All Wales Clinical Biochemistry Audit Group

Clinical Guidance for the Investigation of Hyperprolactinaemia

This is a guideline to aid the investigation of non-physiological increases in prolactin. It has been written in conjunction with the All Wales Clinical Biochemistry Audit Group Laboratory Standards for the Investigation of Hyperprolactinaemia and Macroprolactinaemia, 2012 and The Welsh Endocrine and Diabetes Society.

INTRODUCTION

Prolactin is a peptide hormone synthesised by the anterior pituitary gland. It is under negative regulation by the release of dopamine from the hypothalamus, and to a lesser extent, by positive regulation of thyrotropin releasing hormone (TRH). Its primary physiological role is in breast development during pregnancy and to stimulate lactation; however it can be raised in males and females due to a variety of other conditions. Symptoms of hyperprolactinaemia can be non-specific, and may include menstrual irregularities, infertility, loss of libido, erectile dysfunction and galactorrhoea. Patients with a significant pituitary lesion can present with headaches and visual field disturbances.

INTERPRETATION OF RAISED PROLACTIN RESULTS

If a patient's prolactin is raised above the assay reference range it should be repeated in the first instance after excluding secondary causes – see table 1. It is important to know that stress, pain and breast stimulation (including examination) are frequent causes of raised prolactin concentrations. Other secondary causes to bear in mind are untreated/undiagnosed hypothyroidism and renal impairment. Several medications may cause hyperprolactinaemia, in particular antipsychotics and anti emetics that interfere with the dopaminergic control of prolactin secretion. A list of drugs that may increase prolactin concentration is given in table 2.

Secondary hyperprolactinaemia is associated with prolactin levels up to 5,000 mU/L. Levels over this are usually due to prolactin secreting tumours. If prolactin is still raised on repeat testing and secondary causes have been excluded (including pregnancy) the patient should be referred for an endocrine opinion but an MRI should not be requested at that stage. A result over 10,000 mU/L is usually due to a macroprolactinoma and should prompt urgent telephone referral to endocrinology.

Please contact your Biochemistry department if further advice is required.

Table 1: Secondary causes of raised prolactin

– Any of these can raise prolactin to as much as 5,000 mU/L

Cause	Mechanism	Comments
Drugs	Effects on delivery of dopamine or antagonising dopamine receptors	Drug effects (non-depot preparations) only persist a few days after discontinuation. Clinically meaningful results can be obtained at least 72 hours after
Primary hypothyroidism	TRH stimulates prolactin release	Prolactin will return to normal when the TSH is normalised
Renal failure	Reduced clearance of prolactin	
Chest wall stimulation	Mimics suckling	Includes breast examination
Pregnancy/breastfeeding		
Physical/psychological stress	Including painful venepuncture	
Seizures		
PCOS		
Liver cirrhosis		
Anorexia nervosa		
Marijuana use		

Table 2: Drugs that may increase prolactin concentration

Type of medication	Examples	
Antipsychotics	Phenothiazines	Prochlorperazine, Fluhenazine, Perphenazine, Trifluoroperazine
	Thioxanthenes	
	Butyrophenones	Benperidol, Haloperidol
	Atypical	Risperidone, Molindone, Olanzapine
Antidepressants	Tricyclic/tetracyclic	Clomipramine, Desipramine, Amitriptyline
	SSRIs	Citalopram, Fluoxetine,

		Paroxetine
Opiates and cocaine		
Antihypertensives		Verapamil, Methyldopa, Reserpine
Gastrointestinal	Histamine 2 receptor blockers Others	Cimetidine, Famotidine, Nizatidine, Ranitidine Metoclopramide, Domperidone
Oestrogens		

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Version 1, August 2012.