Aripiprazole use combined with depot antipsychotic medication: two cases demonstrating its ability to reduce prolactin levels in an adolescent forensic hospital

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Abstract: Many patients maintained on depot medication have raised prolactin levels, which can lead to a range of long-term medical problems. The addition of aripiprazole can reduce prolactin levels and restore sexual function in these patients. The cases described demonstrate the potential role of aripiprazole in a forensic setting.

Keywords: antipsychotic, aripiprazole, forensic, hyperprolactinaemia, polypharmacy, prolactin

Introduction

Currently there is little support for antipsychotic polypharmacy [Taylor, 2010]. There is no substantial evidence that it improves treatment of psychosis and some evidence that it increases the potential risk to patients [Langan and Shajahan, 2010]. However we would like to suggest that prescribing oral aripiprazole to patients who need to be on depot antipsychotic medication may be a sensible way to reduce prolactin levels in these patients.

There is some evidence that aripiprazole may play an important role in treating patients with psychosis who are sensitive to elevated prolactin and patients with prolactin-secreting pituitary tumours because aripiprazole reduces prolactin levels by about 75% whereas the other antipsychotics increase levels up to 275% [Hoffer *et al.* 2009]. There is also some evidence that prescribing aripiprazole to patients with antipsychotic-induced hyperprolactinemia reduces prolactin levels [Lorenz and Weinstein, 2007; Shim *et al.* 2007]. Other ways of reducing prolactin levels, such as dopamine agonists, may worsen psychosis [Boyd, 1995]. The addition of testosterone in men or oestrogen replacement in women to protect bone mass and improve sexual function is another option [Casanueva *et al.* 2006]. Many psychiatrists would be wary of prescribing testosterone to a man with a history of aggressive or impulsive behaviour.

Use of depot medication is common practice in Australia, the USA and Europe where a quarter to a third of patients with psychotic illnesses receive long-acting depot antipsychotic medication depending on the clinical settings [Barnes *et al.* 2009]. Guidelines suggest that depot antipsychotic medication should be prescribed in specific circumstances, such as when a patient has expressed a preference [Moore *et al.* 2007] and when partial or complete lack of compliance is a significant issue [National Institute for Health and Clinical Excellence, 2009; Lehman *et al.* 2004]. In a UK-based study it was shown that patients within assertive outreach teams, forensic inpatient settings and acute adult wards more frequently received depot medication [Barnes *et al.* 2009]. The relatively higher use of depot medication in forensic inpatient populations is unsurprising given that these patients pose a high risk to others. The majority of such patients have a history of serious and usually violent offences. Almost all of these patients are detained under the Mental Health Act and are commonly subject to restriction orders [Anderson, 2008].

In these patients, changing to oral antipsychotics is often not a viable option because of a history of poor compliance and insight. If patients with a history of violence related to psychosis are going to achieve discharge it is likely to be on depot medication.

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Hyperprolactinaemia is a commonly seen adverse effect of antipsychotic medication [Petty, 1999] which is caused by D2 receptor drug binding [Markianos *et al.* 2001]. Because all the available depots are potent D2 blockers, raised prolactin levels can be associated with depression, sexual dysfunction, amenorrhoea, galactorrhoea, breast cancer and osteoporosis [Halbreich *et al.* 2003; Maguire, 2002]. There is evidence to show that patients are more concerned with the sexual side effects than any other side effects [Finn *et al.* 1990], which is one of the main reasons why patients stop taking depot medication.

In an adolescent forensic secure hospital we have had clinical experience of reducing prolactin levels and restoring sexual function in two young men with hyperprolactinaemia secondary to depot antipsychotic medication.

Case 1

An 18-year-old man with a history of severe unprovoked violence directly related to psychosis had made a good clinical response to zuclopenthixol decanoate 500 mg taken fortnightly. Prior to the prescription of depot he had been started on orodispersible olanzapine in a youth offender institute. He refused medication on a frequent basis and following transfer to hospital was prescribed a test dose of zuclopenthixol. The dose was titrated up to 500 mg fortnightly over 3 months. He complained of being unable to ejaculate since being on the depot and had a raised prolactin level of 492 mU/ml (normal range in men is 55.4–276). He had mild gynaecomastia. He experienced a worsening of psychotic symptoms when we attempted a dose reduction. Because of his poor insight and statements he made about wanting to stop medication we did not consider that a nondepot would be viable. However, we discussed with him the possibility of prescribing aripiprazole in order to try and restore sexual function and he agreed to try this in addition to the zuclopenthixol decanoate injection. The aripiprazole was commenced at a dose of 10 mg. His prolactin levels fell to 182 mU/ml over a period of a month and he stated that he was able to get an erection again and ejaculate. Because he refused to have further blood tests it was not possible to continue to monitor his prolactin level.

We excluded other potential causes of hyperprolactinaemia.

Case 2

The second case was a 17-year-old man with a psychotic illness and a history of serious violence. Again his lack of insight prevented us from considering an oral antipsychotic when he experienced an inability to sustain an erection or ejaculate on risperidone long-acting injection 50 mg fortnightly. He had been commenced on orodispersible risperidone in a youth offender institute and had never been on an antipsychotic before. A dose reduction led to deterioration in his psychosis. The team considered that changing to a different depot made no sense because they were all likely to raise prolactin levels. The man agreed to a trial of aripiprazole 5 mg in addition to the risperidone long-acting injection and his prolactin level fell from 1152 to 421 mU/ml over a 3-month period. He stated that his sexual function returned. He complained of increased anxiety for about 2 weeks after starting the aripiprazole but this subsided. Because the prolactin level continuing to be above the normal range the aripiprazole dose was increased to 10 mg daily and the prolactin level fell after a month to 319 mU/ml. He again complained of increased anxiety in the first week following the increase in dose.

We excluded other potential causes of hyperprolactinaemia.

Discussion

Evidence of use of aripiprazole in combination with other antipsychotic medication (other than clozapine) is lacking. There has been some concern that coprescribing aripiprazole may result in re-emergence or worsening of psychotic symptoms [Adan-Manes and Garcia-Parajua, 2009], which is thought to have been mediated by its partial antagonism of mainly D2 receptors. However, there is also evidence that such a combination does not change [Henderson *et al.* 2009] or can improve [Kuo and Hwu, 2008] psychotic symptoms. In these two cases we did not observe any deterioration, although we acknowledge that the period of observation was relatively brief. One of our patients did experience increased anxiety for a short period following the addition of aripiprazole. Agitation and anxiety are recognised potential side effects of aripiprazole. In one trial 0.6% of patients stopped taking aripiprazole because of agitation compared with 0% of patients taking haloperidol [Marden *et al.* 2003]. In both cases discussed here we did not add aripiprazole until the patients had made a

reasonable recovery and were not behaviourally disturbed.

In our opinion the addition of aripiprazole to patients on depot antipsychotic is rational prescribing. It is warranted when patients have high prolactin levels on depot antipsychotic medication and dose reductions are ineffective in reducing prolactin or are causing clinical deterioration. Aripiprazole is of particular use in forensic practice when some patients need to be on depot medication for risk reasons, but it could clearly have a role in many other settings as well.

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Conflict of interest statement

None declared.

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