Amiodarone Induced Thyrotoxicosis Treatment? (AIT)

Presentation of a Case Report

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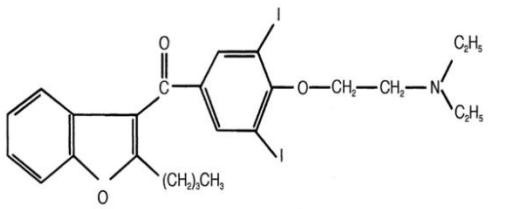
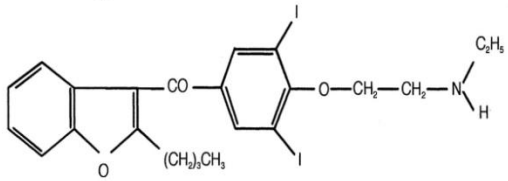
1. Background



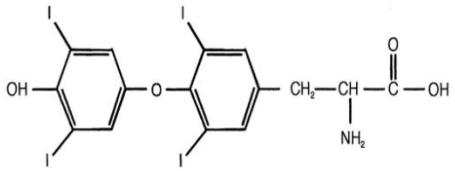
Amiodarone



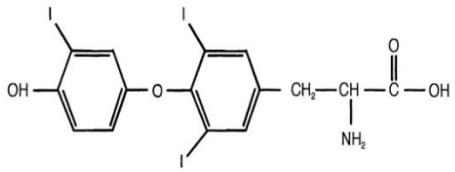
Desethylamiodarone

Amiodarone (Cordarone)

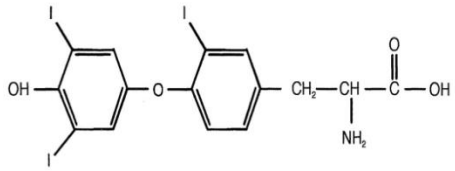
- iodine rich drug
- management of tachyarrhytmias
- distributed in several tissues
- Long elimination half life



Thyroxine (T_4)



3,5,3'-Triiodothyronine (T_3)



3,3',5'-Triiodothyronine (reverseT_3,rT_3)

1. Background

Effect of Amiodarone on thyroid hormones

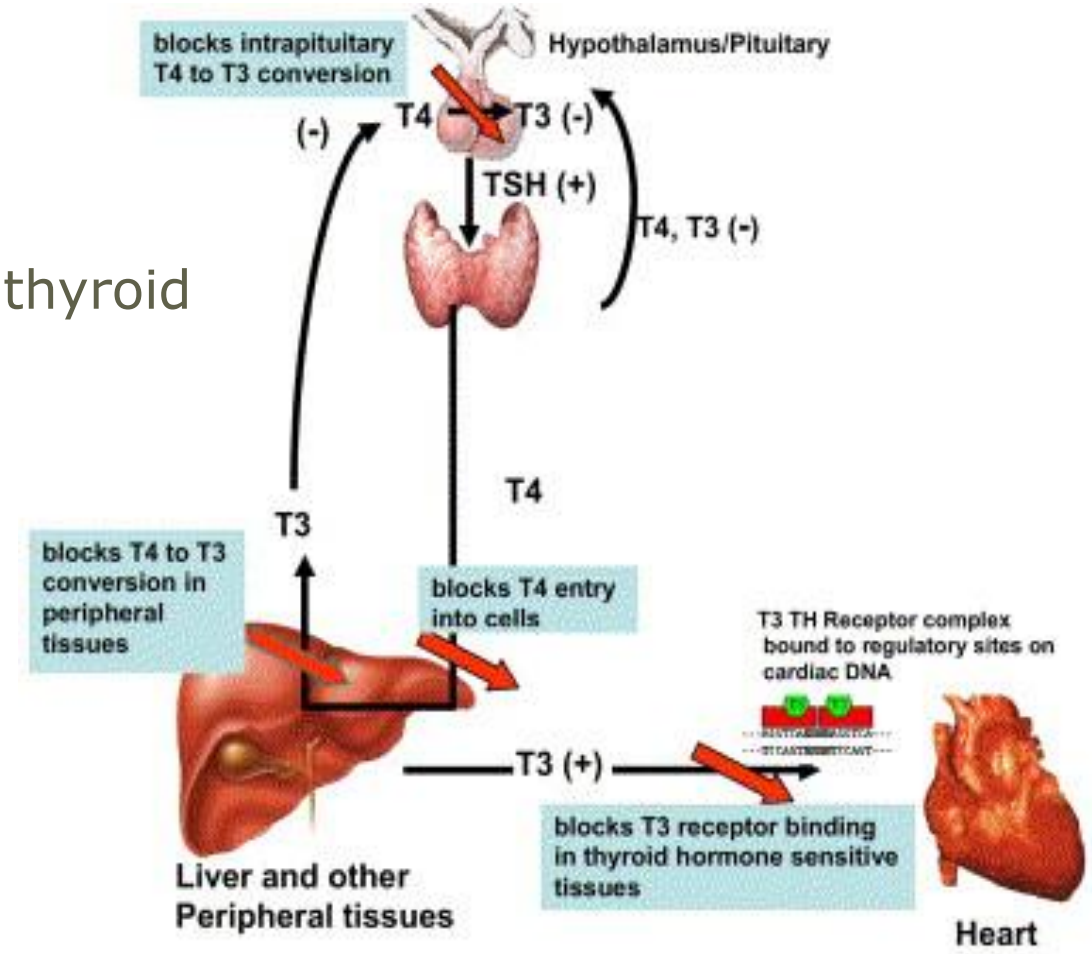


Figure of Basaria S, Cooper D. Amiodarone and the thyroid. Am J Med 2005; 118: 706-14.

1. Background

Overt thyroid dysfunction in 14-18% of patients on Amiodarone

Amiodarone induced hypothyroidism (AIH) or
Amiodarone induced hyperthyroidism (AIT)

AIT:
-Sudden and explosive onset
-Early or late after amiodarone instauration / withdrawal

TYPE I: due to iodine excess in preexisting thyroid disease
TYPE II: due to destructive thyroiditis

2. Case report

62 year, Caucasian man

- atrial fibrillation since 4 years
- on Amiodaron (200mg daily) for 2 years
- no personal/ familial history of thyroid dysfunction
- no information about thyroid tests/ Abs before

Medical history: AF, AI grade 1-2/4, hyperlipidemia, hemorrhagic sigmoiditis, lumbar arthrosis.

2. Case Report

History: tremor, heat intolerance, excessive sweating, weight loss (15kg), palpitations, dyspnea and exercise intolerance.

Routine blood test by general practitioner:

Free T4 of > 40 pmol/L	(12.5-21.2 pmol/L)
Free T3 of 29.6 pmol/L	(3.9-6.6 pmol/L)
TSH < 0.015 mIU/L	(0.27-4.20 mIU/L)

ECG: atrial fibrillation

Diagnose of AIT

2. Case Report

Treatment:

- methylprednisolone (32mg/day)
- thiamazole (30mg/day; then 60mg/day – 40mg/day)

After 2 weeks:

- addition of potassium perchlorate (1g/day)

2. Case Report

REFERRAL TO OUR DEPARTMENT OF ENDOCRINOLOGY

- eight weeks after initiation of treatment

- worsening of symptoms (palpitations, angina pectoris at exercise, excessive sweating, tremor)

- Medical treatment at that moment:

Strumazol 40mg/day, methylprednisolone 32mg/day, potassium perchlorate 1g/day, sotalol 240mg/day, pravastatin, pradaxa, omeprazole, alprazolam, zolpidem

2. Case Report

Clinical examination

BP 149/97 mmHg; pulse 127/’ (irregular)
No fever, normal oxygenation
BMI 25kg/m²

Facial flush, excessive transpiration
Thyroid gland is tender, nl volume, no nodules
No signs of exophthalmia
Normal pulmonary auscultation
No peripheral oedema

3. Investigations

A. Biochemical tests

- fT4 > 98.7 pmol/L (11.9-21.9 pmol/L)
- fT3 = 18.0 pmol/L (4.0-6.8 pmol/L)
- TSH < 0.015 mIU/L (0.27-4.20 mIU/L)

- Anti-TPO Abs, anti-Tg Abs, TSI's were negative

- CRP, ESR, WBC nle

3. Investigations

B. Radiology

Thyroid ultrasound:

- Diffuse hypo-echogenic heterogenous gland
- Estimated volume of 32 ml
- No nodules

Color flow doppler sonography:

- Absent hypervascularity

Thyroid radioactive iodine uptake (RAIU) not done

3. Investigations

C. Cardiac exams

ECG: atrial fibrillation at 125/minute

Echocardiography: normal LVEF, no major valve insufficiencies

4. Diagnosis

Which type of AIT?

Amiodarone induced thyrotoxicosis
– most probably type 2

HYPER

HYPO

IODINE INTAKE	AIT (HYPER)	AIH (HYPO)	COUNTRY
high	1.7%	13.2%	USA, UK (n=295)
intermediate	7.9%	5.7%	Spain, Australia, Holland (n=229)
low	11.9%	6.4%	Italy, Belgium (n=419)
intermediate	8%	6%	The Netherlands 2011 (n=303)

	AIT TYPE I	AIT TYPE II
PATHOGENESIS	IODINE-INDUCED THYROTOXICOSIS	DESTRUCTIVE THYROTOXICOSIS
Preexisting thyroid disease	Yes	No
Physical examination	Usually nodular or diffuse goiter	Sometimes small firm (painful goiter)
Thyroid antibodies	Can be present	Mostly absent
Thyroidal RAIU	Low or normal	Low or absent
Thyroid ultrasound	Diffuse or nodular goiter	Heterogeneous pattern
Doppler sonography	Normal or increased flow	Decreased flow
99mTc-sestaMIBI	Clear thyroid retention	No thyroid uptake
Spontaneous remission	Unlikely	Likely

Treatment of AIT

TABLE 6. Therapeutic strategy in amiodarone-induced thyrotoxicosis

Type I AIT Thionamides (methimazole, 30–40 mg/day) in combination with potassium perchlorate (1 g/day for 16–40 days). Discontinue amiodarone if possible. After restoration of euthyroidism and normalization of urinary iodine excretion, definitive treatment of the underlying thyroid abnormalities by either radioiodine or thyroidectomy. If amiodarone cannot be withdrawn and medical therapy is unsuccessful, consider total thyroidectomy.
Type II AIT Glucocorticoids for 2–3 months (starting dose, prednisone 40 mg/day or equivalent). Discontinue amiodarone if possible. In mixed forms add thionamides and potassium perchlorate. After restoration of euthyroidism, follow-up for possible spontaneous progression to hypothyroidism. If amiodarone cannot be withdrawn and medical therapy is unsuccessful, consider total thyroidectomy.

5. Literature of AIT

Difficult to manage
Increased rate of adverse CV events compared to euthyroid

TREATMENT:

AIT type 1: thionamides in high dose +/- potassium perchlorate

AIT type 2: glucocorticoids

Mixed formes or severe cases: combination

Withdrawal of amiodarone if possible

5. Literature of AIT

In AIT refractory to medical treatment:

Thyroidectomy

Total plasma exchange (TPE)

Radioactive iodine

Iopanoic acid

Lithium

TOTAL THYROIDECTOMY FOR AMIODARONE-INDUCED THYROTOXICOSIS

1. Mayo Clinics, USA
   - 34 pat. (29 M, 5 F), age 60 yr (39-85), 1985-2002
   - 2 type I, 32 type II
   - 3 death, 3 rehospitalization
   - 10 complications

2. Brisbane, Australia
   - 14 pat. (11 M, 3 F), age 50 yr (26-82), 1998-2005
   - 1 type I, 13 type II
   - 0 death
   - 2 complications

How to reduce morbidity and mortality related to total thyroidectomy in AIT?

Is plasmapheresis an alternative to reduce risks related to thyroidectomy in AIT ?

6. Treatment of our patient

Medical treatment:
- methylprednisolone (8weeks)
- thiamazole (40 mg)
- potassium perchlorate (stopped after 4 weeks)

Total plasma exchange (TPE):
- 1 to 1.5 of total plasma volume; 6x
- Human albumine as replacement fluid

Total thyroidectomy

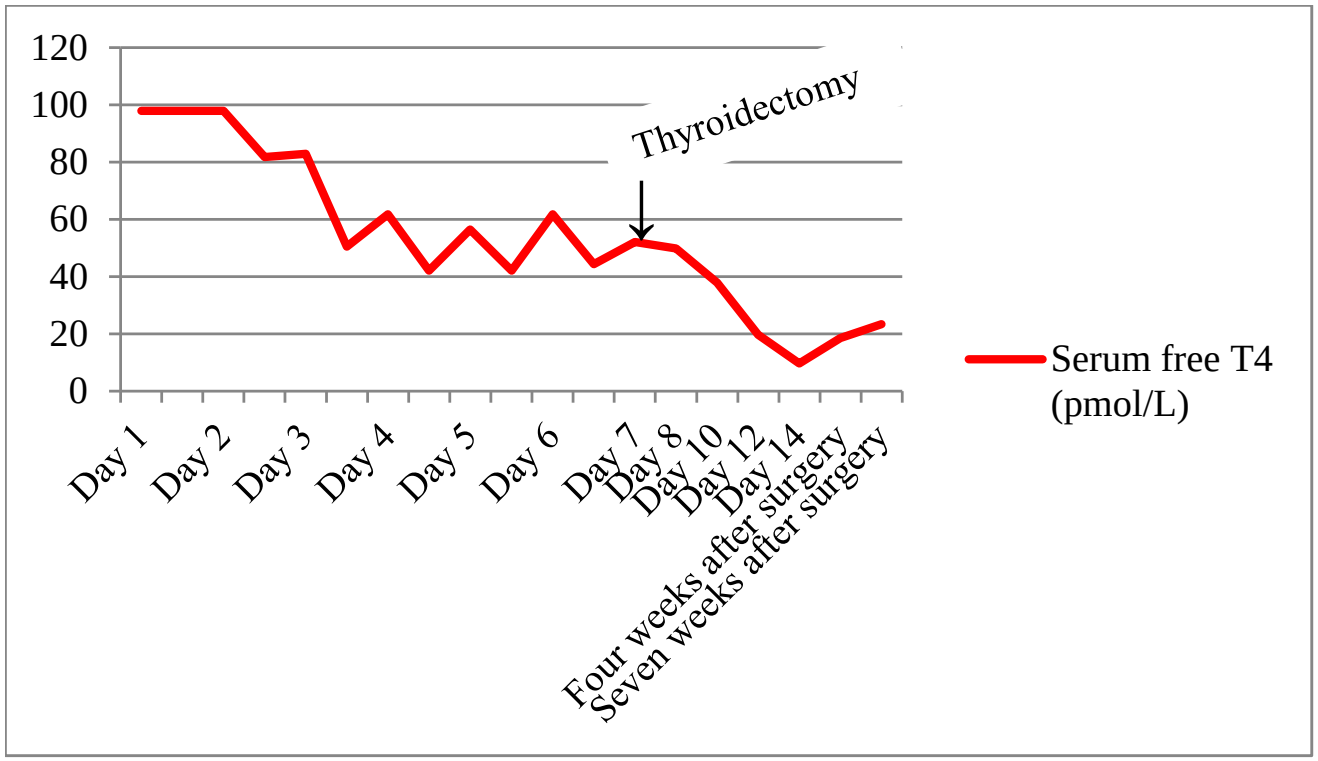
7. Outcome & follow up

	21/5/13		22/5/13		23/5/13		24/5/13		25/5/13	
	preTPE	postTPE	preTPE	postTPE	preTPE	postTPE	preTPE	postTPE	preTPE	postTPE
free T4 (pmol/L)	>97.8	>97.8	>97.8	81.8	82.9	50.5	61.8	42.0	56.5	42.1
free T3 (pmol/L)	18.0	13.4	14.1	10.3	8.6	7.2	6.6	5.5	5.7	4.6
TSH (mIU/L)	<0.015	<0.015	<0.015	0.015	<0.015	0.018	<0.015	0.016	<0.015	0.016

	26/5/13		27/5/13	28/5/13	30/5/13	1/6/13	3/6/13		24/6/13	18/7/13
	preTPE	postTPE		POD1	POD3	POD5	POD7		POD28	POD52
free T4 (pmol/L)	61.8	44.4	52.1	49.8	37.8	19.6	9.7		18.5	23.3
free T3 (pmol/L)	5.8	5.1	5.5	4.0	3.7	2.6	4.8		5.5	
TSH (mIU/L)	<0.015	0.143	<0.015	<0.015	<0.015	<0.015	<0.015		7.77	0.164

7. Outcome & follow up

Figure: Evolution of serum thyroxine level



7. Outcome & follow up

Clinical:

Rapid improvement of symptomatology after TPE

No major complications of surgery

Discharged Day 5 after surgery

Biochemical:

Hypothyroidism – Levothyroxine was prescribed

8. Learning points

Fulminant AIT: treated with glucocorticoids, a thionamide and potassium perchlorate

Thyroidectomy indicated in AIT refractory to medical treatment

Plasmapheresis rapidly reduces thyroid hormone levels and reduces perioperativer risk in patients with thyrotoxicosis

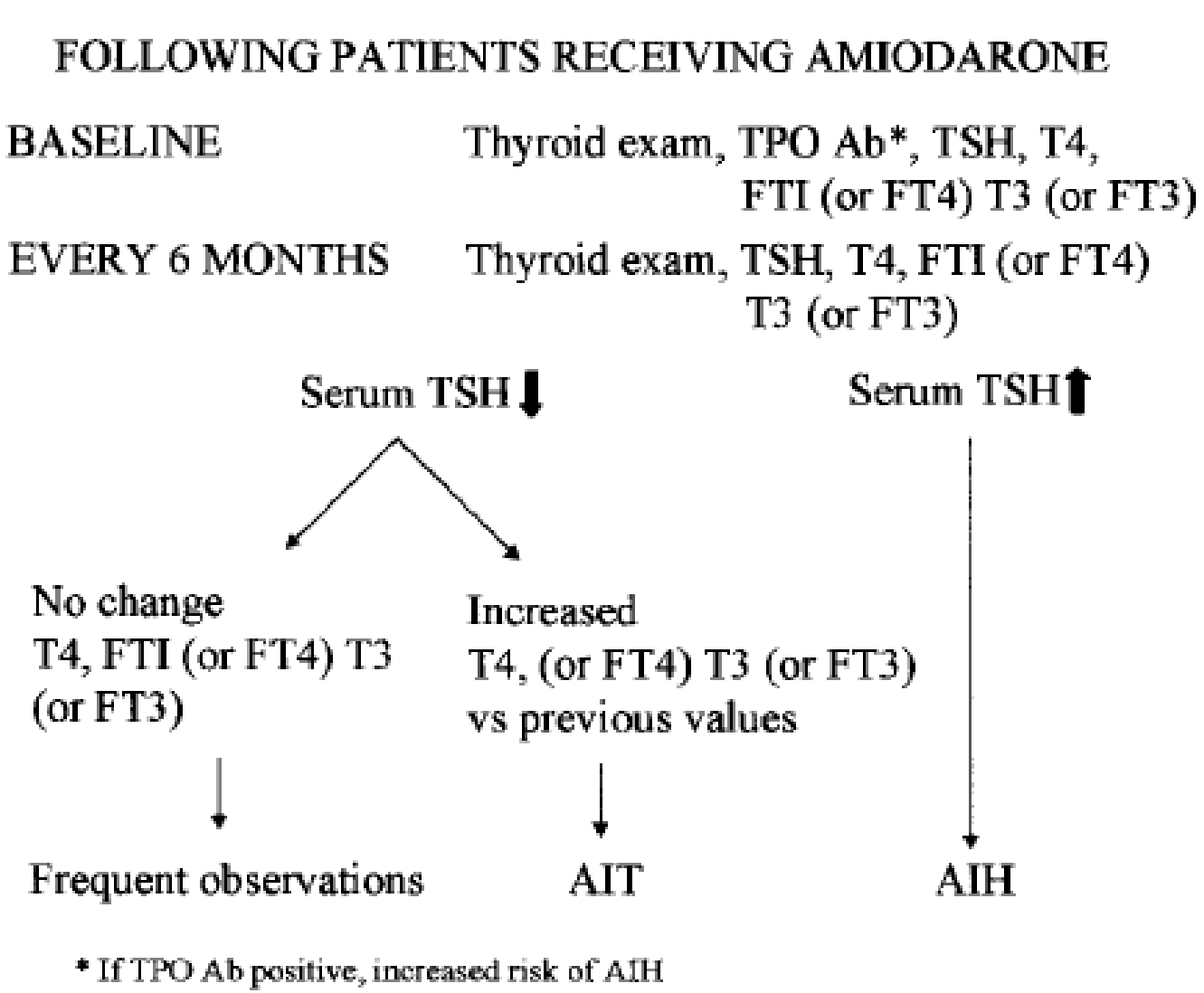


FIG. 8. Flow chart for following patients receiving amiodarone.

J Clin Endocrinol Metab, June 2010, 95(6):2529–2535

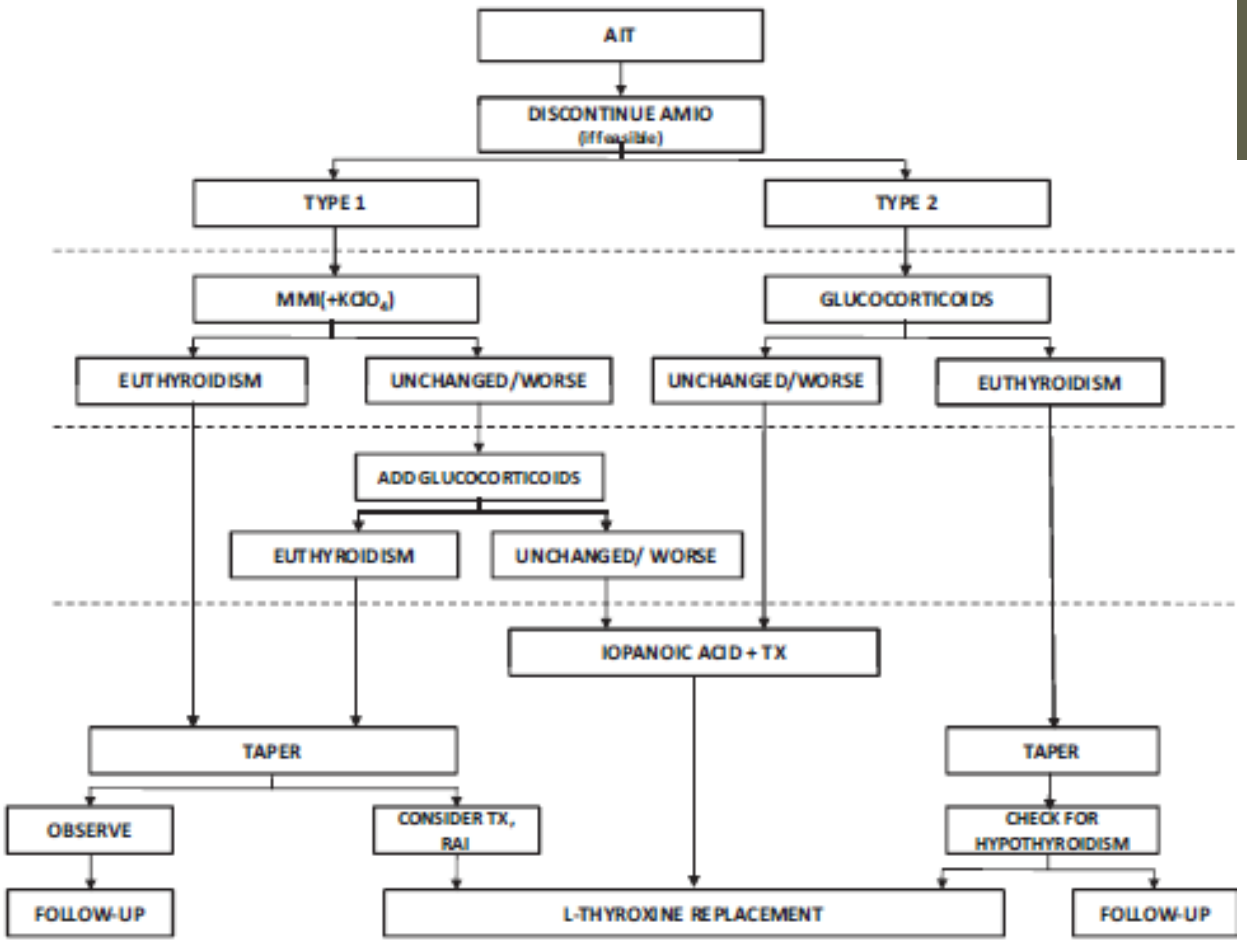


FIG. 1. Proposed algorithm for the management of patients with AIT. Patients with type 1 AIT are preferably treated with methimazole (starting dose, depending on the severity of hyperthyroidism, 40–60 mg/d associated with potassium perchlorate, ≤1 g/d). We continue methimazole, at lower doses, until reaching euthyroidism; potassium perchlorate is given for 4–6 wk. Our preferred medical option for patients with type 2 AIT is glucocorticoids, which are given at a starting dose of 0.5–0.7 mg prednisone/kg body weight per day; treatment is usually continued for 3 months; however, in some cases, a longer period of therapy may be necessary. For further details, see text. AMIO, Amiodarone; TX, total thyroidectomy.