

a dopaminergic agonist. However, in these cases, we run the risk of provoking psychopathological destabilization, as occurred in the case of the patient we are presenting. We currently count on aripiprazole, an atypical antipsychotic of the so-called third generation. It acts on different neurotransmission systems with the special feature that it behaves as a partial agonist of the type D2 and D3 dopaminergic receptors.<sup>13, 14</sup> It has been suggested that aripiprazole can act, depending on the availability of the D2 and dopamine receptors in the synapsis, in each case having agonist or antagonist properties.<sup>15</sup> In relation to its partial agonism, several works have demonstrated that this drug not only increases the serum levels of prolactin, but also corrects the hyperprolactinemia caused by other antipsychotics when associated to them.<sup>16, 17</sup> Normally, the doses used for this purpose, in the works reviewed, were 10-30 mg/day.<sup>17, 18</sup> However, in our case, we have observed that with only 5 mg/day, the prolactin levels have normalized. We carried out the evaluation of said levels after 4 weeks of treatment but the decrease in prolactin appears earlier. On the other hand, it would be interesting to see if this effect is maintained over time.

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