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Research Article

Serum Prolactin Monitoring in Patients on Risperidone admitted to the acute wards at Mount Carmel Hospital

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Abstract. First-generation antipsychotics have been shown to increase prolactin levels in the body. Atypical antipsychotics have a lower tendency to produce hyperprolactinaemia due to a weaker and transient dopamine antagonistic effect. Despite being an atypical antipsychotic, Risperidone, tends to cause a higher increase in prolactin due to a stronger and more prolonged blockade on dopamine receptors.
The purpose of this audit is to assess current practices at Mount Carmel Hospital (MCH) with regards to serum prolactin monitoring in patients taking Risperidone when compared to Maudsley Prescribing Guidelines in Psychiatry, 14th Edition (2021). The audit was based on patients acutely admitted between June and December 2021. Focus was placed on prolactin levels checked during admission in patients previously on Risperidone, prolactin levels checked in the preceding six months if no prolactin level was checked during admission and the appropriate action taken in cases where the serum Prolactin was noted to be high.
From this audit it was concluded that there is inadequate monitoring of serum prolactin levels in patients prescribed Risperidone at MCH. Increased awareness of Risperidone-induced hyperprolactinemia and associated guidelines are required to improve clinical practice.
The recommendations suggested from this audit were to increase awareness of serum prolactin monitoring guidelines amongst all medical and nursing staff at MCH and to create a simple flow-chart outlining the appropriate serum prolactin monitoring guidelines and distribute this to MCH wards.

Keywords: Hyperprolactinemia, Risperidone, Antipsychotics.

1 Introduction

Hyperprolactinemia is clinically defined as a plasma prolactin level of >424 mIU/L for men and >530 mIU/L for women. Serum prolactin levels may be raised as a result of stress, pregnancy and lactation, seizures, renal impairment and in cases of prolactinoma. The blood sample should be taken first thing in the morning and stress during venipuncture should be kept to a minimum. Levels over 2500 mIU/L are considered to be highly elevated and one must rule out the possibility of a prolactinoma by MRI in these cases. Hyperprolactinaemia (in all cases) is more common in female patients.

High serum prolactin levels are often asymptomatic, however may be associated with symptoms pertaining to disruption of the hypothalamic-pituitary-gonadal axis. The clinical manifestations of chronic hyperprolactinemia include:

- Reproductive dysfunction (anovulation, menstrual irregularity, amenorrhea, reduced fertility, decreased oestrogen and testosterone production).
- Sexual impairment (reduced libido, retrograde or painful ejaculation, erectile dysfunction, impotence)
- Breast pathology (galactorrhoea, breast enlargement, prolactin-sensitive dysplasia with increased potential for breast cancer, gynecomastia).
- Chronic hypogonadism complications (decreased bone mineral density and osteoporosis, increased cardiovascular risk, metabolic syndrome, malignancy).
- Psychological effect (depression, anxiety, hostility, memory deficit, psychosis).

First-generation antipsychotics have been shown to increase prolactin levels in the body. The associated mechanism involves dopamine (D2) blockade in the tuberoinfundibular tract of the hypothalamus, which in turn re-

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verses the dopaminergic inhibition of prolactin in the anterior pituitary gland. The time taken for prolactin levels to increase varies between a few hours to approximately nine days.

Atypical antipsychotics have a lower tendency to produce hyperprolactinaemia due to a weaker and transient dopamine antagonistic effect. Although atypical antipsychotic agents, such as olanzapine, quetiapine, and clozapine, have shown to increase prolactin level, this effect is minimal and short-lived. These varying effects can be attributed to the duration of receptor binding. Atypical antipsychotics tend to dissociate from D2 receptors rapidly, therefore having a transient dopamine antagonistic effect. This in turn leads to a smaller rise in plasma prolactin. Despite being an atypical antipsychotic, Risperidone, tends to cause a higher increase in prolactin due to a stronger and more prolonged blockade on dopamine receptors (Besnard et al., 2014).

Risperidone is one of the most commonly used antipsychotics, due to its safety and efficacy in reducing psychotic symptoms. However, the side effects of Risperidone are the most common cause of non-compliance with therapy, resulting in worsening of psychiatric symptoms and hospitalization. Symptoms associated with hyperprolactinaemia may have a significantly negative effect on quality of life (Stojkovic, Radmanovic et al., 2022).

Regular serum prolactin monitoring is recommended in patients taking antipsychotics which are particularly associated with hyperprolactinaemia, i.e. Risperidone, as well as Amisulpiride, Sulpiride, Paliperidone and first-generation antipsychotics. Patients taking Asenapine, Aripiprazole, Clozapine, Olanzapine and Quetiapine do not require regular monitoring but serum prolactin levels are measured if the patient develops symptoms.

Prolactin-elevating drugs should be avoided in patients under the age of 25 (i.e. before peak bone mass), especially females; and in patients with osteoporosis and a history of hormone-dependent breast cancer.

2 Aims and Objectives

The purpose of this audit is to assess current practices at Mount Carmel Hospital (MCH) with regards to serum prolactin monitoring in patients taking Risperidone when compared to Taylor et al. (2021). This audit takes into account all acute admissions between June and December 2021. The following parameters were considered in this audit:

- Prolactin levels checked during admission in patients previously on Risperidone.
- Prolactin levels checked in the preceding six months if no prolactin level was checked during admission.
- Appropriate action taken in cases where the serum Prolactin was noted to be high.

3 Standard used

Clinical practices at Mount Carmel Hospital were compared to the Taylor et al. (2021). These guidelines state that serum Prolactin levels should be checked:

- At baseline (prior to commencing antipsychotic),
- then at 6 months,
- then yearly.

Patients should be assessed for symptoms related to hyperprolactinaemia after being started on a high risk antipsychotic, such as Risperidone.

If the serum prolactin is noted to be above normal range, the following action is recommended:

- Assess for symptoms of hyperprolactinaemia.
- MRI Brain if levels over 2500 mIU/L.
- **Symptomatic hyperprolactinaemia**: Change antipsychotic to one with a lesser effect on serum prolactin. If this is not possible, add adjunctive Aripiprazole.
- **Asymptomatic hyperprolactinaemia**: Discuss risks of chronically raised prolactin levels, i.e. increased risk of osteoporosis and breast cancer. Consider continuing current treatment with annual monitoring for complications. If this is not possible, change antipsychotic to one with a lesser effect on serum prolactin. If this is not possible, add adjunctive Aripiprazole.
- If the above courses of action are not successful, consider adding a dopamine agonist, such as Bromocriptine, or metformin.

4 Methodology

The audit was based on patients acutely admitted between June and December 2021. Patient data was obtained from the acute admissions list, as well as, electronic case summaries (ECS), physical case files and iSOFT results. Ethical clearance was obtained prior to acquiring patient data, and the approval of the chairman of Psychiatry in Malta was also obtained.

The following information was collected from the aforementioned sources:

- Prolactin levels checked during admission in patients previously on Risperidone.
- Prolactin levels checked in the preceding six months if no prolactin level was checked during admission.
- Appropriate action taken in cases where the serum Prolactin was noted to be high.

The medical files of patients with hyperprolactinaemia were obtained and analyzed for any clinical action taken following recognition of the elevated prolactin level. The

data was analyzed and compared to the above-mentioned guidelines.

5 Results

A total of 477 patient records were analyzed; all patients were listed on the acute admissions list between June and December 2021.

RESULTS SUMMARY	
Total Patients: 477	
On Risperidone: 145	
Prolactin Level Taken	
Y	N
15	130
Results	
Elevated	NORMAL
5	10
Appropriate Action Taken	
Y	N
3	2

Table 1: Summary of results.

145 patients were noted to be on Risperidone during the acute admission, amounting to 30.40% of the patient sample.

40 patients out of the total had a serum prolactin checked during the admission; 14 of these were taking Risperidone. Therefore, only 9.66% of patients taking Risperidone had a prolactin level recorded during admission.

Two other patients had a serum prolactin checked in the 6 months prior to the admission, one of whom was noted to be taking Risperidone. This amounts to 15 patients out of 145 who fit into the monitoring guidelines described above, i.e. 10.34%.

18 patients had an elevated serum prolactin level and 5 of these were taking Risperidone. This means that out of all prolactin levels taken in patients on Risperidone, 35.71% had hyperprolactinaemia.

Out of these 18 individuals, the high serum prolactin level was acknowledged in the medical notes in 7 instances and some form of clinical action was taken in all of these patients.

6 Discussion

A total of 477 patient records were analyzed in this audit, taking into account all acute admissions to MCH between June and December 2021. Initially, there were around 530 admissions recorded in this time frame, however some patient data was discarded as the I.D. card numbers did not match the patient details in the acute admissions list and thus, the data could not be collected from iSOFT and ECS.

30.40% of all patients were taking Risperidone, as confirmed by the patients' discharge letters for the admission being studied. Thus, this audit focused on the monitoring of serum prolactin levels of all patients taking Risperidone, rather than whether baseline levels were being checked in patients being started on Risperidone during the admission. This could be an area of possible future audit as baseline prolactin levels are essential in future monitoring and to distinguish between causes of hyperprolactinaemia.

Out of 477 patients, 40 patients had a serum prolactin checked during the admission in question. Only 14 of these patients were prescribed Risperidone. Therefore, 9.66% of the patients taking Risperidone had a serum prolactin level checked during the admission. This result was increased to 10.34% when taking into consideration another two patients who had serum levels checked in the 6 months prior to the admission, thus deeming another serum prolactin level unnecessary according to guidelines. This result showcases a very poor level of monitoring for hyperprolactinaemia in these patients and highlights the need for improvement in this regard.

Out of the 40 patients who had a serum prolactin level checked, 45% had an elevated result. Five of these were taking Risperidone, therefore 35.71% of prolactin results were elevated in patients taking Risperidone. These results are significant in that they highlight the importance of serum prolactin monitoring in all patients on neuroleptic treatment. Despite being an atypical antipsychotic, Risperidone, tends to cause a higher increase in prolactin due to a stronger and more prolonged blockade on dopamine receptors (Aboraya, Fullen et al., 2004). Furthermore, it poorly penetrates the blood-brain barrier, thus having a greater presence at the pituitary gland (Tewksbury & Olander, 2016).

3 out of the 5 patients who had confirmed hyperprolactinaemia on Risperidone in this audit were noted to be on long-acting Risperidone intramuscular depot of doses ranging from 25 to 50mg every 2 weeks. The other two patients were taking a nocte dose of oral treatment; 0.5mg and 2mg respectively. Although a dose-dependent relationship of Risperidone and serum prolactin can be observed, a study by Kinon, Gilmore et al. (2003) showed that even at a low-dose of around 2 mg daily, the serum

prolactin level begins to rise, reaching the upper-limit of normal range.

There were 13 other patients noted to have an elevated serum prolactin whilst not being prescribed Risperidone. The treatment prescribed to these patients was not documented as it was beyond the scope of this audit. However, it is known that hyperprolactinaemia can be induced by other neuroleptic treatment, especially first-generation antipsychotics. Other drug classes that induce sustained hyperprolactinaemia include (La Torre & Faslorni, 2007):

- Antidepressants;
  Tricyclics, ex. Clomipramine, Amitriptyline.
  SSRIs, ex. Fluoxetine, Sertraline
  MAOIs.
- Prokinetics, ex. Metoclopramide.
- Antihypertensive, ex. Verapamil, alpha-methyldopa.
- Opiates, ex. Morphine.
- H2 Antagonists, ex. Ranitidine.
- Chemotherapy.

The medical records of patients with elevated prolactin levels were obtained and the admission notes were reviewed, checking for recognition of hyperprolactinaemia and recording any related clinical action that was taken. Raised prolactin levels were acknowledged in the medical notes in 7 out of 18 cases. The most common action taken was a dose reduction or change in antipsychotic choice. MRI of the pituitary gland was booked in 2 cases. Repeat prolactin levels were planned by the caring teams for all acknowledged cases, however, the plan was lost to follow-up in 5 out of 7 patients.

The above results are in keeping with the established importance of serum prolactin monitoring in these patients. Prolonged hyperprolactinaemia may have serious implications on patient's physical health, namely through distressing sexual side effects, osteoporosis and the resultant increased risk of fractures, as well as the risk of developing breast cancer.

For this reason, the poor results displayed by this audit are concerning and increased awareness of guidelines amongst clinical staff is essential. Furthermore, any acknowledgement of deranged prolactin levels must be documented in the patient's medical notes and any plans to act on the elevated level must be followed through by the caring team.

7 Conclusion

There is inadequate monitoring of serum prolactin levels in patients prescribed Risperidone at MCH. Increased awareness of Risperidone-induced hyperprolactinemia and associated guidelines are required to improve clinical practice.

8 Recommendations

- To increase awareness of serum prolactin monitoring guidelines amongst all medical and nursing staff at MCH.
- To create a simple flow-chart outlining the appropriate serum prolactin monitoring guidelines and distribute this to MCH wards.

References

Aboraya, A., Fullen, J., et al. (2004). Hyperprolactinaemia associated with risperidone. *Psychiatry (Edgmont)*, *1*(3), 29–31.

Besnard, I., Auclair, V., Callery, G., Gabriel-Bordenave, C., & Roberge, C. (2014). Antipsychotic-drug-induced hyperprolactinaemia: Physiopathology, clinical features and guidance. *Encephale*, *40*(1), 86–94.

Kinon, B., Gilmore, J., et al. (2003). Prevalence of hyperprolactinemia in schizophrenic patients treated with conventional antipsychotic medications or risperidone. *Psychoneuroendocrinology*, *28*(2), 55–68.

La Torre, D., & Faslorni, A. (2007). Pharmacological causes of hyperprolactinaemia. *Ther Clin Risk Manag*, *3*(5), 929–951.

Stojkovic, M., Radmanovic, B., et al. (2022). Risperidone induced hyperprolactinaemia: From basics to clinical studies. *Front. Psychiatry*.

Taylor, D. M., Barnes, T. R. E., & Young, A. H. (2021). *Maudsley prescribing guidelines in psychiatry* (14th Edition).

Tewksbury, A., & Olander, A. (2016). Management of antipsychotic-induced hyperprolactinemia. *Ment Health ClinJul; 6*(4), 185–190.