Information for Clinicians

Clinical Biochemistry Department

Hyperprolactinaemia - a guide for GPs

Definition
Prolactin > 700 mIU/L on a single sample without excessive venepuncture stress, at any time of day in both males and females is considered clinically significant hyperprolactinaemia and requires further investigation.

Note: The cut off of 700 mIU/L is a clinical action threshold and not a reference range. If a patient has symptoms of hyperprolactinaemia below this cut off, advise discussion with the Duty Biochemist (01225 824050)

<table>
<thead>
<tr>
<th>Prolactin (mIU/L)</th>
<th>Interpretation</th>
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</thead>
<tbody>
<tr>
<td>700 - 2000</td>
<td>Mild hyperprolactinaemia</td>
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<tr>
<td>2000 - 5000</td>
<td>Significant hyperprolactinaemia</td>
</tr>
<tr>
<td>&gt;5000</td>
<td>Severe hyperprolactinaemia</td>
</tr>
</tbody>
</table>

Symptoms of hyperprolactinaemia

In females
- Oligomenorrhoea/amenorrhoea
- Galactorrhoea (when not pregnant or breast feeding)
- Vaginal dryness
- Acne
- Hirsutism

In males
- Erectile dysfunction
- Decreased body and facial hair
- Gynaecomastia

In both sexes
- Low bone density
- Reduction in other pituitary hormone production
- Decreased libido
- Headaches
- Visual disturbances
- Infertility

In children
- Growth failure
- Delayed puberty
Causes of Hyperprolactinaemia

**Factitious causes of hyperprolactinaemia**
Macroprolactin – Biologically inactive immunoglobulin-bound-prolactin (macroprolactin) can cross react in the prolactin assay causing false hyperprolactinaemia. The laboratory will routinely screen for macroprolactin on every first raised (>700 IU/L) prolactin seen in an individual patient. The presence of macroprolactin is not pathological itself; if present, an estimation of bioactive prolactin is reported with interpretation to guide further investigations.

**Physiological causes of hyperprolactinaemia**
- Pregnancy – measurement of prolactin during pregnancy is not routinely indicated or required
- Breastfeeding – measurement of prolactin during breastfeeding is not routinely indicated or required
- Exercise
- Stress (physical or psychological, including venepuncture)
- Sleep
- Post-ictal (within hours of a seizure)
- Neonatal period
- Chest wall surgery or trauma

**Medication induced hyperprolactinaemia** can be associated with the following:
- TRH
- High dose oestrogens
- Antipsychotic drugs: phenothiazines (e.g. chlorpromazine, promazine, thioridazine, sulphuride, fluphenazine, trifluoperazine), haloperidol, flupentixol, risperidone, paliperidone
- Selective serotonin reuptake inhibitors (citalopram, fluoxetine, fluvoxamine, sertraline, paroxetine)
- Antiemetics (metoclopramide, domperidone)
- Cardiovascular drugs (verapamil, reserpine, methyl dopa)
- Opiates, opioids (transient, rare)
- Monoamine oxidase inhibitors
- Cimetidine (intravenous)
- Verapamil
- Liquorice
- Miscellaneous (bezafibrate, omeprazole, trimethoprim, histamine H2 antagonists)
- Tricyclic antidepressants (rare)

**Pathological causes of hyperprolactinaemia**
- Pituitary tumour (prolactin secreting tumour, or non-secreting pituitary tumour that prevents dopamine reaching normal prolactin producing cells)
- Hypothalamic/pituitary stalk lesion
- Neuraxis irradiation
- Spinal cord lesion
- Head injury (e.g. due to disruption of the pituitary stalk)
- Chronic renal failure (reduced prolactin clearance)
- Severe liver disease (disordered hypothalamic regulation)
- Primary hypothyroidism (increased synthesis of TRH)
- PCOS
Investigations and Management in Primary Care

**Prolactin > 700**
Interference from Macroprolactin will be excluded by the laboratory. Check TFTs and exclude pregnancy.

**Macroprolactin Positive**
Hyperprolactinaemia may be spurious due to the presence of macroprolactin. See bioactive prolactin report for interpretation. If bioactive prolactin is raised – other causes for hyperprolactinaemia should be investigated.

**Macroprolactin Negative**

**Physiological Cause Identified**
Exercise – repeat after rested for 2-3 days
Stress – consider cannulated prolactin (with 30 minutes rest after cannulation before drawing blood)
Pregnancy/Lactation – not recommended to routinely measure prolactin

**Review Physiological Causes**

**Review Medications**

**Consider Repeat/Referral if no obvious cause of hyperprolactinaemia**

**Medication Induced Hyperprolactinaemia**

- **Prolactin < 3000**: Hyperprolactinaemia likely due to medications. If symptomatic, discuss with prescribing clinician or endocrinology. Ideally prolactin should not remain elevated as there is a risk of osteoporosis and infertility. Repeat in 6-12 months to monitor.
- **Prolactin > 3000**: Medications can cause hyperprolactinaemia at this level. Advise discussion with prescribing clinician regarding change in medication/dose. If persistently elevated, referral to endocrinology is indicated for further investigations.

**On first occasion:**
- **Prolactin < 2000**: Repeat in 4 weeks avoiding stress (and other physiological causes) at time of venepuncture
- **Prolactin 2000-5000**: Prompt repeat to confirm and referral to endocrinology
- **Prolactin > 5000**: Urgent endocrinology referral indicated.

**On repeat:**
- **Prolactin < 1000**: If symptomatic, increasing prolactin, or unknown cause, refer to endocrinology.
- **Prolactin > 1000**: Review clinical symptoms. If unknown cause, refer to endocrinology.

If prolactin persistently > 1000 other pituitary function tests are indicated.

Further investigations through endocrinology referral may include pituitary MRI, visual field testing and dynamic testing of anterior pituitary function.
Management

The main principle of management of hyperprolactinaemia is to identify and treat the underlying cause if feasible.

The goals of treatment are:
- Relieve symptoms (if present)
- Prevent complications from osteoporosis or pressure effects
- Restore fertility and sexual function

Patients with prolactinomas are managed by Endocrinology.

All prolactin results are clinically reviewed by the Duty Biochemist and interpretative comments appended to results to guide further investigations and when referral is indicated.

Further sources of Information

For further advice regarding hyperprolactinaemia please contact the duty biochemist on 01225 824050 Monday – Friday 9am -5pm.

Reference Sources

Wass et al. Diagnosis and Treatment of Hyperprolactinaemia: An Endocrine society Clinical Practice Guideline The Journal of Clinical Endocrinology & Metabolism; Volume 96:2 2001; 273-288


Sommerfield. Hyperprolactinaemia. J R Coll Physicians Edinb; 2005; 35; 143-147

UpToDate (Accessed 11/06/2018)

Medscape (Accessed 03/09/2021)