Pharmacology
Team 437

MED437
KING SAUD UNIVERSITY

Endocrine Midterm Summary File

Editing File

Color index: Important Note Extra

Drugs of Endocrine Block

Growth hormone and Pituitary Adenomas

Drug	Key Point	C.I
Treatment of growth hormone deficiency		
Sermorelin	**M.O.A:** Synthetic GHRH **Use:** patient with defective hypothalamic release of GHRH **but** normally functioning anterior pituitary somatotrophs	-
Somatropin /Somatrem	**M.O.A:** Recombinant human growth hormone. **Use:** Growth failure in pediatric associated with (GH deficiency and Turner syndrome), Short bowel syndrome, wasting in patients with AIDS, idiopathic short stature. **ADRs:**Leukemia, rapid growth of melanocytic lesions, Hypothyroidism, Insulin resistance, Arthralgia, Increase in cytochrome P450 activity (side effects seen more in children)	-
Mecasermin	**M.O.A:**Synthetic IGF1 , given S.C **Use:** used for children with severe IGF1 deficiency due to mutations in the GH receptor (**Laron dwarfism**) or development of neutralizing antibodies against GH. **ADRs:**Hypoglycemia "can be avoided by eat meal 20min before or after the drug."	-
Treatment of Acromegaly / Gigantism :		
Octreotide /Lanreotide	-is a synthetic long-lasting peptide analogue of somatostatin -Octreotide more potent than Lanreotide **M.O.A: 1-**Inhibit GH secretion. **2-**partially inhibits GH-induced IGF-1 generation . **3-** reduce GHRH release. **ADRs:** Significant Gastrointestinal disturbances , Gallstones , Cardiac conduction abnormalities	-
Pegvisomant	**M.O.A:** GH receptor antagonist ,given s.c . **Use:**treatment of acromegaly - it reduce IGF-1 (does not affect GH level)	-
Bromocriptine / Cabergoline	**M.O.A:** Dopamine agonists **Use:** as primary and adjuvant treatment ,Response rate low ,high doses (used as last choice) -**Bromocriptine** more effective at inhibiting prolactin release **used** for hyperprolactinemia -**Cabergoline** More effective in GH and IGF1 reductions	-

Drugs of Endocrine Block

Drug	Key Point	C.I
Treatment of Prolactinoma :		
Bromocriptine	**M.O.A:**dopamine agonist , it works by inhibiting prolactin secretion without the uterotonic, vasospastic properties of other ergots. **Use:** in pregnancy -Take with food to reduce side effects	-
Cabergoline	**M.O.A:** dopamine agonist -More effective and more expensive , Well tolerated **ADRs:** Orthostatic hypotension, Nausea, Dizziness. " we can avoid the ADRs by beginning with low-dose therapy."	pregnancy
Pergolide mesylate	**ADRs for all dopamine agonists:** GI intolerance, postural hypotension, constipation, nasal stuffiness	pregnancy

Drugs of Endocrine Block

Hyperthyroidism

Drug	Key Point	C.I
Thioamides **M.O.A:** Inhibit synthesis of thyroid hormones by inhibiting the peroxidase enzyme that catalyzes the iodination of tyrosine residues.		
Propylthiouracil (PTU)	**M.O.A:** Blocks the conversion of T4 to T3 in peripheral tissues. **Advantages:** Recommended in pregnancy and breastfeeding. **ADRs:** Immunoallergic hepatitis, Agranulocytosis, ANCA-positive vasculitis, Arthralgia, Polyarthritis, Urticarial or macular reactions and GIT effects.	-
Methimazole	- Concentrated in Thyroid & crosses placenta - Secreted in breast milk **ADRs:** Abnormal sense of taste or smell, Agranulocytosis, Urticarial or macular reactions, Arthralgia, Polyarthritis and GIT effects.	- Pregnancy - Breastfeeding
Carbimazole (prodrug of Methimazole)		
IODINE		
Organic: iopanoic acid or ipodate	**M.O.A:** Inhibit synthesis and release of thyroid hormone + Blocks the conversion of T4 to T3 in peripheral tissues. - The effect is rapid but not sustained (temporary remission of symptoms) **Uses:** 1/Prior to thyroid surgery to decrease vascularity & size of the gland, 2/Following radioactive iodine therapy, 3/Thyrotoxicosis **May produce iodism symptoms:** Skin rash, Hypersalivation, Metallic taste, Bad breath and Oral ulcers	- As a single therapy - Pregnancy
Potassium iodide		
Adrenoceptor Blocking Agents (β Blockers)		
Propranolol	**Adjunctive therapy to relief the adrenergic symptoms of hyperthyroidism such as:** Tremor, Palpitation, Heat intolerance and Nervousness.	Asthmatic patients
Atenolol		-
Metoprolol		

Drugs of Endocrine Block

Drug	Key Point	C.I
Radioactive Iodine (RAI)		
RAI	**M.O.A:** 131 I isotope (therapeutic effect due to emission of β rays) - Accumulates in the thyroid gland and destroys parenchymal cells, producing a long-term decrease in thyroid hormone levels. - Clinical improvement may take 2-3 months. **Uses:** 1/As a diagnostic. 2/Hyperthyroidism mainly in old patients. 3/Graves. 4/Patients with toxic nodular goiter. **Advantages:** Easy to administer ,effective , painless and less expensive. **Disadvantages:** 1/High incidence of delayed hypothyroidism. 2/Large doses have cytotoxic actions. and fibrosis 3/May cause genetic damage. 4/May cause leukemia & neoplasia	- Pregnancy - Breastfeeding
Management of Thyroid Storm		
- Correct electrolyte abnormalities, Treat cardiac arrhythmia (if present) - Aggressively control hyperthermia by applying ice packs - Rarely, plasmapheresis has been used to treat thyroid storm		
Antiadrenergic drugs	**(e.g. propranolol)** To minimize sympathomimetic symptoms	
High-dose Propylthiouracil (PTU)	Preferred because of its early onset of action (risk of severe liver injury and acute liver failure)	
Hydrocortisone	To prevent shock.	
iodine compounds	Orally or via a nasogastric tube	
Management of Hyperthyroidism due to Graves' disease		
Severe Hyperthyroidism >> Radioiodine preferred in adults >> Normalization of thyroid function with antithyroid drugs before surgery in **elderly** patients and those with **heart disease**		
Mild/Moderate Hyperthyroidism >> Antithyroid drug therapy (Methimazole, PTU in Pregnancy) >> **Euthyroid state** achieved >> Discontinue drug therapy after 12–18 M >> Monitor thyroid function every 2 months for 6 months >> If It **Remission** then monitor every 12 M, if it's **Relapse** start Definitive radioiodine (Second course of anti-thyroid drug therapy in children)		
Subtotal Thyroidectomy is the treatment of choice in very large gland or multinodular goiter		

Hypothyroidism

Drug	Key Point	C.I
synthetic thyroid hormone preparations.		
Levothyroxine T4	Synthetic form of thyroxine (T4) Drug of choice for replacement therapy. regardless of etiology;Congenital,hashimoto&pregnancy Long half life/once daily Given in a dose of 12.5 - 25 ug/day for 2 weeks and then increase every two weeks. Restore normal thyroid levels within 2-3 weeks **MOA**; Major pathway of thyroid hormone metabolism is through sequential deiodination -80% of circulating T3 is derived from peripheral T4 by monodeiodination -80% of the daily dose of T4 is deiodinated to yield equal amounts of T3 and rT3 **ADRs** children: restlessness , insomnia , accelerated bone maturation **ADRs** in adult; arrhythmia (tachycardia , atrial fib), tremor , restlessness, headache , change in appetite, **weight loss ,** heat intolerance , muscle pain PRECAUTION In old patients and in patients with cardiac problems(start treatment with reduced dosage)	
Liothyronine T3	More potent (3-4 times) and rapid onset of action short half life, so not recommended for routine replacement therapy (requires multiple daily doses)	should be avoided in cardiac patients
Liotrix T3+T4	**MOA**: Combination of synthetic T4 & T3 in a ratio 4:1 that attempt to mimic the natural hormonal secretion The major limitations to this product are: 1-High cost 2-Lack of therapeutic rationale because 35% of T4 is peripherally converted to T3	

Myxedema coma

- Life –threatening hypothyroidism
- The treatment of choice is loading dose of **levothyroxine** intravenously.
- I.V. liothyronine T3 for rapid response but it may provoke cardiotoxicity
- I.V. hydrocortisone may be used in case of adrenal and pituitary insufficiency.

Hypothyroidism and pregnancy

In pregnant hypothyroid patient 20-30 % increase in thyroxine is required because of

1. elevated maternal thyroxine binding globulin (TBG) induced by estrogen
2. early development of fetal brain which depends on maternal thyroxine

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References:

✓ Doctors' slides and notes

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