Ipotiroidismo

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Dipartimento di Scienze Mediche e Sperimentali,
Università degli Studi di Brescia

- ✓ IPOTIROIDISMO: NUOVE FORMULAZIONI
- ✓ IPOTIROIDISMO SUB-CLINICO: SELENIO?

Dispensed prescriptions Mn		2009	2010	2011	2012	2013
Total U.S. market		**3,953**	**3,995**	**4,022**	**4,139**	**4,208**
1	acetaminophen/hydrocodone	129.4	132.1	136.7	136.4	129.2
2	levothyroxine	100.2	103.2	104.7	112.2	115.2
3	lisinopril	83.0	87.6	88.8	99.1	101.5
4	metoprolol	76.9	76.6	76.3	82.6	83.9
5	simvastatin	84.1	94.4	96.8	89.3	79.1
6	amlodipine	52.1	57.8	62.5	69.1	74.0
7	metformin	53.8	57.0	59.1	67.8	72.8
8	omeprazole	45.6	53.5	59.4	66.6	70.7
9	atorvastatin	51.7	45.3	43.3	55.5	68.4
10	albuterol	54.5	55.1	56.9	61.2	63.5
11	amoxicillin	52.8	52.4	53.8	52.8	54.2
12	hydrochlorothiazide	47.9	47.8	48.1	51.2	50.2
13	alprazolam	45.3	47.7	49.1	49.5	49.6
14	azithromycin	54.7	53.6	56.2	54.6	48.6
15	fluticasone	30.1	34.8	38.4	42.1	45.3
16	furosemide	43.8	43.6	42.3	44.1	45.0
17	gabapentin	25.7	29.6	33.4	38.6	43.9
18	sertraline	34.8	36.2	37.6	39.7	41.7
19	zolpidem	42.7	43.7	44.6	44.0	41.5
20	tramadol	25.5	28.0	33.9	39.3	41.5
21	citalopram	27.3	32.2	37.8	41.6	39.5
22	prednisone	27.8	28.7	33.7	35.2	36.5
23	acetaminophen/oxycodone	36.7	37.9	38.8	38.0	35.9
24	ibuprofen	30.3	31.1	32.6	34.2	35.1
25	pravastatin	17.2	20.2	23.9	33.3	34.7

Source: IMS Health, National Prescription Audit, Dec 2013

www.imshealth.com

CLINICAL REVIEW

For the full versions of these articles see bmj.com

Management of hypothyroidism in adults

Bijay Vaidya,[1] Simon H S Pearce[2]

[1]Department of Endocrinology, Royal Devon and Exeter Hospital, Exeter EX2 5DW, and Peninsula Medical School, Exeter

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Cite this as: *BMJ* 2008;337:a801
doi:10.1136/bmj.a801

Hypothyroidism is one of the commonest chronic disorders in Western populations. In the United Kingdom, the annual incidence of primary hypothyroidism in women is 3.5 per 1000 and in men 0.6 per 1000.[1] During 2006 12 million prescriptions for levothyroxine (50 µg or 100 µg tablets) were dispensed in England, equivalent to about 1.6 million people taking long term thyroid replacement therapy, about 3% of the population.[2] The management of hypothyroidism is generally considered straightforward and is mostly carried out in primary care in the UK. Cross sectional surveys of patients taking levothyroxine have, however, shown that between 40% and 48% are either over-treated or under-treated.[3 4] Furthermore, a to a severe impairment of consciousness, termed "myxoedema coma" (box 2). Advanced presentations of hypothyroidism are rarely seen nowadays in developed countries.

How to diagnose hypothyroidism?

The diagnosis of primary hypothyroidism is confirmed by an increase in the serum thyroid stimulating hormone concentration above the upper limit of the reference range. Adults presenting with symptomatic hypothyroidism often have a thyroid stimulating hormone level in excess of 10 mU/l, coupled with a reduction in the serum free or total thyroxine concentration below the reference range. Some adults

BMJ. 28:337-348, 2008

http://www.agenziafarmaco.gov.it

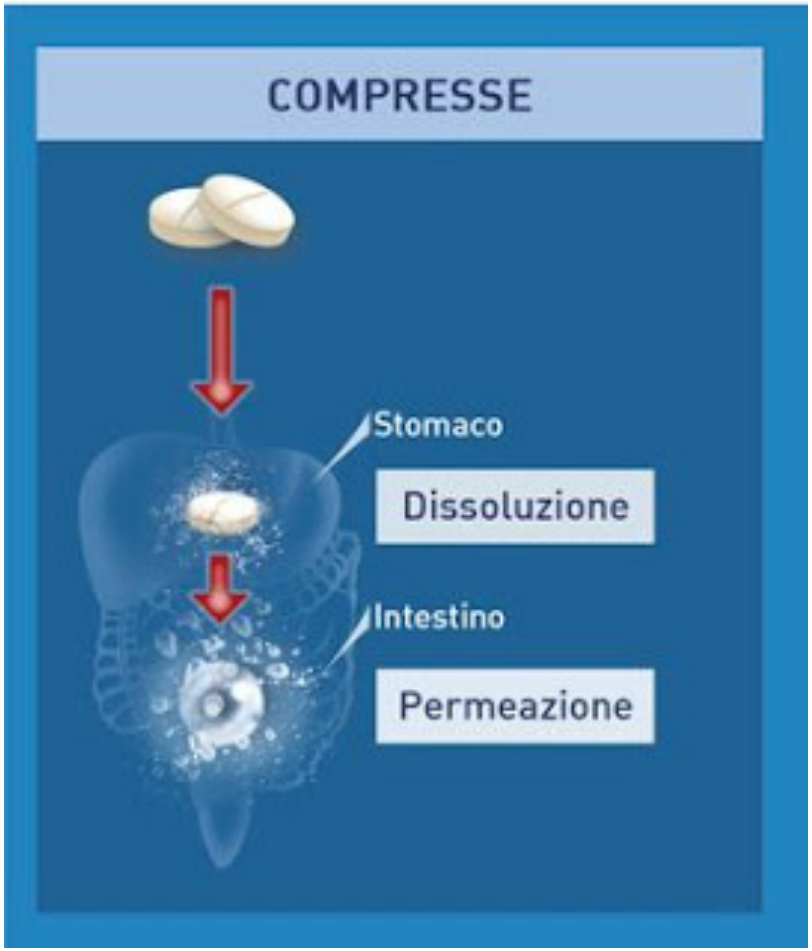
Comunicato Stampa 313, 31/07/2013

Studio AIFA fotografa correttezza cure nella popolazione anziana/fragile

Un anziano su due oltre i 65 anni nel nostro Paese assume dai 5 ai 9 farmaci al giorno.

I pazienti fragili aumentano il numero di farmaci assunti giornalmente di 3 principi attivi nel primo anno.

Quasi il 60% della popolazione ultra-65enne e il 50% dei pazienti fragili manifestano scarsa aderenza alle terapie.



Dopo somministrazione orale il 60-90% di LT4 viene assorbita nell'intestino tenue. La fase di dissoluzione, direttamente correlata al pH gastrico, è elemento chiave per cui la terapia in compresse deve essere somministrata a stomaco vuoto la mattina a digiuno almeno 30 minuti prima di fare colazione.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thyroxine in Goiter, *Helicobacter pylori* Infection, and Chronic Gastritis

Marco Centanni, M.D., Lucilla Gargano, M.D., Gianluca Canettieri, M.D., Nicola Viceconti, M.D., Antonella Franchi, M.D., Gianfranco Delle Fave, M.D., and Bruno Annibale, M.D.

ABSTRACT

CONCLUSIONS

Patients with impaired acid secretion require an increased dose of thyroxine, suggesting that normal gastric acid secretion is necessary for effective absorption of oral thyroxine.

Best Practice & Research Clinical Endocrinology & Metabolism 23 (2009) 781–792

Contents lists available at ScienceDirect

Best Practice & Research Clinical Endocrinology & Metabolism

journal homepage: www.elsevier.com/locate/beem

8

Conditions and drugs interfering with thyroxine absorption

Llanyee Liwanpo, MD, Doctor *, Jerome M. Hershman, MD, Professor

Department of Endocrinology, VA Greater Los Angeles Healthcare System, Los Angeles, CA, USA

Conditions and medications that may affect absorption of levothyroxine.

Foods	Medical conditions	Drugs
Food intake	Jejunoileal bypass or other bowel resection	Cholestyramine
Dietary fiber	Inflammatory bowel disease	Colesevelam
Espresso coffee	Celiac disease	Ferrous sulfate
	Lactose intolerance	Sucralfate
	H. pylori infection	Calcium carbonate
	Chronic gastritis of the stomach body	Aluminum hydroxide
		Sevelamer hydrochloride
		Lanthanum carbonate
		Raloxifene
		Proton pump inhibitors
		Orlistat

THYROID
Volume 24, Number 12, 2014

DOI: 10.1089/thy.2014.0028

SPECIAL ARTICLE

Guidelines for the Treatment of Hypothyroidism

Prepared by the American Thyroid Association
Task Force on Thyroid Hormone Replacement

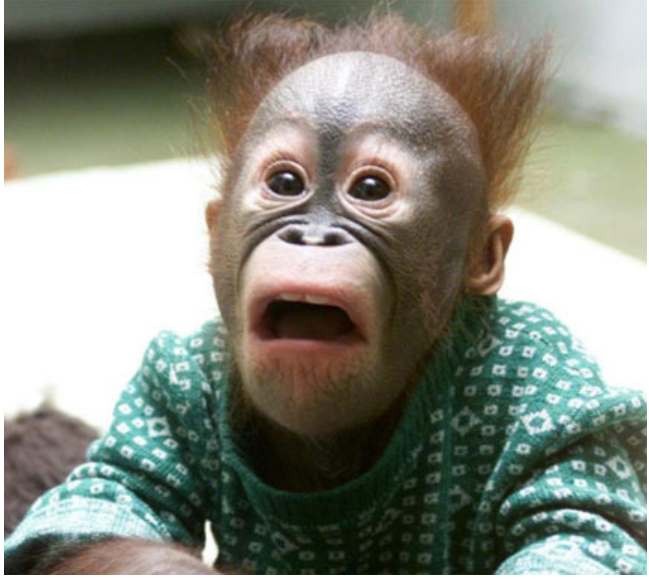
Jacqueline Jonklaas,[1*†] Antonio C. Bianco,[2*‡] Andrew J. Bauer,[3†] Kenneth D. Burman,[4†] Anne R. Cappola,[5†] Francesco S. Celi,[6‡] David S. Cooper,[7†] Brian W. Kim,[2‡] Robin P. Peeters,[8‡] M. Sara Rosenthal,[9†] and Anna M. Sawka[10†]

3a. How should levothyroxine administration be timed with respect to meals and beverages in order to maintain maximum, consistent absorption?

■ RECOMMENDATION

Because co-administration of food and levothyroxine is likely to impair levothyroxine absorption, we recommend that, if possible, levothyroxine be consistently taken either 60 minutes before breakfast or at bedtime (3 or more hours after the evening meal) for optimal, consistent absorption.

Weak recommendation. Moderate quality of evidence.



Abstract

Am J Health Syst Pharm. 2015 Mar 1;72(5):373-7. doi: 10.2146/ajhp140250.

Alternative schedules of levothyroxine administration.

Geer M[1], Potter DM[1], Ulrich H[1].

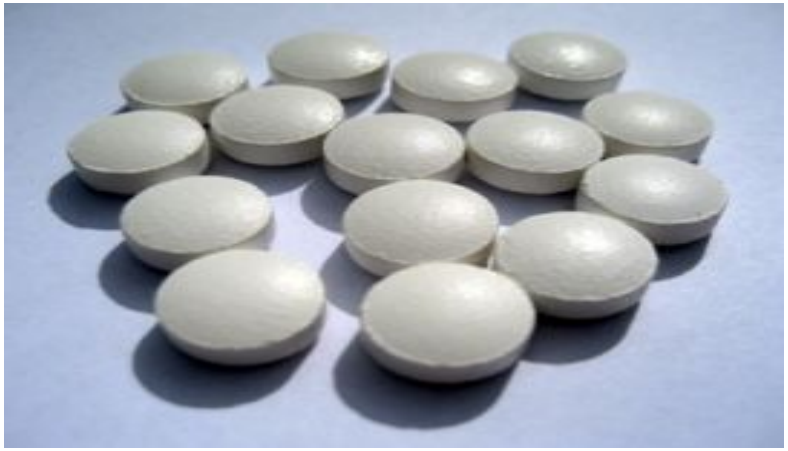
Author information

Abstract

PURPOSE: Published evidence on bedtime versus prebreakfast administration of levothyroxine is reviewed.

SUMMARY: Because levothyroxine absorption has been shown to increase when the drug is administered to patients in a fasted state, the standard recommendation is that levothyroxine be taken one half to one hour prior to breakfast and at least four hours before or after potentially interacting drugs. However, compliance with this recommendation may be problematic for patients with unpredictable or variable schedules. A literature search identified four published studies of bedtime levothyroxine dosing. Two of the studies demonstrated a significant decrease in levels of thyroid-stimulating hormone (TSH) with levothyroxine administration at bedtime versus 30 minutes before breakfast, one study showed an increase in TSH when levothyroxine was taken at bedtime versus one hour before breakfast, and one study found no significant differences in TSH levels or other thyroid function monitoring limitations with bedtime versus standard dosing in subjects naive to levothyroxine therapy. The inconsistent study findings may be attributable to a number of variables, including dietary differences among the study populations, the use of potentially interacting supplements in one study, and variable intervals between levothyroxine administration and food intake. Neither dosing method correlated with substantial changes in assessments of quality of life or symptom severity; in two of the studies, patients indicated a preference for bedtime levothyroxine administration.

CONCLUSION: Based on the available literature, bedtime administration of levothyroxine is an option for patients with hypothyroidism who want to avoid taking their medication with food.



timeline

1970

2012

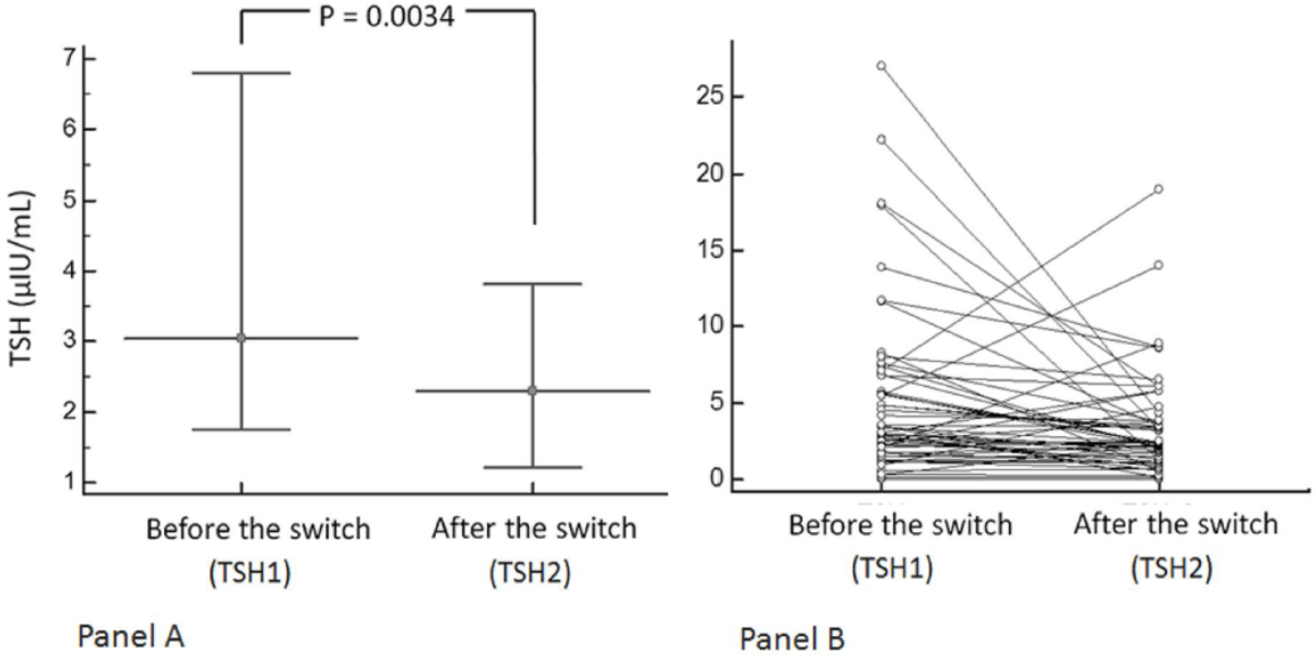
3 Aprile 1973

I farmaci in forma liquida non necessitano della fase di dissoluzione, si miscelano direttamente con I fluidi gastrointestinali, rendendosi subito disponibili, anche in casi di patologie come la celiachia e l'intolleranza al lattosio. Le soluzioni liquide, inoltre, garantiscono una migliore permeazione del principio attivo.

COMPARISON OF TSH LEVELS WITH LIQUID FORMULATION VERSUS TABLET FORMULATIONS OF LEVOTHYROXINE IN THE TREATMENT OF ADULT HYPOTHYROIDISM.

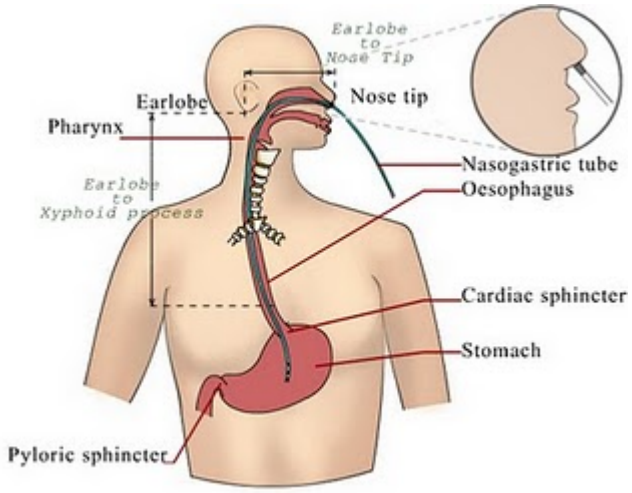
Running title: LT4 tablets versus oral solution

Davide Brancato, MD, Alessandro Scorsone, MD, Gabriella Saura, MD, Lidia Ferrara, MD, Anna Di Noto, MD, Vito Aiello, MD, Mattia Fleres, MD, Vincenzo Provenzano, MD.

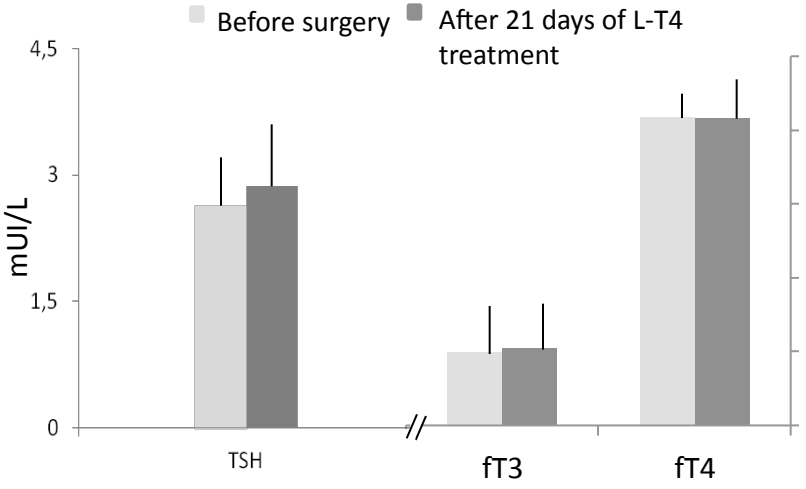


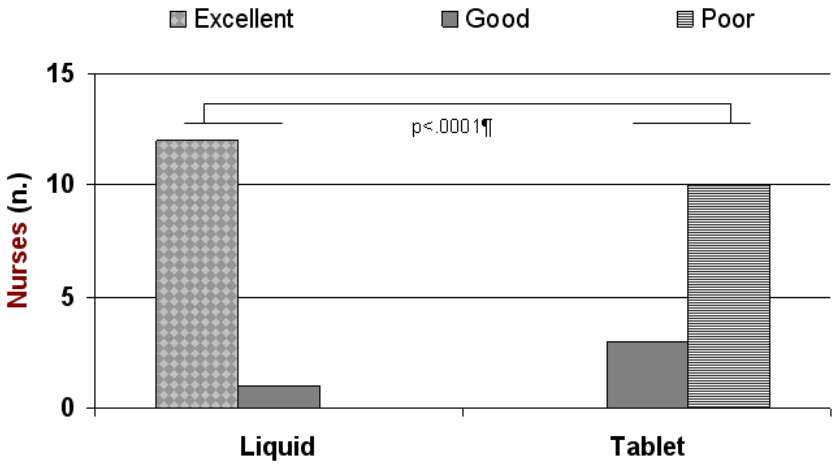
Conclusion. Our study confirms that LT4-OS could have an increased absorption rate in comparison to LT4 tablets, especially when other factors interfering with LT4 absorption are present.

Comparison between liquid and tablet levothyroxine formulations in patients treated through enteral feeding tube.



	Patients treated with L-T4 *Tablet form*	Patients treated with L-T4 in *Liquid form*	P value
Patients (n.)	10	10	-
Gender (M/F)	9/1	9/1	Ns
Age (yrs)	68±5.8	69.1±5.1	Ns
BMI (Kg/cm^2)	23±2.1	23.1±1.9	Ns
TSH (mUI/L)	2.50±1.18	2.79±1.03	Ns
fT4 (pg/mL)	12.31±1.89	12.68±2.68	Ns
fT3 (pg/mL)	3.21±0.56	3.09±0.62	Ns





Pirola I et al, J Endocrinol Invest. 2014 Jun;37(6):583-7

J Clin Endocrinol Metab, December 2014, 99(12):4481–4486

Switching Levothyroxine From the Tablet to the Oral Solution Formulation Corrects the Impaired Absorption of Levothyroxine Induced by Proton-Pump Inhibitors

Roberto Vita, Giovanna Saraceno, Francesco Trimarchi, and Salvatore Benvenga

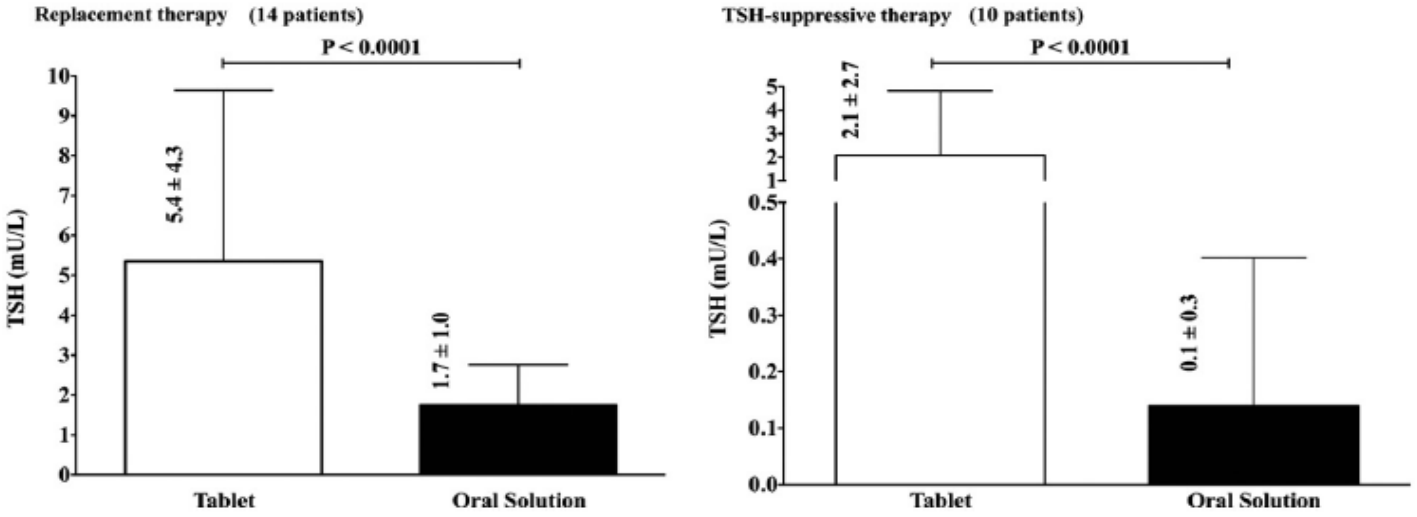


Figure 1. Serum TSH values (means ± SD) with LT4 therapy (□, tablet LT4; ■, oral solution) while maintaining therapy with PPIs. The switch was performed at the same daily dose.

Fallahi et al. BMC Gastroenterology (2016) 16:22
DOI 10.1186/s12876-016-0439-y

BMC Gastroenterology

RESEARCH ARTICLE Open Access

Reversible normalisation of serum TSH levels in patients with autoimmune atrophic gastritis who received L-T4 in tablet form after switching to an oral liquid formulation: a case series

Poupak Fallahi, Silvia Martina Ferrari, Ilaria Ruffilli and Alessando Antonelli*

Abstract

Background: L-thyroxine (L-T4) malabsorption is a potential concern in patients with autoimmune atrophic gastritis.

Methods: We evaluated five patients with autoimmune gastritis, who showed high serum thyrotropin (TSH) levels (in the hypothyroid range) while in therapy with L-T4 in tablet. All patients were switched to receive an oral L-T4 liquid formulation maintaining the same dosage.

Results: In all patients who received L-T4 in tablet form after switching to an oral liquid formulation with the same L-T4 dosage, TSH circulating levels were normalized. In four patients who were switched back again to receive L-T4 in tablets, maintaining the dosage, TSH levels worsened again reaching levels in the hypothyroid range.

Conclusions: The fact that the change from tablets to liquid oral formulation normalised serum TSH levels, and that switching back to tablets caused thyrotropin levels to worsen, leads us to believe that absorption of L-T4 is greater with oral liquid formulations in these patients. These results suggest that the L-T4 oral liquid formulation could circumvent the pH alteration resulting from atrophic gastritis.

Keywords: L-thyroxine, Liquid L-thyroxine, Hypothyroidism, Gastritis

A Double-Blind Placebo-Controlled Trial of Liquid Thyroxine Ingested at Breakfast: Results of the TICO Study

Carlo Cappelli,[1] Ilenia Pirola,[1] Linda Daffini,[1] Annamaria Formenti,[1] Carmelo Iacobello,[2] Alessandra Cristiano,[1] Elena Gandossi,[1] Enrico Agabiti Rosei,[1] and Maurizio Castellano[1]

TABLE 1. BASELINE DEMOGRAPHIC AND CLINICAL CHARACTERISTICS ACCORDING TO REGIMEN SEQUENCE OF LT4 ADMINISTRATION

	All patients	*Sequence "at" → "before"*	*Sequence "before" → "at"*	p-*Value*
Number of patients	77	38	39	
Sex (female/male)	64/13	32/6	32/7	NS
Age (years)	45.4 ± 13.7	46.2 ± 14.1	44.8 ± 13.4	NS
BMI	24.2 ± 4.7	24.1 ± 4.1	24.3 ± 4.6	NS
Hashimoto thyroiditis (*n*)	66	33	33	NS
Total thyroidectomy (*n*)	11	5	6	
TSH (mIU/L)	15.3 (8.13–87.1)	15.1 (8.13–33.2)	16.2 (10.1–87.1)	NS
fT4 (pg/mL)	10.8 (5.3–17.5)	10.3 (5.7–17.5)	11.1 (5.3–16.1)	NS
fT3 (pg/mL)	3.0 (2.1–4.4)	3.0 (2.1–4.4)	3.0 (2.1–4.2)	NS

Values are reported as mean ± standard deviation or as median (min–max) values for variables with normal or non-normal distribution, respectively.

LT4, levothyroxine; NS, not significant; BMI, body mass index; TSH, thyrotropin; fT4, free thyroxine; fT3, free triiodothyronine.

Conclusions: The TICO study suggests that a liquid LT4 formulation can be ingested directly at breakfast, thus potentially improving therapeutic compliance. This observation is of considerable clinical relevance, since non-adherence to LT4 therapy requirements is more likely to cause variability in serum TSH concentrations.

Thyroid. 2016 Feb;26(2):197-202

Endocrine
DOI 10.1007/s12020-015-0788-2

ORIGINAL ARTICLE

Timing of breakfast does not influence therapeutic efficacy of liquid levothyroxine formulation

Silvia Morelli[1,2] · Gianpaolo Reboldi[1] · Sonia Moretti[1,2] · Elisa Menicali[1,2]
Nicola Avenia[2,3] · Efisio Puxeddu[1,2]

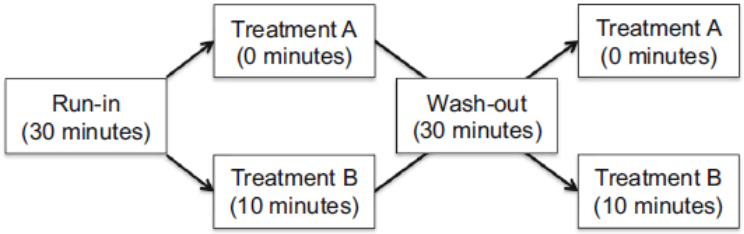
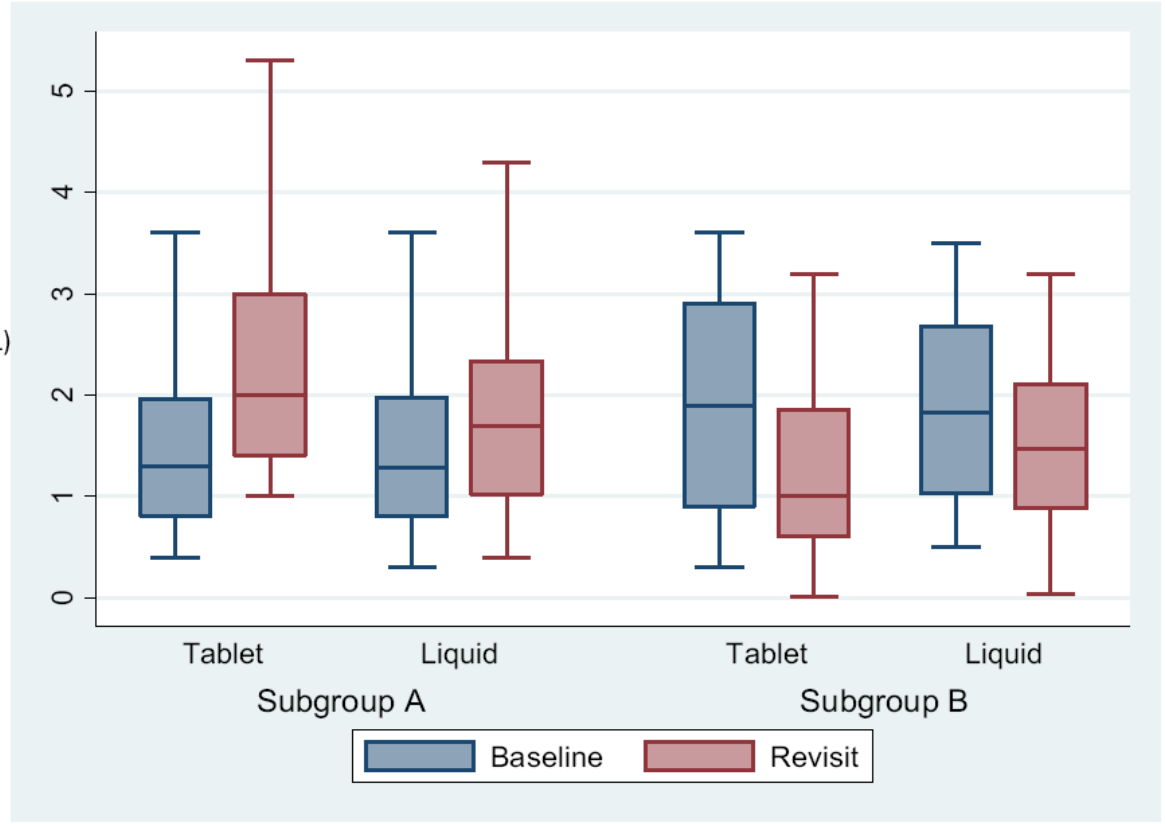


Fig. 1 Design of the study. After L-T4 oral solution dose titration, enrolled patients entered a 6-week run-in phase taking the drug 30 min before breakfast. At the end of this phase, the patients were randomized to the AB or BA treatment sequences, where A stays for a 6-week period in which the interval between the assumption of the drug and breakfast was 0 min and B for a 6-week period in which the interval was 10 min. A 6-week washout phase, in which the interval between the assumption of the drug and breakfast was 30 min, separated periods one and two of each treatment sequence in order to minimize a possible carry-over effect

Abstract Oral levothyroxine (L-T4) is the mainstay of hypothyroidism treatment. Many factors may influence its absorption, including the timing of administration. Objective of the study is to demonstrate the therapeutic equivalence of administering liquid L-T4 with breakfast or 10 min before breakfast. This was a pilot study conducted with a crossover design AB/BA where A stays for L-T4 with breakfast and B for L-T4 10 min before breakfast. A post hoc analysis was conducted to compare L-T4 administered at breakfast or 10 min before breakfast with L-T4 administered 30 min before breakfast. Sixty-one hypothyroid patients were enrolled and assigned to one of the two treatment sequences. All patients were evaluated for TSH levels at the end of each period. Fifty-nine patients completed the study. The mean thyrotropin concentration was 1.52 ± 0.73 μU/ml when L-T4 was administered with breakfast and 1.46 ± 0.81 μU/ml when it was taken 10 min before breakfast, without clinically and statistically significant differences ($P = 0.59$), regardless of treatment sequence and period. The mean thyrotropin concentration was 1.54 ± 0.9 μU/ml when L-T4 was administered at 0–10 min intervals before breakfast and 1.25 ± 0.7 μU/ml when it was taken 30 min before breakfast (ratio = 1.23, within our definition of equivalence set at 0.8–1.25). There is therapeutic equivalence between liquid L-T4 administration at breakfast or 10 min before breakfast.

Levothyroxine Liquid Solution Versus Tablet for Replacement Treatment in Hypothyroid Patients.



Conclusions. The use of L-thyroxine liquid formulation compared to tablet resulted in a significantly higher number of hypothyroid patients who maintained the euthyroid state in a 12 months of follow up, and a reduced variability in TSH values.

Negro N et al. Endocr Pract, 2014, in press

European Geriatric Medicine xxx (2014) xxx–xxx

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Research paper

Thyroid hormonal profile in elderly patients treated with two different levothyroxine formulations: A single institute survey

C. Cappelli *, I. Pirola, L. Daffini, E. Gandossi, B. Agosti, M. Castellano

Department of Clinical and Experimental Sciences, Endocrine and Metabolic Unit, Clinica Medica, University of Brescia, c/o 1 Medicina Spedali Civili di Brescia, Piazzale Spedali Civili no 1, 25100 Brescia, Italy

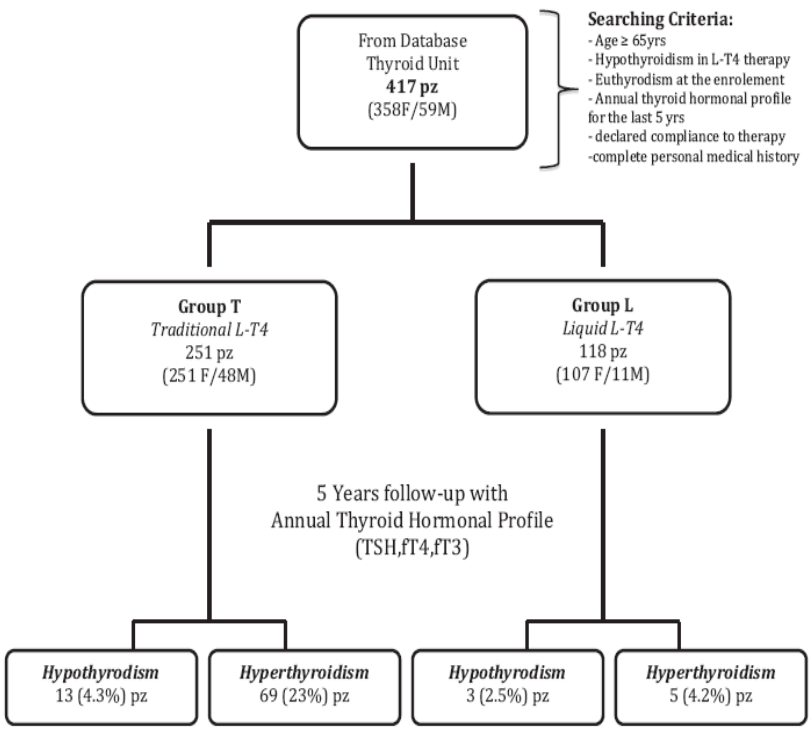

Fig. 1. Schematic diagram of the study design and data collection.

Table 2
Logistic regression analysis of developing subclinical or hyperthyroidism in the study population.

	Odds ratio (95% CI)	*P* value
Age (yrs)	1.00 (0.96–1.05)	NS
Gender (female)	1.51 (0.76–3.01)	NS
BMI (kg/cm^2)	0.54 (0.25–1.10) NS	NS
Thyroid disorder (Hashimoto thyroiditis)	0.72 (0.36–1.56) NS	NS
Concomitant drugs therapy	0.56 (0.25–1.10)	NS
Levothyroxine (tablets)	2.35 (1.14–4.83)	0.021

INTERNATIONAL THYROID CONGRESS

Orlando

17-23, October, 2015

http://www.ncbi.nlm.nih.gov/pubmed/?term=soft+gel+capsule+AND+thyroid

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1. The administration of L-thyroxine as **soft gel capsule** or liquid solution.
Vita R, Fallahi P, Antonelli A, Benvenga S.
Expert Opin Drug Deliv. 2014 Jul;11(7):1103-11. doi: 10.1517/17425247.2014.918101. Epub 2014 Jun 4. Review.
PMID: 24896369 [PubMed - indexed for MEDLINE]
Related citations

2. Tablet levothyroxine (L-T4) malabsorption induced by proton pump inhibitor; a problem that was solved by switching to L-T4 in **soft gel capsule**.

Abstract

OBJECTIVE:

To report a patient in whom the impaired absorption of tablet levothyroxine (L-T4) due to a proton pump inhibitor (PPI) use was corrected by switching the patient to the soft gel capsule.

4. A novel formulation of L-thyroxine (L-T4) reduces the problem of L-T4 malabsorption by coffee observed with traditional tablet formulations.

In 7 patients, post-switch TSH was 0.41 ± 0.46 (PH) versus 0.28 ± 0.20 pre-switch (PH) (P = 0.61) and 0.34 ± 0.30 (IH) versus 1.23 ± 1.47 pre-switch (IH) (P < 0.001)

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THYROID HORMONE PROFILE IN PATIENTS INGESTING SOFT GEL CAPSULE OR LIQUID LEVOTHYROXINE FORMULATIONS WITH BREAKFAST

	6 months before recruitment	At enrolment	6 months after soft gel capsule
TSH (mIU/L)	1.9 (0.5-4.1)	1.9 (0.5-4.0)	2.2 (0.5-4.5)
fT4 (pg/mL)	10.5 (8.6-13.8)	10.6 (8.6-13.8)	9.9 (8.0-13)*
fT3 (pg/mL)	2.7 (2.4-3.6)	2.7 (2.4-3.3)	2.5 (2.4-3.1)+

Median (min-max)

*p<0.0001 vs. 6 months before recruitment and at enrolment; +p<0.05 vs. 6 months before recruitment and at enrolment

Conclusion: Both liquid and soft gel formulations of L-T4 can be taken with breakfast. However, liquid L-T4 would be the preferred formulation for patients in whom even small changes in fT4 and fT3 levels is to be avoided.

Cappelli C et al, Int J Endocrinol in press

- ✓ IPOTIROIDISMO: NUOVE FORMULAZIONI
- ✓ IPOTIROIDISMO SUB-CLINICO: SELENIO?

Guidelines

European
Thyroid Journal

Eur Thyroid J 2013;2:215–228
DOI: 10.1159/000356507

Received: September 26, 2013
Accepted: October 7, 2013
Published online: November 27, 2013

2013 ETA Guideline: Management of Subclinical Hypothyroidism

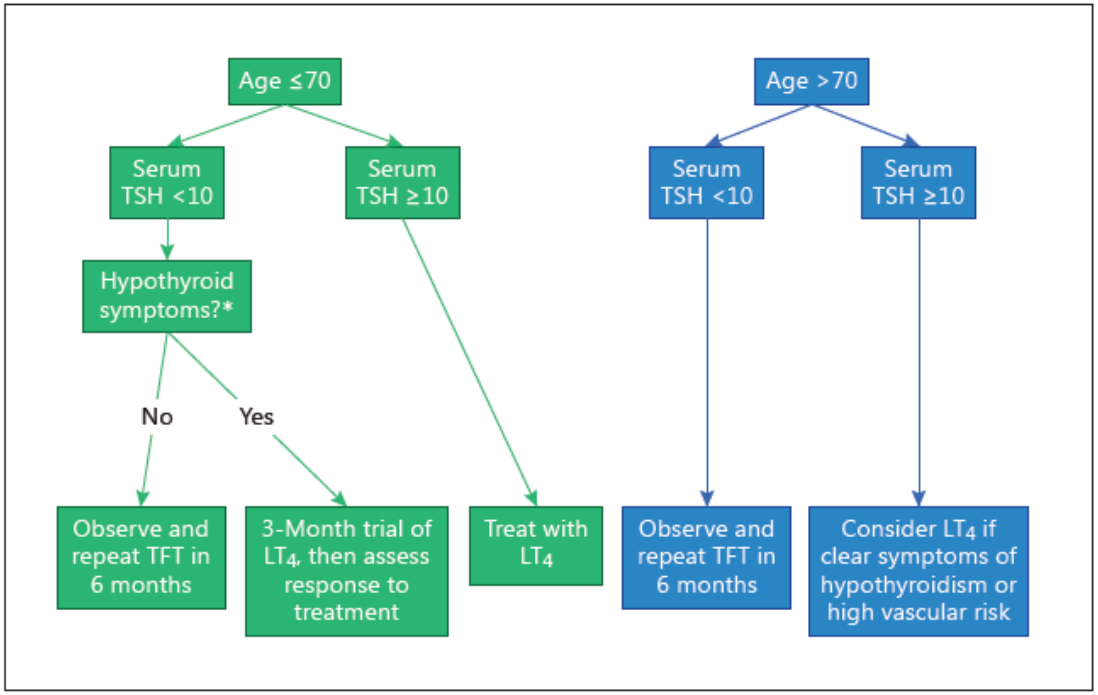
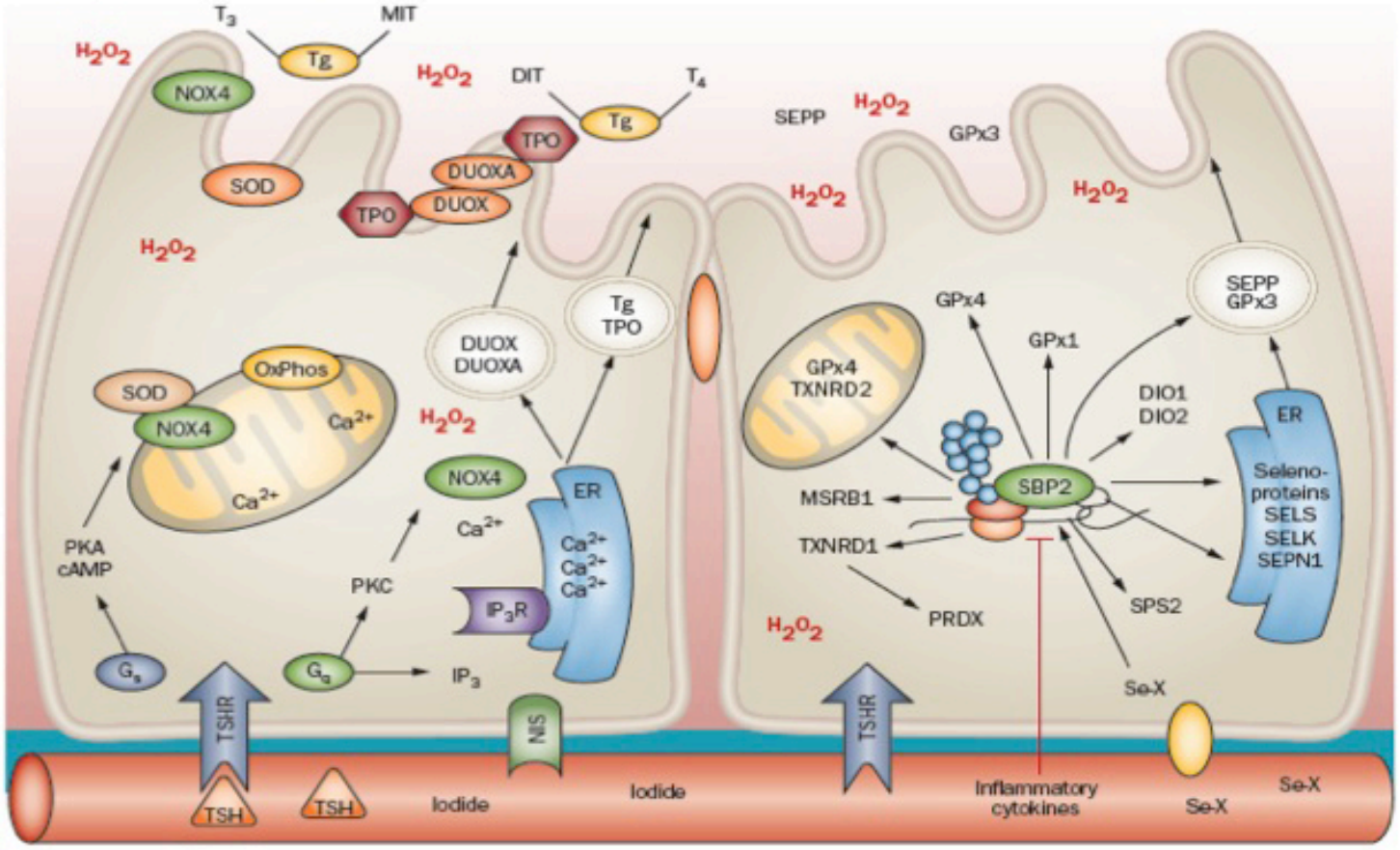


Fig. 1. Suggested management algorithm. Initial management of persistent subclinical hypothyroidism in non-pregnant adults: persistent subclinical hypothyroidism describes patients with elevated serum TSH and within reference range serum FT_4 on two occasions separated by at least 3 months. This algorithm is meant as a guide and clinicians are expected to use their discretion and judgement in interpreting the age threshold around 70 years. * Depending on circumstances, individuals with goitre, dyslipidaemia, and diabetes may also be considered for treatment, along with those with planning pregnancy in the near future.

Selenoproteine: glutatione perossidasi (GPx1 e GPx3)

Vie coinvolte nella generazione di perossido nella tiroide (sinistra) e nella protezione cellulare selenio-dipendente (destra)

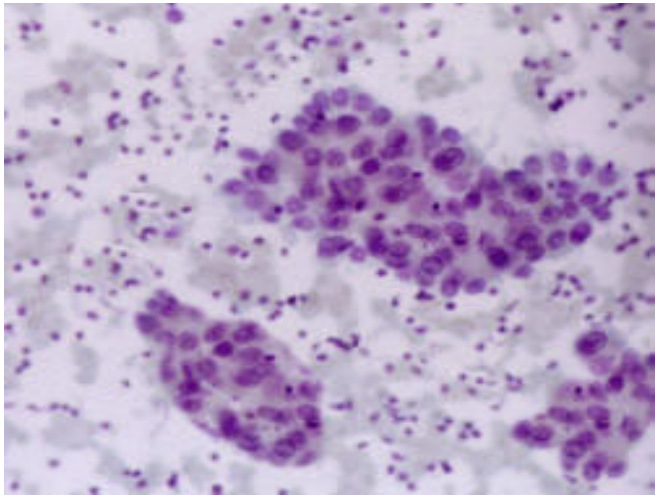


Modificata da Schomburg L. *Nat Rev Endocrinol* 2011 Oct 18 [Epub ahead of print]

IMPORTANZA DEL SELENIO

E'micronutriente essenziale ***necessario*** per la biosintesi di ***selenoproteine.***
La maggior parte delle selenoproteine note sono espressi nella tiroide
(tra cui alcuni con funzioni ancora sconosciute)

Selenoproteina	Abbreviazione	Funzione
Glutatione perossidasi	GPX	Catalizza la riduzione di H_2O_2 Protegge dallo stress ossidativo
GPx1 citosolica	GPX1	Attività antiossidante
GPx extracellulare	GPX3	Azione antinfiammatoria
GPx fosfolipidica	GPX4	Riduce gli idroperossidi fosfolipidici e regola l'apoptosi
Iodotironina deiodinasi	DIO	Catalizza la conversione di T4 e T3
DIO di tipo I	DIO1	Conversione di T4 in T3
DIO di tipo II	DIO2	Produzione locale (intracellulare) di T3 da T4
DIO di tipo III	DIO3	Produzione di rT3 da T4 e di T2 da T3
Tioredoxina reduttasi	TXNRD	Attività ossidoriducente con nicotinamide adenina dinucleotide fosfato (NADPH) come cofattore
Tioredoxina reduttasi citosolica	TXNRD1	Principale strumento antiossidante a livello cellulare
Tioredoxina reduttasi mitocondriale	TXNRD2	Regola la proliferazione cellulare

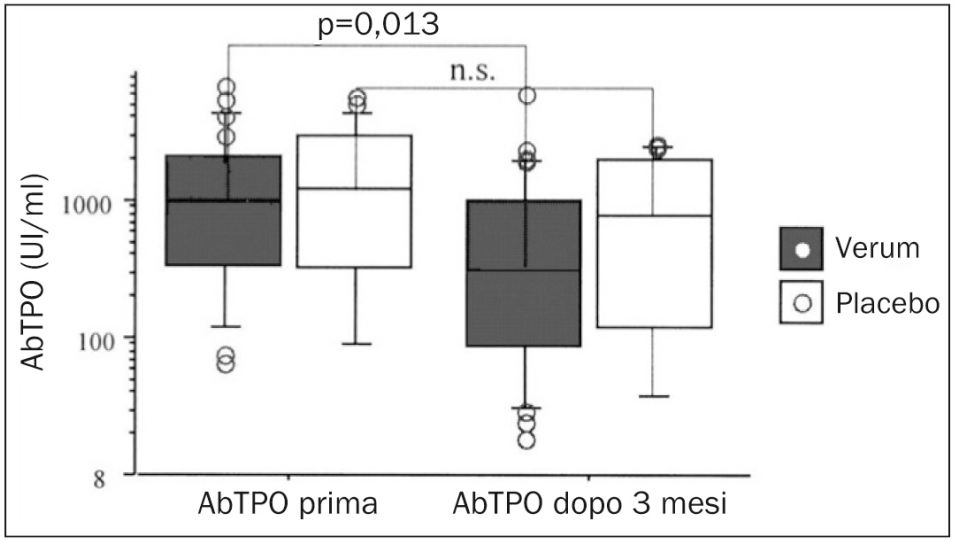


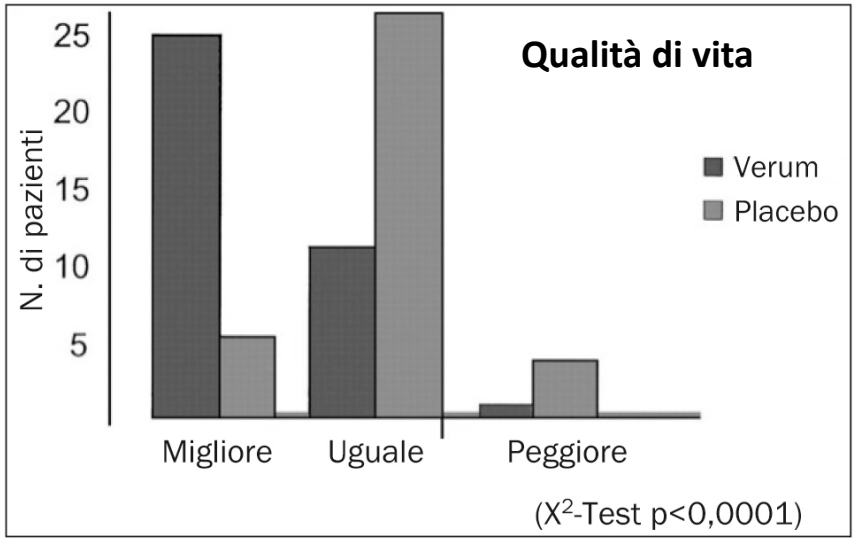
TIROIDITE CRONICA
Infiltrazione linfocitaria cronica
=
infiammazione cronica
=
cronica produzione di radicali liberi

J Clin Endocrinol Metab. 2002 Apr;87(4):1687-91.

Selenium supplementation in patients with autoimmune thyroiditis decreases thyroid peroxidase antibodies concentrations.

Gärtner R[1], Gasnier BC, Dietrich JW, Krebs B, Angstwurm MW.





SPECIAL FEATURE

Clinical Review

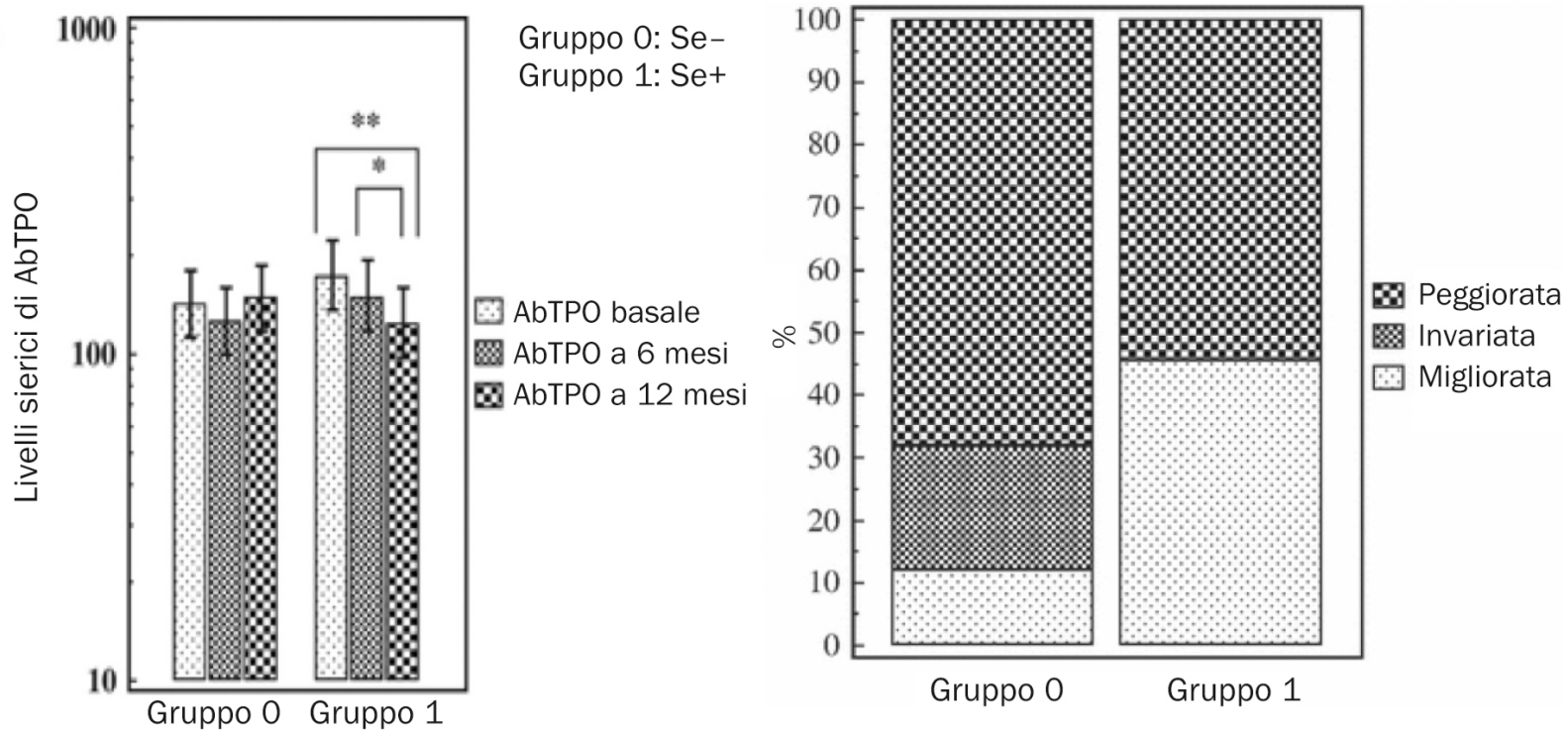
Selenium and the Thyroid: A Close-Knit Connection

Leonidas H. Duntas

Conclusions: Maintenance of "selenostasis" via optimal intake not only aids preservation of general health but also contributes substantially to the prevention of thyroid disease. (*J Clin Endocrinol Metab* 95: 5180–5188, 2010)

Supplementazione con selenio, AbTPO nella tiroidite di Hashimoto ed ecogenicità tiroidea

Pazienti affetti da HT in eutiroidismo

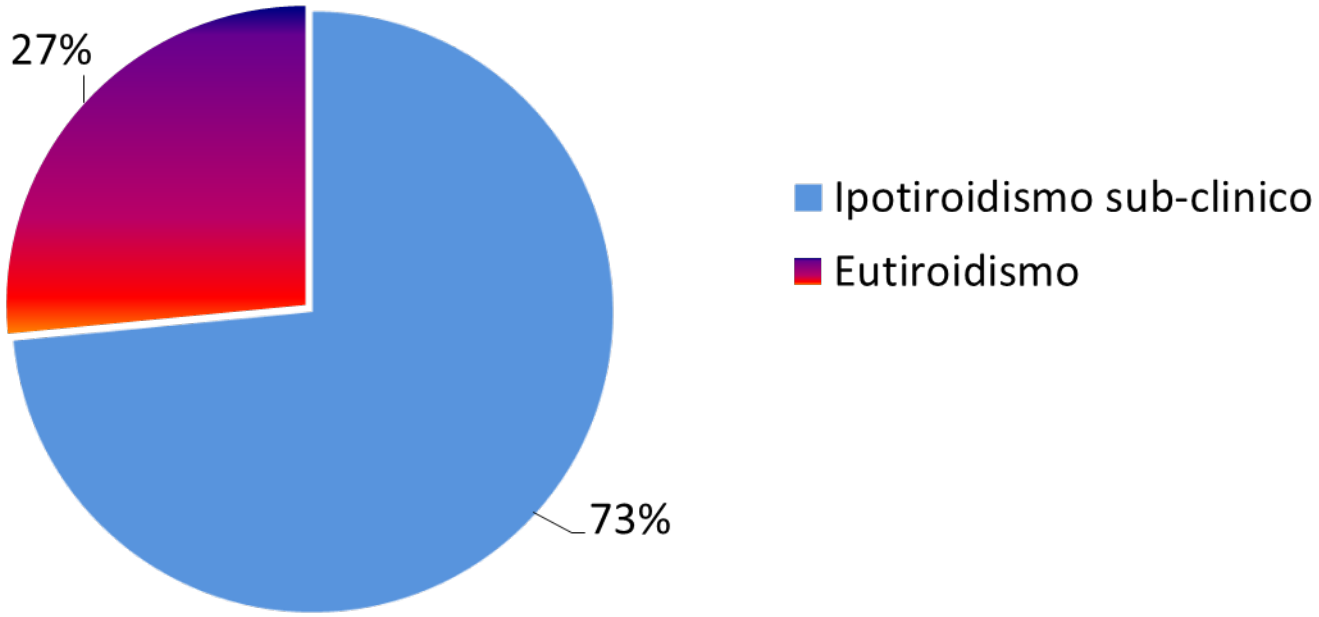


Conclusioni: effetti protettivi del selenio sul corso naturale della TH manifesti dopo 6 mesi, evidenti dopo 12 mesi. Nessun cambiamento dei valori di TSH o fT_4.

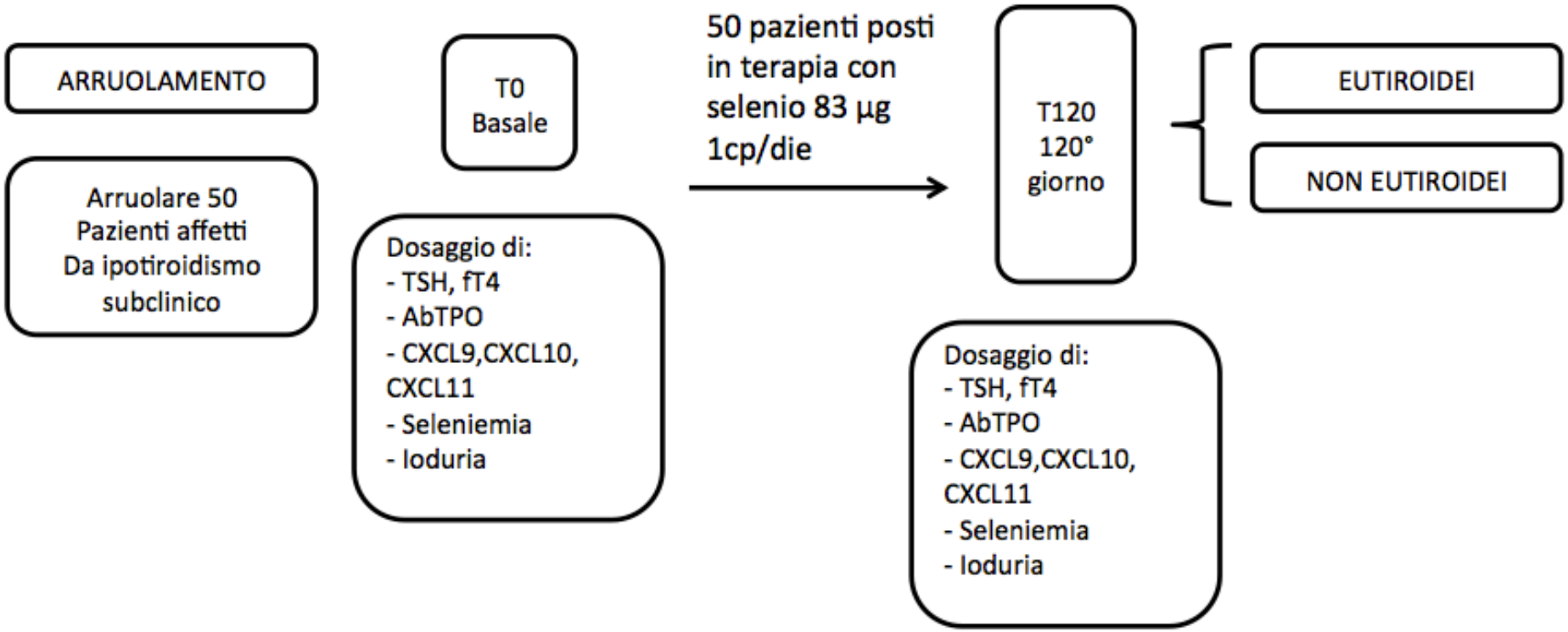
Nacamulli D, et al. *Clin Endocrinol (Oxf)* 2010;73(4):535-9

Ambulatorio Malattie della Tiroide

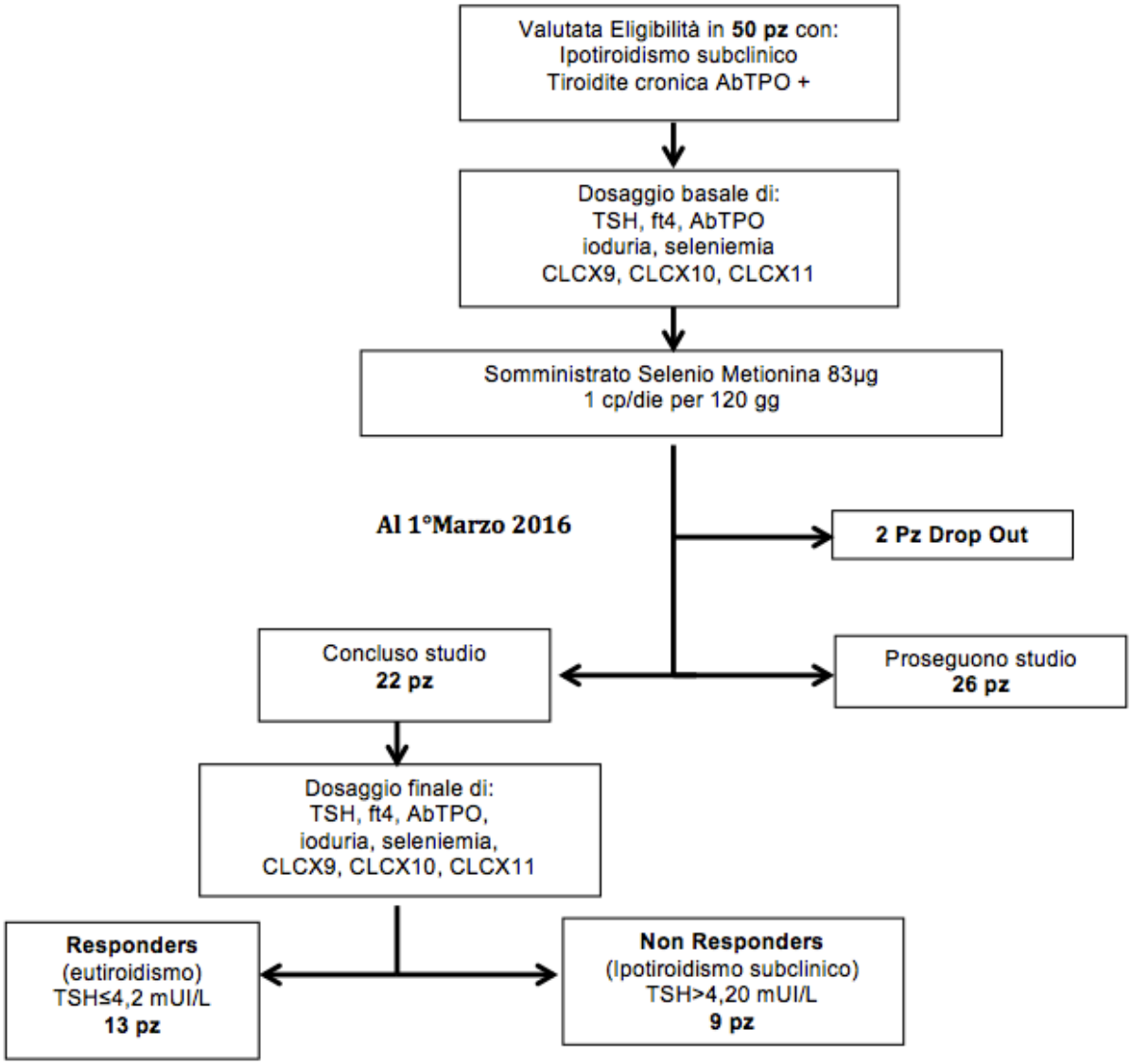
294 pazienti trattati con Selenio (Syrel®) per 4 mesi



Studio SETI (N.PROTOCOLLO 1981)



RISULTATI PRELIMINARI: Risultati al 1° marzo



Risultati

Caratteristiche della popolazione all'atto dell'arruolamento

Variabili	
Sesso (femmine/maschi)	18/4
Età (anni)	45.23±10.9 (22-64)
TSH (mUI/L)	6.31±2.57 (4.31-14.94)
fT4 (pg/mL)	10.2±1.3 (7.1-13.2)
AbTPO (UI/mL)	363.4±215.5 (118.2-1000)
Seleniemia (µg/L)	92.6±12.8 (64.4-116.8)
Ioduria (µg/L)	84.3±62.4 (19-256)
CXCL9 (pg/mL)	74.54±39.04 (57.23-91.84)
CXCL10 (pg/mL)	123.67±61.92 (96.22-151.12)
CXCL11(pg/mL)	49.66±41.41 (28.46-56.42)

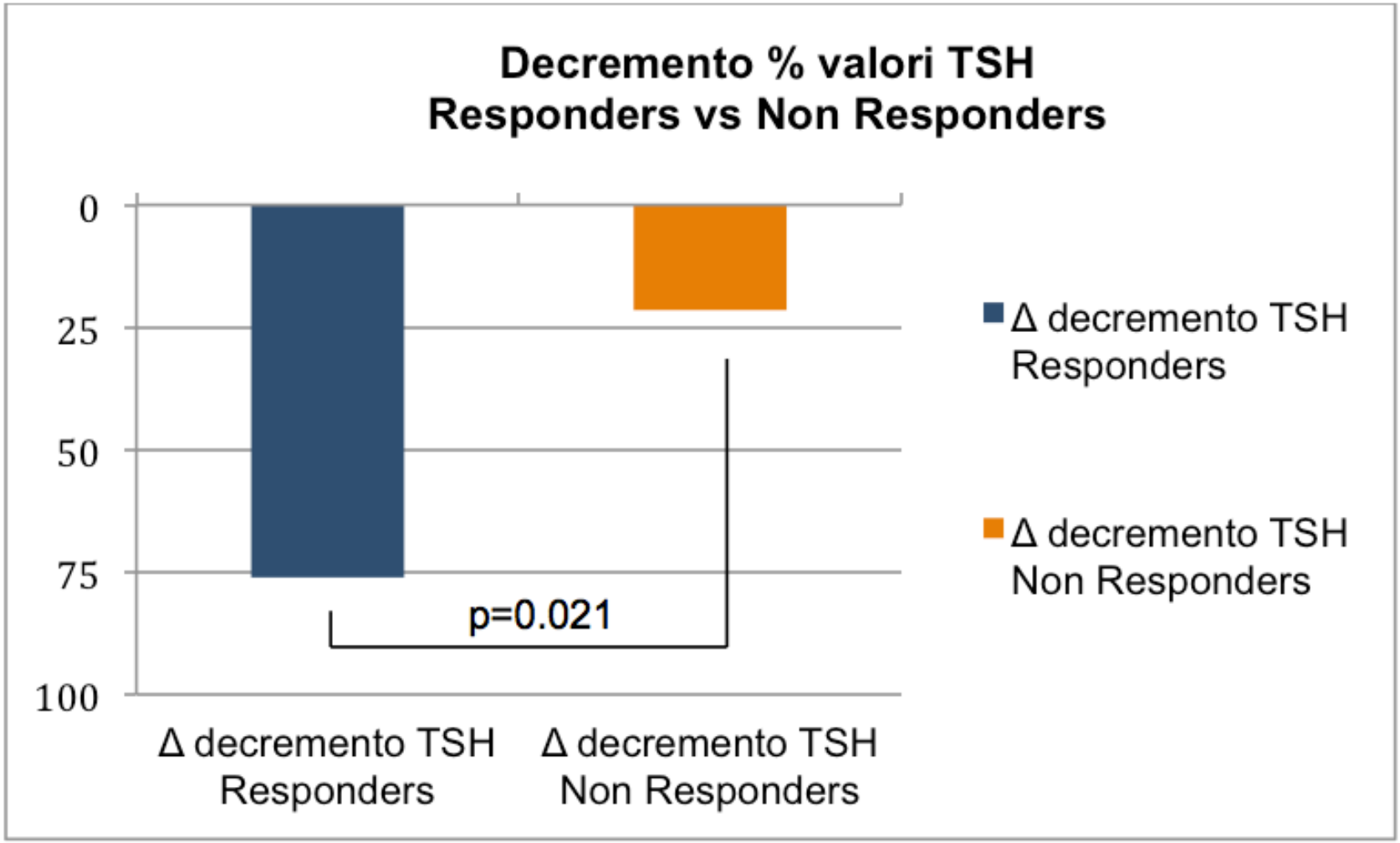
Risultati 1

p=0.021

	Pazienti Responders			Pazienti Non Responders		
	Pre-trattamento	Post-trattamento	P	Pre-trattamento	Post-trattamento	P
TSH (mUI/L)	5.33±0.93	3.22±0.79	**<0.001**	7.71±3.50	7.09±4.81	0.665
fT4 (pg/mL)	10.043±1.76	9.354±0.992	0.110	10.311±0.84	9.567±1.222	0.058
TPO_Ab (UI/mL)	408.9±428.7	381.38±363.39	0.756	297.8±411.3	304.14±384.75	0.962
Seleniemia (µg/L)	93.7±12.9	159.9±27.4	**<0.001**	91.0±13.3	145.6±25.8	**<0.001**
Ioduria (µg/L)	75.72±57.07	76.60±48.64	0.962	96.78±71.08	130.56±42.36	0.199
CXCL9 (pg/mL)	77.06±35.28	37.61±20.08	**<0.001**	70.91±45.92	52.54±30.40	0.276
CXCL10 (pg/mL)	124.89±61.24	125.17±48.19	0.980	121.90±66.58	127.80±50.51	0.681
CXCL11(pg/mL)	49.02±35.89	41.92±29.66	0.384	50.59±50.67	43.19±35.92	0.486

Seleniemia: incremento significativo dei valori di seleniemia post-trattamento sia nei Responders che nei Non Responders.

Decremento TSH



Risultati 1

	Pazienti Responders			Pazienti Non Responders		
	Pre-trattamento	Post-trattamento	P	Pre-trattamento	Post-trattamento	P
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Clinical Thyroidology / Original Paper

European
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Eur Thyroid J 2015;4:226–233
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IFNγ-Inducible Chemokines Decrease upon Selenomethionine Supplementation in Women with Euthyroid Autoimmune Thyroiditis: Comparison between Two Doses of Selenomethionine (80 or 160 µg) versus Placebo

Conclusions: Semet supplementation had no positive effect on thyroid echogenicity or TPOAb in our patients. However, we observed a Semet-dependent downregulation of the IFNγ-inducible chemokines, especially CXCL-9 and -10, which may serve as helpful biomarkers in future selenium supplementation trials.

Risultati 2

	Pazienti Responders			Pazienti Non Responders		
	Pre-trattamento	Post-trattamento	P	Pre-trattamento	Post-trattamento	P
TSH (mUI/L)	5.33±0.93	3.22±0.79	**<0.001**	7.71±3.50	7.09±4.81	0.665
fT4 (pg/mL)	10.043±1.76	9.354±0.992	0.110	10.311±0.84	9.567±1.222	0.058
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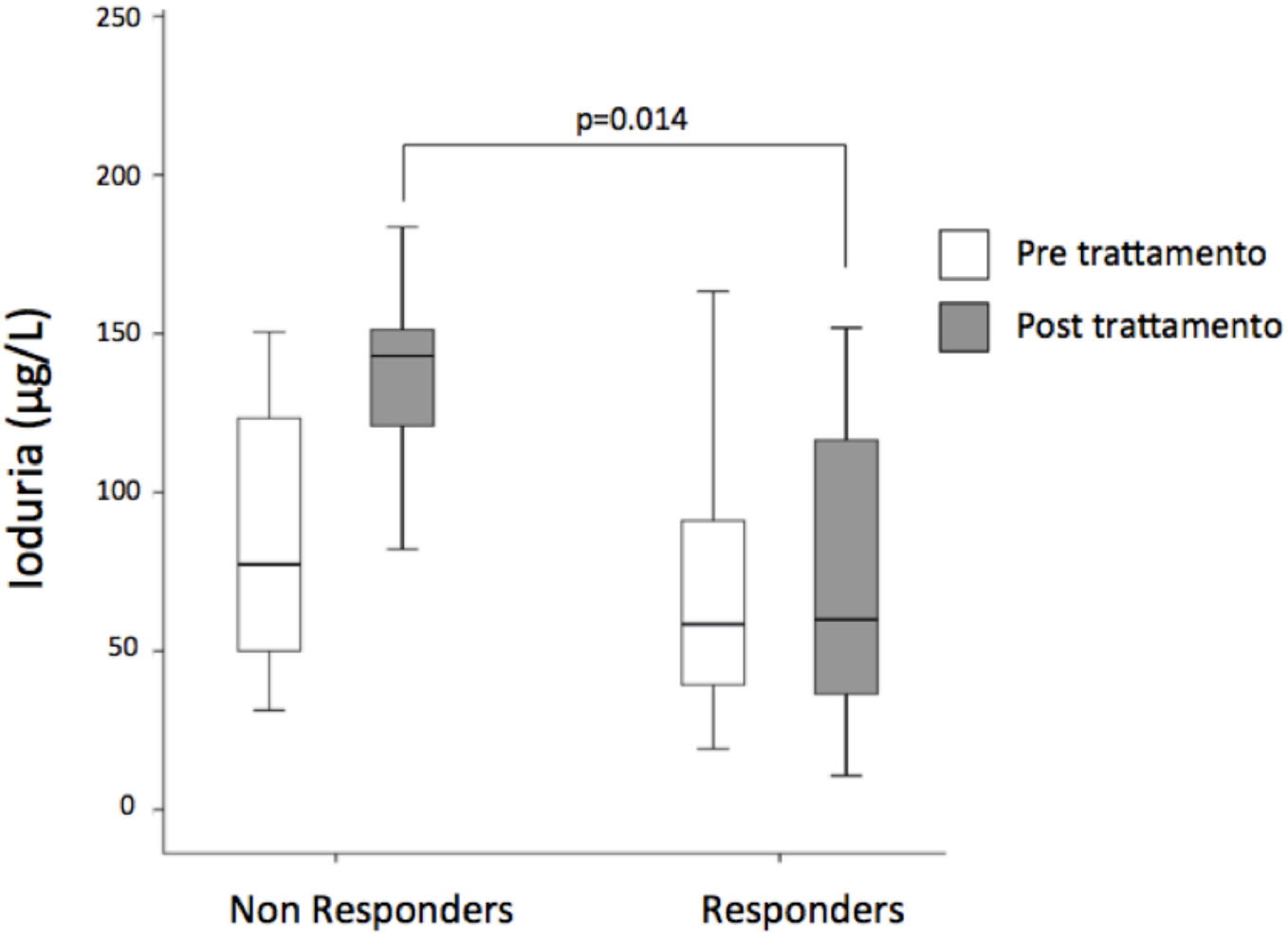
CXCL11(pg/mL)	49.02±35.89	41.92±29.66	0.384	50.59±50.67	43.19±35.92	0.486

Ioduria


250
200
150
100
50
0
Ioduria (µg/L)
p=0.014
Pre trattamento
Post trattamento
Non Responders
Responders

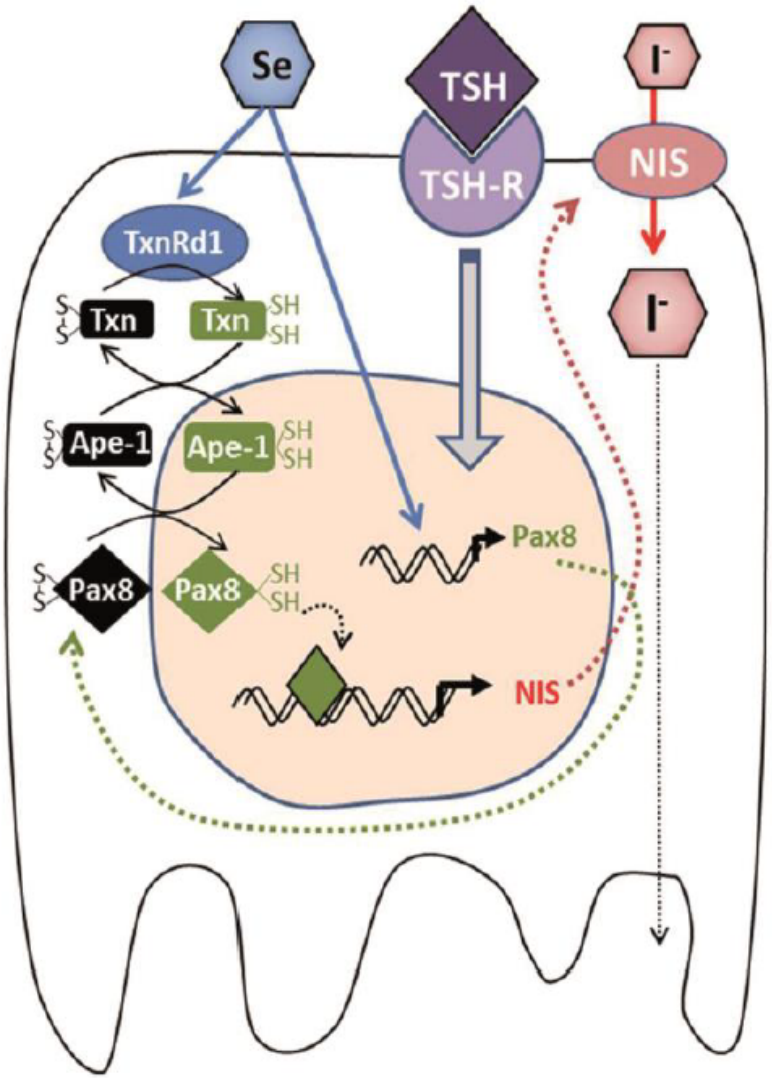
Antioxid Redox Signal. 2015 Dec 9. [Epub ahead of print]

Selenium increases TSH-induced sodium/iodide symporter expression through Txn/Ape1-dependent regulation of Pax8 binding activity.

Leoni SG[1], Sastre-Perona A[2], De la Vieja A[3], Santisteban P[4].

Abstract

Aims: The Sodium iodide symporter (NIS) mediates the uptake of I⁻ by the thyroid follicular cell and is essential for thyroid hormone biosynthesis. Nis expression is stimulated by TSH and also requires Pax8 to bind to its promoter. Pax8 binding activity depends on its redox state by a mechanism involving Txn/TxnRd1 (thioredoxin/thioredoxin reductase 1) reduction of Ape1 (apurinic/apyrimidinic endonuclease 1). In this study we investigate the role of Se in Nis expression. **Results:** Selenium increases TSH-induced Nis expression and activity in rat thyroid cells. The stimulatory effect of Se occurs at the transcriptional level and is only observed for Nis promoters containing a Pax8 binding site in the NUE (*Nis upstream enhancer*), suggesting that Pax8 is involved in this effect. In fact, Se increases Pax8 expression and its DNA-binding capacity, and in Pax8-silenced rat thyroid cells Nis is not Se-responsive. By inhibiting Ape1 and TxnRd1 functions we found that both enzymes are crucial for TSH and TSH *plus* Se stimulation of Pax8 activity and mediate the Nis response to Se treatment. **Innovation:** We describe that Se increases Nis expression and activity. We demonstrate that this effect is dependent on the redox functions of Ape1 and Txn/TxnRd1 through control of the DNA-binding activity of Pax8. **Conclusion:** Nis expression is controlled by Txn/Ape1 through a TSH/Se-dependent mechanism. These findings open a new field of study regarding the regulation of Nis activity in thyroid cells.



CONCLUSIONI

- I nostri dati sottolineano ancora una significativa carenza iodica nella nostra popolazione;
- Il titolo anticorpale non sembra avere una grande influenza sul processo di organificazione degli ormoni tiroidei;
- Nell'ipotiroidismo subclinico, il selenio potrebbe essere un tentativo NON farmacologico per ripristinare l'eutiroidismo nelle fasi precoci della tiroidite cronica.