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Treatment of antipsychotic-induced galactorrhoea

Prolactin is a hormone which plays an important role in lactation, gonadal function, reproductive and parental behavior. It affects angiogenesis, osmoregulation and regulation of the immune system. Hyperprolactinaemia can be physiological, pathological or iatrogenically induced (3). Many of drugs can cause increasing of prolactin's level, among other things neuroleptics. Galactorrhoea is one of clinical consequences of hyperprolactinaemia.

The aim of this paper is a short review of the literature on therapeutic research into the cause of antipsychotic-induced galactorrhoea.

Antipsychotic agents are dopamine receptor blockers. Dopamine is the predominant physiological inhibitory factor and blockade of endogenous dopamine receptors by neuroleptics, causes prolactin secretion to incsease (5). Hyperprolactinaemia can develop gynaecomastia in men and galactorrhoea in both sexes. Galactorrhoea is much more common in women than men (1). In women treated with conventional antipsychotic agents spontaneous galactorrhoea of varying severity has been reported to have prevalence of 10-57% (5). Potential risk factors for developing galactorrhoea include depot antipsychotic, traditional antipsychotic treatment, especially long term treatment, prior pregnancy, oral contraceptives, history of antipsychotic-induced galactorrhoea (4).

However, every patient should be considered individually, in patients taking medications known to cause galactorrhoea, it is critical to establish that the medication is the cause. It is known that conventional neuroleptic than atypical antipsychotic agents more often develop hyperprolactinaemia. Although risperidone causes elevations in prolactin level even higher than those caused by the typical antipsychotics. In contrast, clozapine, olanzapine, quetiapine much less commonly elevate prolactin levels (5). Many others drugs affect prolactin levels, such as antidepressants, antihypertensive or gastrointestinal medications. It is important to remember about it because very often psychiatric patients take several drugs and its side effects are summed. Interestingly, lithium carbonate appears to decrease prolactin levels by about 40% (5).

The first step is prolactin level measurement. Mild-to-moderate elevations should be checked with a second sample to exclude physiological surges above the laboratory's upper reference value. Antipsychotics usually produce moderate prolactin elevation of up to six times the upper limit of reference range. The likelihood of antipsychotic-induced galactorrhoea is high when the onset symptom appears shortly after starting the treatment or increasing the dose. Galactorrhoea usually occurs about 20 days (range 7–75 days) after commencement of antipsychotic treatment (1).

Before starting treatment it is necessary to rule out other reasons of this problem, pituitary tumor, hypothyroidism, end-stage renal disease and hepatic failure first of all. In these cases, suggested by the clinical history and examination, structural brain imaging (MRI or CT) and laboratory tests (levels of thyroid hormone, thyroid-stimulating hormone, serum electrolytes, blood urea nitrogen, creatinine

and hepatic transaminases) are helpful (1). The simplest approach is to have the patient discontinue the medications and measurement of prolactinaemia again. Baseline prolactin levels may take up to 3 weeks to return to the normal range, depending on the half-life of the drug and its metabolites as well as storage in fatty tissues. In the case of depot medication may take as long as 6 months (2). But most of psychiatric patients need continuation of antipsychotic treatment. Part of strategy is a reduction in dose but its effectiveness is unpredictable and it carries the risk of precipitating an exacerbation or relapse of psychotic symptoms. Switching the patient to a prolactin-sparing antipsychotic (i.e. olanzapine, quetiapine or clozapine) is another commendable option, although there is also a risk of relapse (1, 4). Patients receiving a traditional antipsychotic who cannot change to a novel agent (depot antipsychotics because of noncompliance), may be candidates for a prolactin-lowering agent such as bromocriptine–dopamine receptor agonist. Bromocriptine is administered twice daily at a starting dosage of 1.25 mg twice a day given with meals. The dosage may gradually be increased to 15 mg/day in divided doses to normalize prolactin levels. The patient should be monitored with attention for exacerbation of psychosis and for other clinical adverse effects associated with bromocriptine such as nausea, emesis, rhinitis, fatigue and postural hypotension. Before initiating bromocriptine therapy, the patient should be maintained on the lowest effective antipsychotic dose to minimize prolactin effects as much as possible. Amantadine lowers prolactin level too. The most often applied doses are 100–300 mg/day. The most common adverse effects during taking include nausea, dizziness or lightheadedness and insomnia. Anticholinergic adverse effects may also occur. In patient with renal failure the dose must be reduced. Exacerbation of anxiety, depression, agitation, confusions and hallucinations have also been reported. Cabergoline is a selective and long-lasting dopamine agonist which has recently been approved by the FDA. Results of the study are encouraging (4).

CONCLUSIONS

Hyperprolactinaemic symptoms in psychiatric patients treated with antipsychotic drugs are poorly researched. Secondary after-effects to hypreprolactinaemia should be taken into account, such as increased risk of osteoporosis, cardiovascular disease. So hyperprolactinaemia should be the focus of interest, particularly given the introduction of prolactin-sparing antipsychotics and increasing knowledge about its possible long-term adverse effects.

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SUMMARY

Antipsychotic drugs can increase prolactin level. Galactorrhoea is a clinical consequence of this. Prevalence in women treated with conventional antipsychotic agents is estimated at 10–57%. Treatment strategies should be considered individually and include reduction of doses, switching to an alternative medication, which does not cause hyperprolactinaemia, or cautiously adding a dopamine receptors agonist.

Leczenie mlekotoku w przebiegu kuracji neuroleptykami

Większość neuroleptyków wpływa na poziom prolaktyny. Kliniczną konsekwencją podwyższonego poziomu prolaktyny jest m. in. mlekotok. Rozpowszechnienie tego zjawiska wśród kobiet leczonych neuroleptykami starej generacji jest oceniane na 10–57%. Strategie postępowania powinny być rozważane indywidualnie i obejmują następujące możliwości: redukcję dawki dotychczas stosowanego leku, zamianę na inny, niewpływający w tak dużym stopniu na poziom prolaktyny, bądź ostatecznie dołączenie agonisty receptorów dopaminy.