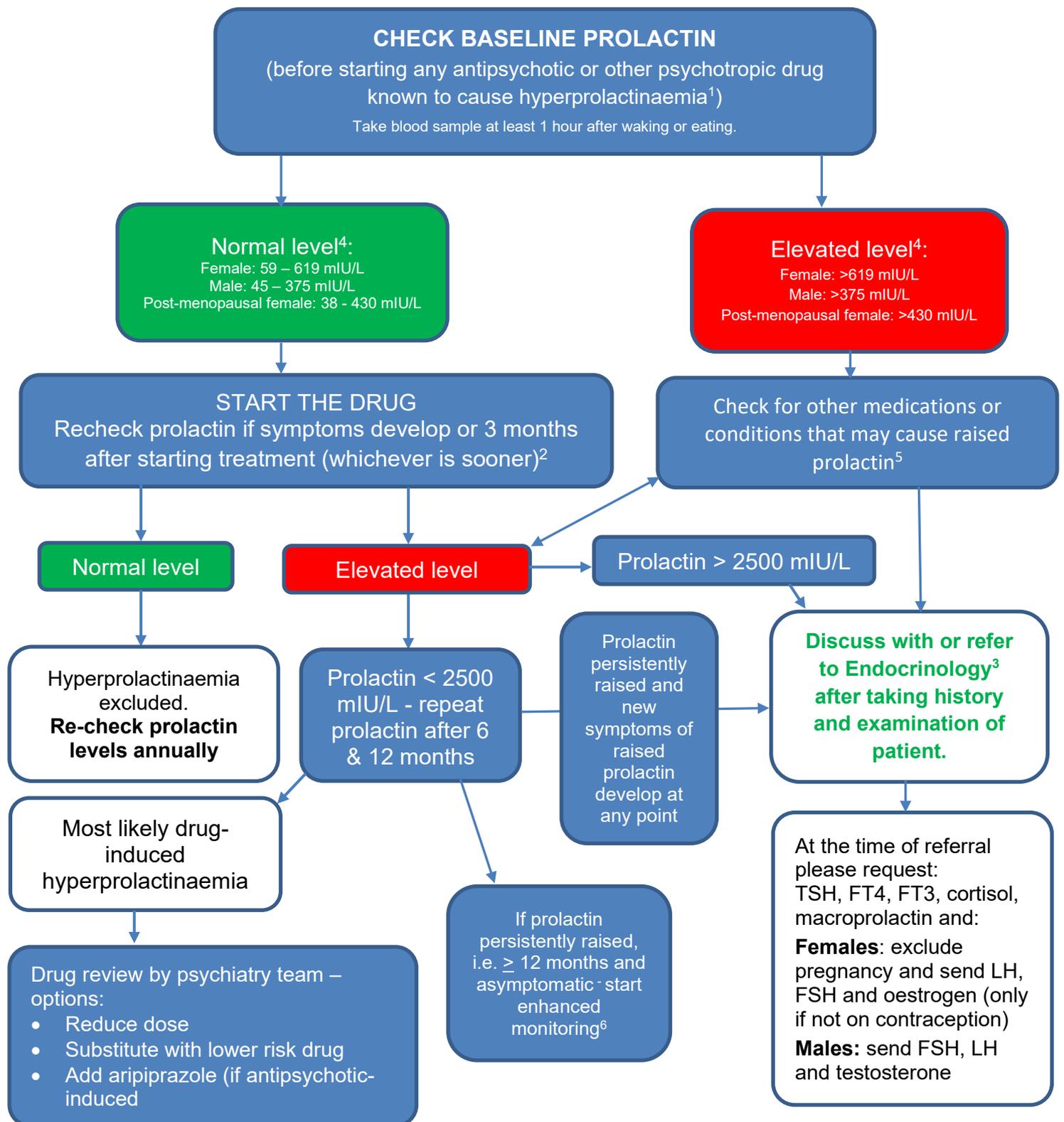


GUIDANCE ON MANAGING THE EFFECTS OF PSYCHOTROPIC DRUGS ON PROLACTIN (IN ADULTS)



1. Avoid drugs known to cause hyperprolactinaemia in patients <25 years (who have not attained peak bone mass), women planning pregnancy, and patients with history of breast cancer, prolactinoma or osteoporosis.
2. Symptoms in premenopausal females: infertility, oligomenorrhoea, or amenorrhoea and galactorrhoea. Symptoms in males: reduced libido, erectile dysfunction, infertility, gynecomastia or galactorrhoea.
3. Symptoms of mass effect: headaches and/or visual impairment (loss of peripheral vision, reduced visual acuity, double vision).
4. 95% of female patients will have a prolactin level of <500 mIU/L and 95% of male patients will have a prolactin level of <325 mIU/L. Levels up to 700 mIU/L for both female and male patients are rarely pathological and may be due to stress of venepuncture.
5. See table 2 in detailed guidance below.
6. See Enhanced Monitoring section in detailed guidance below

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MEDICATIONS CAUSING HYPERPROLACTINAEMIA

Medication	Frequency of prolactin elevation*
First generation antipsychotics	
Chlorpromazine	+++
Flupentixol	+++
Fluphenazine	+++
Haloperidol	+++
Sulpiride	+++
Trifluoperazine	+++
Zuclopenthixol	+++
Second generation antipsychotics	
Aripiprazole	-
Amisulpride	+++
Asenapine	-
Cariprazine	-
Clozapine	-
Lurasidone	+
Olanzapine	+
Paliperidone	+++
Quetiapine	-
Risperidone	+++
Antidepressants	
Agomelatine	-
Amitriptyline	+
Clomipramine	+++
Nortriptyline	+/-
MAOIs	+/-
SSRIs (es/citalopram, fluoxetine, fluvoxamine, sertraline)	+
Others (bupropion, mirtazapine, trazodone)	+/-
Venlafaxine	++
Vortioxetine	-
Antiemetic and gastrointestinal	
Metoclopramide	+++
Domperidone	+++
Prochlorperazine	+
Antihypertensives	
Verapamil	+
Methyldopa	++
Most antihypertensives including calcium channel blockers	+/-
Opioid analgesics	
Methadone, morphine, others	Transient increase for several hours following dose

+++ = high; ++ = moderate; + = low; - = very low / case reports only. Effect may be dose dependent.

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Introduction

Sufficient evidence has emerged that both typical and atypical antipsychotic medications are associated with hyperprolactinaemia. The degree to which they are likely to raise levels and by how much varies within the groups to some extent. However, there is also evidence that antidepressants and other commonly prescribed medications can have the same effects. Hyperprolactinaemia commonly causes menstrual problems in females and sexual problems in males.

In the past treatment was recommended only in symptomatic patients, but over the past few years it has become clear that persistent asymptomatic hyperprolactinaemia can be associated with long term physical morbidities such as osteoporosis, breast cancer etc. Therefore, it is essential that hyperprolactinaemia, if detected, irrespective of its clinical manifestation, should be taken seriously and current guidance has been updated to reflect this¹⁸.

Prolactin

Prolactin is secreted by the pituitary gland and is under the inhibitory control of dopamine (in most cases). Other factors also influence prolactin secretions, such as serotonin, TSH, oestrogen etc. Prolactin is released in a pulsatile manner; its level reaches peak at night and troughs in the afternoon. Prolactin levels increase temporarily soon after food intake, exercise, sex and after stressful events including venepuncture. Prolactin levels also increase at the end of pregnancy and after delivery.

Normal range

Female: 59 – 619 mIU/L

Male: 45 – 375 mIU/L

Post-menopausal female: 38 - 430 mIU/L

Reference ranges are set differently by different organisations and laboratories.

Raised prolactin (hyperprolactinaemia)

The signs and symptoms of hyperprolactinaemia are not entirely correlated with serum levels of prolactin. Even mild increases in serum prolactin levels can be associated with severe symptoms and vice versa. Women are more likely to suffer from symptoms associated with hyperprolactinaemia including sexual adverse effects. Hyperprolactinaemia is often missed, as it can be asymptomatic, or patients may hesitate to disclose the symptoms unless specifically asked about these adverse effects. Regular screening of these symptoms is important, as these could also lead to noncompliance with the treatment.

Table 1: Symptoms associated with hyperprolactinaemia (adapted from Peveler 2008)¹

Degree of raised prolactin	Reference range	Symptomatology
Mild	<1000 mIU/L	Decreased libido, infertility
Moderate	1000- 2000 mIU/L	Oligomenorrhoea
Severe	>2000 mIU/L	Amenorrhoea, hypogonadism, gynaecomastia & galactorrhoea

Long-term effects of hyperprolactinaemia

Hyperprolactinaemia is associated with many long-term consequences, but the most clinically significant effects are osteoporosis and increased risks of breast cancer (especially

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in those with previous history of breast cancer or family history of the disease). Because of these factors, it is important that even in clinically asymptomatic patients, we should try to restore/carefully monitor prolactin levels.

Osteoporosis

Raised prolactin levels result in suppression of gonadal hormones, oestrogen and testosterone. These hormones play an important role in preserving bone mass. There are some suggestions that prolactin might also have a direct effect on osteoblasts (cells that form bone tissue)². The reduction in bone mass (osteopenia and osteoporosis) result in reduced strength and increased fragility of bones, which, in turn, increases risk of fracture (particularly at spine, hip and wrist). Prolactin elevation is particularly detrimental in men and women who have not reached their peak bone mass (i.e. under the age of 25 years), but can have effect well into adulthood and up to the age of about 60 years. Decreased bone marrow density occurs in women with hyperprolactinaemia and amenorrhoea, but not in women with hyperprolactinaemia with normal gonadal function^{3,4}, so it is particularly important to ask patients about possible symptoms. Restoration of prolactin levels leads to partial reversal of bone mass, but there can be other factors associated with osteoporosis that may be in play (age, poor diet, decreased mobility and weight bearing activities, smoking, and alcohol intake and reduced sun light exposure).

Restoration of prolactin by changing the antipsychotic medication or treatment with gonadal steroid hormone has shown to improve bone density⁵. Other treatment alternatives are Vitamin D, calcium supplement and bisphosphonates. In established cases of osteoporosis, it would also be advisable to avoid the prolactin-increasing antipsychotic drugs.

Breast cancer

In the past no causal link was established between use of antipsychotic drugs and risk of breast cancer. However, many genes that are activated by the prolactin receptor are associated with tumorigenesis and cancer cell proliferation⁶. More recent evidence has come to light that prolactin-increasing antipsychotic use over 5 or more years is associated with an increased risk of breast cancer⁷.

In clinical practice it is, therefore, prudent to prefer prolactin-sparing antipsychotic medications in patients who have either suffered from breast cancer or are at a high risk of breast cancer⁶.

Causes of hyperprolactinaemia

Stress response

Acute stress, including venepuncture, can lead to transient hyperprolactinaemia. It may result in two-to-three-fold rises in prolactin level; however it reverts back to the baseline within few hours.

Pituitary adenoma

This is one of the most common causes of hyperprolactinaemia. Prolactin secreting tumours are benign neoplasm that accounts for 40% of all pituitary tumours. Over 90% are small, intrasellar tumours that rarely increase in size. Prevalence of asymptomatic pituitary tumour in the general public is very high (14.4% in autopsy studies and 22.5% in radiological studies^{8, 9}). When endocrinologically active, they can be associated with very high levels of prolactin and related symptoms and can also lead to other symptoms, such as headache, visual field defects and diplopia; mainly because of the pressure effects on the surrounding structures. Pituitary adenoma is detected on an MRI scan, but small adenoma still can be missed and might present as idiopathic hyperprolactinaemia. The treatment involves use of dopaminergic drugs (bromocriptine and cabergoline) and/or surgical resection.

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Table 2: Common causes of Hyperprolactinaemia

Physiological	Medications associated with hyperprolactinaemia	Other conditions
Stress	Antipsychotic drugs	Pituitary adenoma
Physical exercise	Metoclopramide/domperidone	Hypothyroidism
Sex or breast stimulation/examination	Oestrogen	Chronic kidney disease
Food intake (high protein)	Verapamil	Polycystic ovary disease
Pregnancy	Cimetidine	Cirrhosis
Lactation	Omeprazole	Epileptic seizure
Venepuncture	Opiates	Chest wall injury/irritation
	SSRIs	Disease of the hypothalamus
	Cannabis products	
	Biotin (Vitamin B7 supplement) ²⁹	

Antidepressants associated with hyperprolactinaemia

Antidepressant drugs, especially SSRIs, can be associated with hyperprolactinaemia. However, the increase in prolactin level is generally very little with minimum clinical significance⁹. There are case reports suggestive of hyperprolactinaemia due to sertraline, paroxetine, citalopram, fluoxetine, tricyclic antidepressant drugs (amitriptyline, clomipramine etc.) and MAO inhibitors. As this is not a very commonly encountered adverse effect, routine serum prolactin levels are not recommended. Nevertheless, if a patient presents with signs and symptoms suggestive of hyperprolactinaemia then blood tests should be carried out to confirm the diagnosis. Change of medication will usually rectify this problem, but as in psychosis there is risk of relapse and response of the disorder being treated to the new medication may vary

Antipsychotics associated with hyperprolactinaemia

Almost all antipsychotic drugs can increase prolactin levels. Differential effect of antipsychotic medications is thought to be due to the interplay of different factors namely, antagonistic effect on D2 receptors, rate of dissociation from D2 receptor and concentration in brain (depending on the permeability through blood brain barrier)¹⁰. Furthermore, it has been suggested that the degree of elevation of prolactin correlated with D2 receptor occupancy in excess of 50%; which is less than the D2 occupancy postulated to be required for antipsychotic effect¹¹.

Cross-sectional studies have indicated that the prevalence of hyperprolactinaemia ranges from 42–93% in women and 18–72% in men. One naturalistic study assessed the prevalence of hyperprolactinaemia in a Community Mental Health Team. It assessed prolactin levels of 194 schizophrenia and bipolar patients who were taking antipsychotic medications. The population did not exhibit any signs or symptoms suggestive of hyperprolactinaemia. The study reported that hyperprolactinaemia was more common in females than males (52% vs. 26%). Female patients also suffered more from significantly raised prolactin levels than males. Prolactin levels of 1000 mIU/L were reported in 25% of females and 5% of males and levels of 2000 mIU/L were reported in 13% of females and 2 % of males.

Most patients on risperidone and amisulpride suffered from hyperprolactinaemia¹².

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Medication	Percentage elevation	Estimated range of prolactin elevation
Typical antipsychotic drugs	34-75% (++)	600- 1000 mIU/L
Risperidone/Paliperidone	45-87% (++++)	800 to >2000 mIU/L
Amisulpride	40-100%(++++)	800 to >2000 mIU/L
Olanzapine	30-47% (+, more frequent at higher dosages)	500-700 mIU/L
Quetiapine	<5% (+/--sometime transient, at higher dosages)	Minimal
Clozapine	<5% (+/-)	Minimal
Asenapine	<5% (?/-)	Minimal
Aripiprazole	<1% (-/↓)	May lower prolactin

Prolactin levels increase within a few hours of initiation of antipsychotic medications. Levels peak within 1-2 months then gradually the level decreases¹³. Some reports suggest that tolerance develops and prolactin level decreases, but in most cases it remains above the normal range. Prolactin level generally normalises within 48-96 hours of discontinuation of an antipsychotic drug.

Drugs like risperidone and amisulpride can be associated with much higher levels of prolactin and studies have reported prolactin levels up to 6000 mIU/L due to antipsychotic medications¹. These drugs can also be associated with microadenoma, which can disappear after withdrawing of the offending agent or addition of aripiprazole¹⁴.

Even a single dose of antipsychotic medication can increase prolactin levels. Because of these factors, it becomes important to get a baseline prolactin level.

Lowered prolactin (hypoprolactinaemia)

Low prolactin levels (hypoprolactinemia) seem to be much less common and accurate data on its occurrence and causes is less detailed. However, it can also lead to some serious immediate and long-term effects.

Levels that define hypoprolactinaemia below 63 mIU/L in women, and 106 mIU/L in men

In women low prolactin has a direct effect on ovarian function in terms of suppression of follicular development and inhibited corpus luteum formation. This can, in turn, affect fertility and cause irregular menstrual cycles. In women, it can also be a cause of lactation failure after childbirth.

In men, metabolic syndrome is a prominent symptom. Metabolic syndrome (MetS) is a clustering of at least three of the following five medical conditions:

- abdominal obesity
- high blood pressure
- high blood sugar
- high serum triglycerides
- low serum high-density lipoprotein (HDL)

Other common symptoms in males are anxiety, erectile dysfunction, and premature ejaculation. Unseen effects can be on fertility with low concentration of sperm in semen (oligozoospermia), reduced sperm motility (asthenospermia), hypofunction of seminal vesicles, and hypoandrogenism.

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Long-term effects of hypoprolactinaemia

In both men and women fertility issues and sexual dysfunctions are the main effect in the long term²³.

In men metabolic syndrome is associated with increased risk of developing cardiovascular disease and type 2 diabetes.

In a handful of studies published in the 1980s' those with low serum prolactin concentration during maintenance neuroleptic treatment relapsed earlier than those with higher serum prolactin^{24, 25}.

Causes of hypoprolactinaemia

Hypoprolactinemia can result from autoimmune disease, hypopituitarism, growth hormone deficiency, hypothyroidism, excessive dopamine action in the tuberoinfundibular pathway and/or the anterior pituitary, and ingestion of drugs that activate the D2 receptor, such as direct D2 receptor agonists like bromocriptine and pergolide, and indirect D2 receptor activators like amphetamines and aripiprazole (through the induction of dopamine release). Psychiatric drugs most likely to cause low prolactin levels are aripiprazole and ADHD stimulants, though other NRI action medications (reboxetine, atomoxetine, venlafaxine and duloxetine) may also theoretically increase dopamine production as may bupropion, a NDRI, which in turn could lower prolactin.

Conflicting evidence exists with some studies reporting no changes in prolactin levels with these medications and others reporting prolactin reductions or no change²⁷.

Currently there is no robust evidence for monitoring prolactin in patients on ADHD medications.

Monitoring of prolactin levels

NICE Guidelines (Schizophrenia and Bipolar disorder, 2014) have suggested baseline prolactin levels with antipsychotics, but these guidelines have not specified any follow up monitoring of prolactin levels in asymptomatic patients^{16, 17}. However, updated NICE Clinical Knowledge Summaries in 2021 state that prolactin should also be monitored 6 months after starting treatment, then every 12 months, and prescribers and staff monitoring medication should also ask about symptoms of raised prolactin (these include low libido, sexual dysfunction, menstrual abnormalities, gynaecomastia, and galactorrhoea)¹⁸.

Monitoring is not required for aripiprazole, clozapine, quetiapine, or olanzapine (less than 20 mg daily). However, cases of raised prolactin have been reported with some of these medications¹⁸.

Ideally baseline test should be a morning fasting sample. Excessive stress due to venepuncture should be avoided. The morning dose of medication should be omitted before the test.

Based on the fact that patients stable for 3 months could be stepped down to primary care services we have recommended retesting at 3 months, rather than the CKS guidance of 6 months, and then every 12 months once stabilised.

In the absence of a baseline prolactin level, it becomes difficult to attribute the raised prolactin to the psychotropic drug. In a patient with suspected antipsychotic induced hyperprolactinaemia, where baseline prolactin level is not available, consideration should be given to stop the drug for three days and repeating the prolactin levels. If prolactin levels decrease significantly or normalisation occurs, then it would confirm the suspicion.

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In case of mild to moderate increase of prolactin level or if in doubt then the blood test should be repeated in the ideal condition. A single blood test showing a very high level of prolactin (>2500 mIU/L) or a high level in a symptomatic patient is usually sufficient to confirm hyperprolactinaemia.

Management of hyperprolactinaemia

Raised prolactin levels should not always be assumed to be secondary to psychotropic drugs, unless there is clear evidence of temporal relationship and baseline level was normal. In absence of a baseline level, other factors such as prevalence of hyperprolactinaemia with the particular drug, temporal association of symptom emergence with the initiation of the drug and severity of hyperprolactinaemia (<2500 mIU/L) might suggest a psychotropic induced hyperprolactinaemia. Though other common causes of hyperprolactinaemia such as hypothyroidism, pregnancy, chronic kidney disease and pituitary adenoma should always be considered and excluded.

The management of hyperprolactinaemia should be aimed at normalisation of prolactin level, restoration of gonadal dysfunctions (menstruation and sexual problems) and lastly to prevent osteopenia/osteoporosis and increased risk of breast cancer.

If a patient presents with moderate to severe hyperprolactinaemia or symptomatic hyperprolactinaemia (irrespective of serum level) or low levels of gonadal hormones then serious consideration should be given to actively manage the hyperprolactinaemia.

Hyperprolactinaemia can be managed by reducing the dose of causative drug, switching to a prolactin sparing alternative medication, adding aripiprazole (in the case of antipsychotic-induced hyperprolactinaemia) or a dopamine agonist (bromocriptine or cabergoline). The management strategy will depend on the distress associated with hyperprolactinaemia symptoms, benefit from the causative drug and the risk of relapse should the dose of causative drug be substantially reduced or stopped.

Reduction of dose of antipsychotic medication

As there is some evidence that raised prolactin levels might be a dose related adverse effect of antipsychotic medications, it makes clinical sense that reductions of antipsychotic dosages should be tried initially. However, one has to be aware of the risk of relapse, especially in patients with psychotic illnesses. One study has indicated that lower occupancy of D2 receptor is required for elevation of prolactin elevation than the D2 receptor occupancy required for antipsychotic response; hence reduction of dose of antipsychotic drug might not be an effective strategy in psychotic patients¹⁹.

One study compared reduction of risperidone dose with change to another antipsychotic medication in patients who suffered from risperidone induced amenorrhoea. It was reported that switching antipsychotic medication was more effective strategy. Most patients, where the dose of risperidone was reduced, either did not experience any improvement in the adverse effects or relapsed²⁰.

Switching to a prolactin sparing antipsychotic medication (aripiprazole, quetiapine)

Antipsychotics, especially atypical antipsychotic drugs, vary significantly regarding their propensity to increase prolactin levels. Antipsychotic induced hyperprolactinaemia can also be managed by switching to a prolactin sparing antipsychotic drug. Most of the studies report significant improvement of symptoms along with normalisation of prolactin levels within few weeks. However, it is difficult to predict antipsychotic response to the prolactin sparing antipsychotic drugs. Therefore, this option should be chosen only after careful risks and benefits consideration. This might not be a suitable option for a patient who has been

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resistant to several antipsychotic drugs and have done exceptionally well on the current antipsychotic medication.

Addition of aripiprazole

Aripiprazole, due to its partial dopamine agonist effect, usually does not increase prolactin levels. In fact, it reduces prolactin levels in patients who suffer from antipsychotic induced hyperprolactinaemia. Over the past few years, there have been many case reports, case series and a few randomised controlled trials showing its effectiveness in reducing the serum prolactin. It leads to normalisation of prolactin levels in up to 79% of patients, when used as an adjunctive drug in patients, developing antipsychotic induced hyperprolactinaemia²⁰. Low dose of aripiprazole is usually sufficient to normalise prolactin levels. In most cases aripiprazole 5 mg/day will be sufficient; a few patients might require higher dosages. Usually, normalisation of prolactin occurs quite rapidly, if there is no improvement within three months then it is unlikely to be effective. Commonly reported adverse effects are headache, hypersomnia and insomnia. Addition of aripiprazole is not associated with worsening of psychotic illness, neither does it result in significant improvement of psychotic symptoms²¹. Studies up to 26 weeks have not reported any significant adverse effects; however, there are no studies with regards to long-term effect of adjunctive aripiprazole. This approach, however, appears to be less effective with sulpiride/amisulpride.

As most psychiatric prescribers are very familiar with the drug and it has a relatively benign adverse effect profile and more importantly it is unlikely to worsen the psychotic symptoms, it should be preferred over dopaminergic agents. However, aripiprazole is not licensed for treating hyperprolactinaemia and its addition might lead to high dose antipsychotic treatment²⁶.

Addition of dopaminergic drugs by endocrinologist

Bromocriptine & cabergoline are the most commonly used dopaminergic agents to treat hyperprolactinaemia due to pituitary adenoma, but should only be initiated by an endocrinologist. These drugs have been used to treat antipsychotic induced hyperprolactinaemia. The studies have not shown any worsening of psychosis, although psychotic symptoms have been reported when these drugs have been used to treat pituitary adenoma and for other indications. **They should not be initiated by prescribers within TEWV.**

Treatment with oestrogen and testosterone

In patients with long-term hypogonadism and / or osteoporosis, the use of oestrogen in women and testosterone in men can be considered. **They should not be initiated by prescribers within TEWV.**

Referral to endocrinologist

- Serum prolactin level of > 2500 mIU/L
- If associated with symptoms suggestive of mass effect such as headache, visual disturbances etc. (loss of peripheral vision, reduced visual acuity, double vision).
- If the aetiology is not clear and associated with symptoms suggestive of other endocrinal problems.
- If prolactin levels continue to increase and the patient is symptomatic despite interventions.
- Osteoporosis and persistent low levels of gonadal hormones.

Enhanced monitoring

In cases where a solution to raised prolactin cannot be found and changing medication is considered unwise due to the current medication being the only one to gain response then enhanced monitoring can be considered²⁸.

- Bone Mineral Density (BMD) testing every 2 years.

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- More frequent BMD testing may be warranted in certain clinical situations (people with family histories of osteoporosis or bone fractures/breakages at young age).
- The interval between repeat BMD screenings may be longer for patients without major risk factors and who have an initial T-score in the normal range.

If there is variance from normal range (for age and gender) then options would be:

- to change treatment to lower prolactin
- or
- Refer to endocrinologist of evidence of osteoporosis

With regards to prolactin monitoring in people who are transgender, the advice from endocrine society is:

“Though current guidelines do not recommend measuring a prolactin level in transgender males, current guidelines for transgender females do recommend measuring a baseline and annual prolactin level during transition and then every 2 years after that.”³⁰

Management of hypoprolactinaemia

Where a medication is suspected to be lowering prolactin levels and having effect on functioning or producing symptoms, dose reduction should be considered or exchange to a different medication.

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Quick Guide to Hyperprolactinaemia for staff, patients and carers

Information for patients and carers is available on the Choice & Medication website here:

<https://www.choiceandmedication.org/tees-esk-and-wear-valleys/generate/handyfactsheethyperprolactinaemiauk.pdf>

What is prolactin?

Prolactin is a hormone that is best known for helping women to produce milk following childbirth. It also plays an essential role in metabolism (processes that enable life in cells), control of the immune system, and development of the pancreas.

Where is it found and how does it work?

Prolactin is secreted by pituitary gland in the brain where dopamine reduces its production and action. Other factors also influence prolactin secretions, such as serotonin, thyroid hormones, oestrogen etc. Prolactin is released in pulses soon after food intake, exercise, sex and after stressful events including venepuncture and epileptic seizures. Levels also increase after birth and during breastfeeding.

How much prolactin is normal?

There is great debate about what are high levels of prolactin, but normal ranges tend to be:

Female: 59 – 619 mIU/L

Male: 45 – 375 mIU/L

Post-menopausal female: 38 - 430 mIU/L

What is hyperprolactinaemia?

Prolactin levels in the body are raised above normal.

How would I know if I have signs of hyperprolactinaemia?

Women tend to suffer from hyperprolactinaemia more than men (mainly because their hormone systems are different).

Symptoms:

- Loss of libido (interest in sex) and sexual problems (not achieving orgasm, in females sex may become painful because of vaginal dryness, in males problems getting an erection)
- Breast pain/tenderness, development of breast tissue in men
- Breast milk production in men and women who are not pregnant
- In women, periods may disappear altogether or become irregular
- Problems with getting pregnant or in males problems with getting their partner pregnant if trying
- Headaches or eye problems

If any of these symptoms develop; report to a healthcare professional for further investigation

Long term effects of raised prolactin

In the long term raised prolactin levels can lead to an increased risk of osteoporosis (brittle bones) and there is some new evidence, though only a small amount, that it could also increase the risks of breast cancer (so if you have a family history make sure the healthcare professionals know about this).

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Causes of hyperprolactinaemia:

Broadly speaking there are 3 main types of cause for high prolactin levels. These are:

- Changes in your body, e.g. pregnancy, breastfeeding
- Drugs and medicines, e.g. antipsychotics, antidepressants, other medications
- Things wrong with your body, possibly from birth, e.g. diseases of hormone systems within the body, tumours, brain trauma, underactive thyroid, cirrhosis, kidney problems etc.

So why do I have to have prolactin levels monitored?

If you start certain medications for treatment of your mental health, there is a possibility that they could raise your prolactin levels. These medications can be the following types:

Antipsychotics - Most antipsychotic medications, used mainly for treating schizophrenia, bipolar mania and psychotic episodes, can cause raised prolactin levels.

Antidepressants - Some of the newer antidepressants such as fluoxetine, citalopram and paroxetine have been noted to cause raised levels in a minority of people. Older antidepressants such as amitriptyline and clomipramine may also alter levels.

Other medications also may increase prolactin levels such as drugs to reduce blood pressure (verapamil), antiepileptic drugs (phenytoin), drugs used to treat nausea and vertigo (metoclopramide, domperidone) and other drugs such as oestrogens, anaesthetics, cimetidine, ranitidine, opiates, methadone, morphine, heroin, cocaine, marijuana, alcohol etc.

How we will monitor your prolactin levels

We will do a baseline level before you start the medication to see what your normal levels are. Ideally this will be at least one hour after waking or eating.

Prolactin levels will be repeated after 3 months or sooner if symptoms develop and then annually. (Not required for aripiprazole, clozapine, quetiapine, or olanzapine)

If a baseline prolactin level has not been done it is more difficult to see if the drug may be the cause. In this case you team may stop the drug for three days and repeat the prolactin test. If prolactin levels decrease significantly or return to normal range then it would confirm the suspicion that the medication is the cause.

Managing hyperprolactinaemia

It may be obvious that a medication is responsible for high prolactin levels, due to time starting medication and symptom onset. However, your clinician should consider other possible causes such as underactive thyroid, pregnancy, chronic kidney disease and pituitary adenoma (tumour) and exclude these.

The aim of the management will be to get your prolactin levels within the normal range, stop any immediate symptoms and to prevent any long-term problems such as osteoporosis.

If there has been a rise in prolactin levels and you have symptoms, your team may reduce the dose of your medication, or switch to a medication less likely to alter prolactin levels. If this is not possible, because it may affect your mental wellbeing too much, then they may add in another medication that could help reduce the prolactin levels (aripiprazole) or monitor for associated risks e.g. bone scans.

What happens if this does not work?

If there are problems in managing the prolactin levels then your team will refer you to a specialist endocrinologist who will be able to look at the hormone levels in more detail and offer advice on management, perhaps with other medications or through other methods that they commonly use in these departments.

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