

PRACTICAL THYROID MANAGEMENT

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Financial disclosure

- I am a paid speaker for Boehringer Ingelheim Pharmaceuticals for Jardiance

About me

- Married with 4 kids
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Overview

- Goal: practical approach for thyroid probs for PCP
- Discuss
 - Hypothyroidism
 - Hyperthyroidism
 - Thyroid nodules
 - Thyroid CA
- Management keys and common pitfalls

Hypothyroidism

- Etiologies
 - Hashimoto's (>70-90% *etiology- based on various studies*)
 - Postsurgical vs post ablative
 - Idiopathic
 - Others
- MC Sxs
 - Fatigue
 - Weight gain
 - Cold intolerance
 - Dry skin
 - Constipation

Hypothyroidism

- Which labs
 - TSH and FT₄ only
 - Rarely require FT₃
 - Avoid: TT₄, T₄ index, T₃ index
 - +/- TPO or TG Abs (Hashimoto's Abs)
 - (+) test tells etiology only
 - by far MC etiology for hypothyroidism
 - may be helpful in pts struggling w/ fertility (*some a/w infertility and period irregularity*)
 - Do not need to refer for pos TPO Abs

Hypothyroidism

- Interpretation (more art than science)
 - TSH (.4-4.5)
 - FT₄ (.8-1.8)
 - field goal analogy
- FT₄ more likely accurate
 - Examples of falsely low TSH
 - Pregnancy
 - Weight loss
 - Pituitary d/o
 - Lab assay abnormality (falsely low or falsely high)
- Story of 70 YO on 250 mcg LT₄ w/ tremors/palpitations, but high TSH

Hypothyroidism

- Management
 - Levothyroxine (or other generic LT₄ Rx's)
 - Cheap & easy
 - ATA guidelines for the treatment of hypothyroidism (2014)
 - "We concluded that levothyroxine should remain the standard of care for treating hypothyroidism. We found no consistently strong evidence for the superiority of alternative preparations (e.g., levothyroxine–liothyronine combination therapy, or thyroid extract therapy, or others) over monotherapy with levothyroxine, in improving health outcomes."
 - Synthroid (brand name LT₄)
 - More \$, consistent dosing, gluten free
 - Tirosint (water based filler)
 - Most \$, maximal absorption
 - Tirosint solution: ~increased absorption independent of pH
 - Celiac, pts w/ GERD on PPI, malabsorptive d/o, hx bariatric sx
 - LT₄ Rx w/ ~1 wk half-life
 - LT₃ Rx (Cytomel/liothyronine): onset ~2-3 hrs, ~2 day half-life

Hypothyroidism

- Management
 - Once starting on Rx
 - Goal mid nl range TFTs (field goal analogy)
 - "Thyroid hormone therapy should be initiated as an initial full replacement or as partial replacement with gradual increments in the dose titrated upward using serum thyrotropin as the goal." (ATA guidelines for hypothyroidism)
 - Set clear expectations for pts
 - "not all fatigue is d/t thyroid"
 - Repeat TFTs Q 2-3 mo (not earlier)
 - My approach- TSH & FT₄ both→ improved accuracy of dosing

Hypothyroidism management

- My principles for management:
 - If increasing or decreasing dosage, go 1 step at a time
 - Example: FT₄ from 1.0-1.2 after LT₄ from 88 – 100 mcg → may increase to 112 mcg LT₄
 - use only 1 dosage strength at a time
 - Ex: do not use 88 and 100 mcg and alternate dosage- just use 100 mcg 6.5 weekly
 - Titrate to optimal TFTs and sx's
 - Example: FT₄ from 1.4-1.6 after increase to 112 mcg- pt now w/ slight palpitations
 - May lower to 112 mcg 6.5 pills weekly (slightly lower FT₄, lower sx's, but keep FT₄ at mid nl range goal)

Hypothyroidism

- What about desiccated thyroid hormone
 - Human ratio ~14/1 T₄/T₃
 - Pigs ~4/1 T₄/T₃
 - Desiccated thyroid hormone examples
 - Naturethroid, Armour thyroid, NP thyroid
 - LT₄ Rx= all T₄
 - Desiccated thyroid Rx: ~4/1 ratio of T₄/T₃ (pig thyroid extract)
- ATA guidelines for the treatment of hypothyroidism- section regarding desiccated thyroid extracts:

"We recommend that levothyroxine be considered as routine care for patients with primary hypothyroidism, in preference to use of thyroid extracts. Although there is preliminary evidence from a short-duration study that some patients may prefer treatment using thyroid extracts, high-quality controlled long-term outcome data are lacking to document superiority of this treatment compared to levothyroxine therapy. Furthermore, there are potential safety concerns related to the use of thyroid extracts, such as the presence of supraphysiologic serum triiodothyronine levels and a paucity of long-term safety outcome data."

Hypothyroidism management

- My approach:
 - T₄ Rx predominantly, occasional LT₃ if low/nl FT₃ w/ nl FT₄
 - If using LT₄ + LT₃- check TSH, FT₄ and FT₃
 - If using LT₄ only- check TSH and FT₄ only
 - If using desiccated thyroid hormone
 - Set clear expectations for pt
 - Check TSH, FT₄, FT₃
- If pts cannot convert T₄/T₃- can add T₃ back individually (*liothyronine*)
 - check TSH, FT₄, FT₃

Thyroid Rx absorption

- Empty stomach:
 - Take Rx 1 hr before breakfast, or 3 hrs after dinner
 - 3-4 hrs away from Ca, Fe, Vit D, PO estrogen
- If missing dosage of LT₄- can double next day
 - Remember 1 wk half-life
 - Routinely recommend weekly pillbox

Hypothyroidism- special circumstances

- Pregnancy:
 - require ~30-50% more thyroid Rx in pregnancy
 - Trimester specific TSH goals (*ATA guidelines for thyroid disease in pregnancy*)
 - 0.1–2.5 mIU/L for the first trimester,
 - 0.2–3.0 mIU/L for the second trimester
 - 0.3–3.0 mIU/L for the third trimester,
 - If morning sickness- can take LT₄ in evening (3 hrs after dinner)
- Malabsorptive d/o, bariatric surgeries, celiac
 - Likely need higher dosage
 - Consider tirosint for maximal absorption
- Thyroid CA:
 - Keep TFTs upper nl range to lower risk of recurrence
 - Goal TSH .1- .4 if active CA vs .4-2 if in remission

Hyperthyroidism

- Sxs:
 - Palpitations
 - Tremors
 - Wt loss
 - Diaphoresis
 - Exophthalmia (graves eye disease)
- Etiologies:
 - Graves (autoimmune)
 - Acute thyroiditis
 - Autonomous nodule
 - Postpartum thyroiditis
 - Gestational Hyperthyrotoxicosis

Hyperthyroidism

- Which labs?
 - TSH, FT₄, FT₃
 - Graves Abs labs: TSI (thyroid stimulating immunoglobulin), TRAb (thyrotropin R Abs)
 - Avoid: TPO, TG Abs (Hashimoto's), thyroid antibody panel (usually TPO, TG Abs)
- Interpretation
 - TSH ↓, FT₄ or FT₃ moderately/very ↑ = usu graves vs autonomous nodule
 - TSH ↓ w/ nl FT₄ and FT₃ = usu acute thyroiditis vs wt loss vs pituitary disease
 - if TSH low, review hx, repeat TFTs in 2-3 mo- if FT₄/FT₃ nl, may be resolving thyroiditis
 - Key: if unsure and pt asxs, repeat labs 2-3 mo later

Hyperthyroidism

- Dx: history remains key
 - Graves
 - personal/Fam hx autoimmunity
 - Acute onset
 - Sxs more predominant
 - Thyroiditis
 - Subacute onset
 - Preceding URI within months
 - Preceding contrast study w/ iodine
 - Usually resolves w/in 3-6 mo
 - Autonomous nodule:
 - Requires RAI uptake and scan- "hot nodule" = autonomous nodule

Hyperthyroidism- special cases

- pregnancy
 - Postpartum thyroiditis:
 - TFTs high over few months- ~resolve within 3-6 mo
 - Generally do not treat (particularly if breast feeding)- repeat TFTs in 2-3 mo
 - Gestational hyperthyrotoxicosis
 - During peak hCG (10 to 12 weeks), T₄ + T₃ both ↑ (~Upper nl limits), & TSH slightly ↓.
 - Very common during 1st trimester, or in pregnancies with high hCG levels
 - Usually asxs, usu do not treat
 - if sxs present in 2nd trimester, recheck TFTs

Hyperthyroidism

- What about RAI uptake and scan
 - Diagnostic modality for underlying etiology
 - Graves- high diffuse uptake
 - Autonomous nodule: focal high uptake
 - Thyroiditis: very low uptake throughout
- Order if Graves Abs neg and TFTs still high
- My approach for hyperthyroidism:
 - Order TSH, FT₄, FT₃, TSI Abs
 - very rarely require RAI uptake and scan
 - TSI Abs ~95-98% sensitivity and specificity for graves
 - If TSI Abs neg & TFTs still high- then get RAI uptake and scan

Hyperthyroidism

- When to refer vs when to wait
- My approach:
 - FT₄ or FT₃ moderately high- refer
 - TSH low, but FT₄/FT₃ nl- wait (majority will be thyroiditis)
 - repeat TFTs 2-3 months later
- Good idea to always get TSH + FT₄ + FT₃
 - Some forms of hyperthyroidism can be T₃ predominant

Hyperthyroidism management

- B-blockers for palpitations
 - My approach: propranolol 10-20 mg Q6 hrs PRN palpitations
- Anti-thyroid RX
 - Start after confirming dx (pos Abs for pos RAI uptake and scan)
 - Typical to refer these pts to endo for Rx management
 - Methimazole
 - My typical dosing 5-10 mg QD vs BID
 - 5 mg QD for mild FT₄/FT₃ elevation
 - 10 mg QD for moderate FT₄/FT₃ elevation
 - 10 mg BID for significant FT₄/FT₃ elevation
 - PTU: Use only during 1st trimester pregnancy- higher AE profile than MTZ
- if considering total thyroidectomy vs RAI ablation: rec'd endo referral first

Hyperthyroidism management

- IF using MTZ or PTU for management
 - Repeat TFTs Q 2-3 mo for dosage adjustment (just like hypothyroidism)
- Rec'd using FT₄/FT₃ for dosing rather than TSH value
 - TSH will take months to normalize

Thyroid nodule

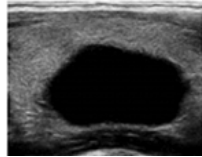
- Frequently present (~50% by age 50 based on multiple studies)
- Etiologies from FNA (% below based on avg over multiple studies)
 - Benign (~70%)
 - Malignant (~1-10%)
 - Inadequate cellularity (~5-10%)
 - AUS (~10-30%)
- No Labs needed if asxs

Thyroid nodule

- When to biopsy vs observe vs refer
 - Very low risk: observe (<1-3% risk of CA)
 - low risk- consider FNA if nodules >1.5 cm
 - Intermediate vs high risk- FNA vs refer

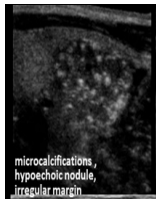
Thyroid nodule

- Examples of very low risk nodules- <1-3% risk of CA- do not need FNA
 - Anechoic (cystic)- regardless of size- do not FNA (pic on R)
 - Spongiform (pic on L)
- (all US Images via *ATA guidelines for assessment of thyroid nodules 2015*)



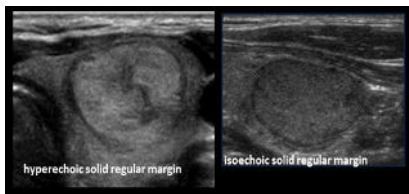
Thyroid nodule

- Examples of high risk nodules- (~70-90% risk of CA)
 - Calcifications, large, hypoechoic, irregular borders, extrathyroidal extension, etc



Thyroid nodule

- Examples of low risk nodules- ~5-10% risk CA- consider bx if >1.5 cm
 - solid, iso/hyperechoic



Thyroid nodule

- FNA w/ AUS (*atypia of undetermined significance- an indeterminate read*)
- Different than inadequate cellularity
- Options for management
 - Observe
 - Repeat FNA
 - Cytogenetic study
 - Examples: ThyraMIR, AFFIRMA
 - Gene classifiers- use genetic material to classify relative risk of CA

Thyroid nodule

- Long-term management
 - ATA guidelines: Q 1-2 yr US surveillance (*low to intermediate risk nodules*)
 - if stable in size/characteristics- may continue monitoring
 - Always can refer to endo if unsure of progression
 - If pts w/ dyspnea/dysphagia, or considering total thyroidectomy- refer to endo
- Note on GLP1s use
 - GLP1s are contraindicated in personal or fam hx of medullary thyroid CA (MTC)
 - MTC very rare, familial
 - Pts w/ thyroid nodules CAN be on GLP1s

Thyroid Cancer

- Etiologies
 - Differentiated thyroid CA (*papillary and follicular*)
 - Medullary Thyroid CA (*rare, a/w MEN syndromes*)
 - Anaplastic (*very rare, high mortality rate*)
- If (+) FNA for DTC- refer to endo
 - Endo can assist in finding surgeon, planning for short/long term surveillance
- If (+) FNA for MTC or anaplastic- urgent endo referral
- If pos hx of thyroid CA in remote past- may not need endo referral (*pt preference*)

Thyroid Cancer

- DTC cases
 - Majority w/ low mortality rate
 - Rarely metastasize beyond cervical LNs
- Surveillance
 - Thyroid US yearly
 - TG, TG Abs yearly (*tumor markers*)-
 - Generally do not require CT/PET scans
- Note: Fam hx of MEN syndromes
 - a/w Pancreatic, parathyroid, pituitary masses, rarely MTC, pheochromocytomas
 - Refer all these to endo for surveillance

Summary

- Hypothyroidism
 - TSH & FT₄
 - goal mid nl range (*splitting the uprights*)
 - optimize absorption
 - small dosage adjustments
- Hyperthyroidism
 - TSH, FT₄, FT₃- do not rely on TSH only
 - TSI or TRAb Abs for graves
 - Rarely require RAI uptake and scan
 - Refer for graves or autonomous nodules

Summary

- Thyroid nodules
 - Majority benign
 - Not all require FNA
 - Refer if worrisome, large, high risk, abnl FNA
 - GLP1s ok if no MTC
- Thyroid CA
 - Majority non-aggressive (DTC)
 - Referral if new or longstanding w/ worrisome features
 - May not require referral if stable and longstanding

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