Hypothyroidism

Pharmacology Clinical Correlations
GSN 0606
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Objectives

- Recognize S/S of hypothyroidism
- Identify goals of pharmacotherapy
- Devise appropriate dosing regimen for euthyroid state
- Select appropriate thyroid hormone replacement
- Educate patients re: thyroid replacement therapy

Hypothyroidism

- Definition: clinical and biochemical syndrome resulting from decreased thyroid hormone production
- Prevalence: 1.5%-2% women and 0.2% men and incidence increases with age
- Majority have primary hypothyroidism
- Pituitary fx rare but should be suspect if decreased levels of T_4 and low TSH levels

Thyroid hormone

- Essential for normal growth and development during embryonic life
- Deficiency during fetal and neonatal development results in mental retardation
- Child with hypothyroidism - growth retardation
- Adult symptoms: varied and nonspecific

Pathogenesis

- Primary
  - Most likely autoimmune
  - Often as sequelae of Hashimoto's disease (chronic thyroiditis)
- Post therapeutic resulting from:
  - Radioactive Iodine
  - Surgery or thyroidectomy
  - Thioamide drugs

Pathogenesis . . .

- Transient thyroiditis of viral etiology
- Postpartum thyroiditis
- Less common: iodine ingestion, neck irradiation and certain medications such as lithium or para-aminosalicylic acid
- Hypothalamic-pituitary axis dysfunction

Patient Presentation

CC: "I simply don't feel well, I must be getting old"

HPI: 60 yo woman c/o feeling "run down" X 6 months. Lacks energy to perform daily activities; complains of being cold; noted recent "aging" of skin/hair causing her to withdraw socially; reports crying episodes and periods of mental depression. Patient attributes sx to "getting old".

Patient Presentation (cont)

PMH: Post menopausal X 10 yrs; G_2P_2 with no chronic medical or psychiatric illnesses

FH: Father deceased-age 76 (black lung)

Mother deceased-age 92(CHF); 1 brother, 2 sisters alive and well

SH: Married homemaker X 40 yrs. ETOH-rare; tobacco-none; husband has CHD and chronic anxiety disorder

Patient Presentation (cont)

Meds: Calcium 2 tabs Q day;

MVI 1 tab Q day; Occasional ASA (headaches and myalgia)

ROS:

Headaches once every 1-2 weeks

Skin changes as per HPI

Occasional aching in muscles/joints of hands

Psychiatric complaints noted in HPI

Physical Examination

Gen: Well-developed, slightly obese white woman NAD; slightly anxious

VS: 110/75 60 16 36.4° Wt: 74 kg

Skin: Coarse/dry especially dorsal aspect of arms and lower extremities

HEENT: Normocephalic with coarsening of hair; periorbital edema; full ↑↓ dentures

Neck: Supple, no adenopathy/masses/goiter

CV: NSR, 60 bpm, Grade II/VI SEM heard best at upper left sternal border

Physical examination

Abd: Soft, mod obese, no tenderness/guarding or rebound

GU: Deferred. Recent negative Pap smear

Ext: Trace edema below knees, bilaterally

Neuro: CN II-XII intact; DTRs mildly diminished (3/5)

Labs: Na-142 K-3.8 Cl-102 CO_2-23

Creat-0.8 BUN-14 Chol-256

Hgb-11.8 Hct-34.1 MCV-86 Plat-175

WBC-7200 TSH-10.8 Tot T_4-3.6
Free T_4-0.5

Problem Identification

- Common symptoms
  - dry skin, cold intolerance, weight gain, constipation, weakness,lethargy, fatigue, loss of ambition,depression, hoarse speech, coarse hair and skin, cold skin, periorbital edema, bradycardia, carpal tunnel syndrome, polyneuropathy, cerebellar dysfunction, muscle cramps , stiffness, relaxation of DTRs
- Labs: ↑ TSH
  - ↓ T_4 (normal if compensated) T_3 often nl

Systemic manifestations of hypothyroidism

- **Cardiovascular**: reduced SV and HR causing decreased CO; increased SVR to maintain BP; normal exercise response, but resting alterations resulting in cool skin, cold intolerance; enlarged heart; diminished heart sounds, bradycardia, prolonged PR interval, depressed P waves, flattened or inverted t waves, low amplitude QRS complexes; rarely cardiac tamponade

Systemic . . .

- **Pulmonary:**

  Dyspnea, myxedematous changes in respiratory muscles leading to hypoventilation and CO_2 retention which may contribute to myxedema coma

Systemic . . .

- **Renal:**

  Reduced renal blood flow and GFR leading to decreased renal excretion of water; increase in total body water and dilutional hyponatremia; reduced production of erythropoieten

Systemic . . .

- **GI:** Decreased appetite; constipation, weight gain, fluid retention; decreased absorption of nutrients; decreased protein metabolism; edema; decreased glucose absorption and uptake; elevated serum lipid values

Systemic . . .

- **Musculoskeletal:** Myalgia, stiffness; slow movement, slow tendon jerk reflexes; decreased bone formation, resorption, increased bone density, arthralgias

Systemic . . .

- **Integumentary:**
  Dry, flaky skin; dry brittle head and body hair; reduced growth nails and hair, slow wound healing, myxedema, cool skin

McCance, K.L. & Heuther, S.E. (1998). Pathophysiology (3rd ed.). Chicago: Mosby.

Laboratory diagnosis

- Primary hypothyroidism
  - Increase in TSH levels (lack of feedback)
  - Serum T_4 and free T_4 usually low
- Secondary hypothyroidism (due to pituitary dysfunction)
  - Decreased TSH levels (also be alert to other decreased hormone levels produced by pituitary)

Goals of Pharmacotherapy

- Restore thyroid hormone to normal tissue concentrations
- Provide symptomatic relief
- Correct biochemical aberrations due to hypothyroidism

Laboratory normals

- T_3 87-178 ng/dl
- T_4 5.53-11 µg/dl
- Free T_4 0.58-1.64 µg/dl
- TSH 0.465-4.68 Iu/ml

Therapeutic Alternatives

- **Thyroid (USP)-desiccated hog, beef, sheep (*unpredictable, inexpensive, may not be bioequivalent*)**
- **Thyroglobulin-Partially purified hog thyroglob (*stable, expensive, no advantage)***
- **$_L$-Thyroxine-Synthetic T_4(*stable, predictable, $t_{1/2}$,- 7 days, daily dosing)***
- **Liothyroine-Synthetic T_3 (*stable, $t_{1/2}$-1.5 days)***
- **Liotrix-Synthetic T_4T_3 in 4:1 ratio(*stable, expensive, no advantage)***

Thyroid Preparations

Drug	Content	Relative dose
Thyroid,USP	Dessicated	1 gr=60µg T_4
Thyroglobulin	Purified pork	1 gr
Levothyroxine	Synthetic T_4	50-60µg
Liothyroine	Synthetic T_3	15-37µg
Liotrix	Syn $T_4T_{3(4:1)}$	60:15µg

Costs

Thyroid, USP	$22/100 tabs
Thyroglobulin	N/A
L-Thyroxine	$40/100
» generic	$23/100
Lyothyroine	$75/100 tabs
Liotrix	N/A

Optimal plan for replacement

- Initial dose - dependent on patient's age, presence of associated disorders, severity/duration of hypothyroidism
  - Longstanding dz, <45yrs, no CAD: 50µg Q day of levothyroxine and increase to 100µg daily after 1 month
  - Older patients with CAD: 25µg/d, titrating upward in increments of 25µg at monthly intervals to prevent cardiac stress (use for this patient)

Drug Monitoring

TSH concentrations most sensitive and specific monitoring parameter for dosing

- falls within hours of initial dosing and usually normal within 2-6 weeks
- Check TSH monthly until euthyroid (appropriate dose will keep TSH in normal range-<6 U/ml), then yearly checks
- May use T_4 levels to detect noncompliance (TSH >20 indicates undertreatment or noncompliance)

- If needed, increase dose in 25µg increments

Patient Education

- Patients are usually compliant because they feel better with medication
- Education should include drug-drug interactions
  - Digoxin: may need lower dose (decreased VD)
  - Insulin: may need lower dose (decreased met)
  - Warfarin: may need lower dose (delays met)
  - Barbiturates, phenothiazines, opioids - avoid may cause respiratory depression

Patient education

- May need to increase levothyroxine dose with the following:
  - phenytoin
  - carbamazepine
  - rifampin
- Dose levothyroxine 4 hours from:
  - cholestyramine
  - ferrous sulfate
  - sucralfate
  - antacids

Patient education

- 5-15% lithium-treated patients (females) develop goiters with lithium and/or hypothyroidism
- TSH >5, give Synthroid 0.05 mg/d
- Check TSH in 1 month
- May increase up to 0.2 mg/d or higher to achieve TSH <0.1-<5mIU/ml

Patient education

- Not applicable in this case, however, if patient in child-bearing age, caution that thyroid must be monitored carefully during pregnancy (fetal development dependent upon this).

Remember . . .

In the words of Dr. Bustos, "Every woman over 50 years deserves thyroid function tests"

References

Bakerman, S. (1994). ABC's of Interpretretive Laboratory Data (3rd ed.). Myrtle Beach: Interpretive Laboratory Data, Inc.

Degowan, R.L. (1994). Diagnostic Examination (6th ed.). St Louis: McGraw-Hill.

Dipiro, J.(1997). Pharmacotherapy: A pathophysiologic approach (3rd ed.). Stamford: Appleton & Lange

References

McCance, K.L. & Huether, S.E. (1994). Pathophysiology (3rd ed.). St Louis: Mosby.

Uphold, C.R. & Graham, M.V. (1999). Clinical Guidelines in Adult Health. (2nd ed.). Gainesville: Barmarrae Books.

Wells, B.G., Dipiro, J.T., et al. (2000). Pharmacotherapy Handbook. Stamford: Appleton & Lange.