

Salenio: clinical study design

Abstract

In the last 20 years there has been a marked increase in thyroid disease, although partly due to increased attention to screening, possibilities for more extensive and more sensitive laboratory diagnostic tests, and the availability of more advanced imaging technologies, nevertheless appears to be evidence of a profound dietary, biological, and environmental change.^{1,2} Autoimmune thyroiditis is the most frequent cause of hypothyroidism in iodine-replete populations.³ It is now estimated that 1/3 of the female population and 1/8 of the male population in goitrogenic endemic countries such as ours, have thyroid disease, and of these 80% are autoimmune thyroiditis. The complexity of this phenomenon is certainly partly due to the extreme thyroid sensitivity to ionizing radiation,⁴ but it can also be explained by nutritional deficiency of other factors such as Iodine and Selenium:⁵ the therapy of these patients is increasingly focused on the use of dietary supplements of Iodine and Selenium, meanwhile the latest international guidelines⁶ are increasingly scaling back the use of thyroid hormone (L-Tyroxine) in this huge plethora of patients in normofunctioning patients with nodular thyroidopathy and patients with subclinical hypothyroidism.^{7,8} This leaves on the market a sizeable slice of patients receptive to Iodine and Selenium treatments; our research aims precisely to test in these patients the efficacy of a salt that is already supplemented with Iodine and Selenium, comparing it in a double-blind randomized trial with a control group using neither iodized salt nor supplements, a group using iodized salt and a Selenium supplement, and finally a third group using an Iodine and Selenium supplement.

Keywords: thyroiditis, Iodine, Selenium, hypothyroidism, autoimmune

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Abbreviations: fT3, free triiodothyronine; fT4, free thyroxine; TSH, thyroid stimulating hormone; hTg, Thyroglobulin; HtgAb, thyroglobulin antibody; TPOAb, antibody tireperoxidase; ESR, erythrocyte sedimentation rate; TAS, anti-streptolysin O; PCR, polymerase chain reaction; Na, sodium; K, potassium

Introduction

The purpose of the Salenio study is to demonstrate that the use of salt supplemented with Iodine and Selenium or the use of Iodine and Selenium dietary supplements improves inflammatory indices and brings thyroid hormones back into the normal range in patients with thyroiditis.

Material and methods

Beginning with the availability of salt samples for testing, the following patients will be enrolled: all patients with clinical (chronic thyroid symptomatology), laboratory (increased antiHtg, antiTPO or antiMicrosomal antibodies) with normal TSH values or < 8mUI and/or with ultrasound alteration compatible with chronic inflammatory thyroid disease and micro-macronodular thyroid disease.

Thus, 4 macro groups are created, randomized to double-blind:

- Control group: without use of iodized salt and Selenium.
- Group with Iodine and Selenium intergrated salt.
- Group with Iodine salt and Selenium supplement (Selima, Syrel or similar)
- Group with Iodine and Selenium supplement (Iosel or similar).

Each group should have a minimum number of 150 patients, and it is estimated with current outpatient regimens to reach this endpoint in about 6-12 months. Each patient will be checked at least 2 times over this period: they must give informed consent upon enrollment in the study and ensure consistent use of the prescribed prescriptions.

At checkups, weight, blood pressure levels, biohumoral levels of FT3, FT4, TSH, Htg, HtgAb, TPOAb, TmicrAb, ESR, TAS, PCR, Na, K, and Ioduria are checked, and ultrasound is performed to monitor and compare thyroid dimensions, any nodular ultrasound features such as ultrasound density, echo-structural inhomogeneity, vascularization according to Lagalla Patterns, if possible quantitative elastosonographic pattern, presence and characteristics of any locoregional lymphadenopathy.

In view of Reg.(EU)1169/2011, the % VNR of Selenium is 55 mcg/day and Iodine 150 mcg/day, in determining which dosage is best for the purpose of proper dietary supplementation, the B group will be divided into 3 subgroups all provided with single-serving sachets for salting to be used at lunch and dinner (Table 1).

Table 1 Subgroups of patients that assume Iodine and Selenium supplement (Iosel or similar)

D group	How we divide group D
D1	Supplementation with 25mcg/day Selenium and 50 mcg/day Iodine content sachets (50 patients)
D2	Supplementation with Selenium-containing sachets of 30 mcg/day and Iodine of 75 mcg/day (50 patients)
D3	Integration with 40 mcg/day Selenium-containing sachets and 100 mcg/day Iodine (50 patients)

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Results

At present, our data are not yet conclusive as our analysis is not yet finished. Until now we can say that in the enrolled patients with

inflammatory thyroid disease who do not supplement either iodine or selenium, there is no improvement in inflammatory indices assessed both laboratorically (ft3 ft4 TSH and PCR) and ultrasonographically (mean elastosonographic index expressed in kPa). Early data look extremely promising with marked reduction in PCR, elastosonographic index, and normalization of TSH, ft3, ft4 in patients supplementing selenium and/or iodine either in salt form or as a dietary supplement (Table 2).

Table 2 Analysis medium index in the four groups

	Group A	Group B	Group C	Group D
TSH medium (mcU/ml)	6.215	3.111	2.805	2.566
ft3 medium(pg/ml)	8.2	3.1	3.9	3.2
ft4 medium (pg/ml)	25	15.4	16.2	15.7
PCR Medium (mg/dl)	1.95	0.17	0.12	0.15
Elastography Index (kPa)	57	42	45	43

A Control group: without use of iodized salt and Selenium

B Group with Iodine and Selenium intergrated salt

C Group with Iodine salt and Selenium supplement (Selima, Syrel or similar)

D Group with Iodine and Selenium supplement (Iosel or similar)

Discussion

Our preliminary results show that dietary supplementation of sodium and selenium, either with salt or dietary supplements, appears to have a positive impact on the course of inflammatory thyroid disease. To obtain these results, 3 groups of patients taking both salt and dietary supplements of sodium and selenium were compared with 1 control group of patients taking neither selenium nor iodine. The data are promising and urge us to continue research along these lines.

Conclusion

Although the results of our study are not yet conclusive, we think, and the data until now seem to confirm, that it is important to continue the study to understand how great an impact sodium and selenium have on the lives of patients with inflammatory thyroid disease.

Acknowledgments

None.

Conflicts of interest

The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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