



## "ALTERNATIVE TREATMENT AS AN ADJUNCT TO LEVOTHYROXINE IN HYPOTHYROIDISM"

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### ABSTRACT

**Introduction:** Hypothyroidism has a worldwide incidence of 750 million people, it also triggers several subsequent pathologies such as diabetes mellitus, arterial hypertension and dyslipidemia; its physiopathology lies in suppressing the formation or synthesis of "thyroid hormones", its main manifestations are weight gain, constipation, and the signs are ataxia, yellowish skin, rough hair; as there is documentation indicating that hormone therapy based on Levothyroxine does not offer benefits to individuals suffering from this condition, new therapeutic approaches are being sought, which will be described in this article.

**Objective:** To describe the use of alternative treatment as an adjunct to Levothyroxine therapy in hypothyroidism.

**Methodology:** Research was carried out in "databases" such as PubMed, Scielo, Web of Science, Latindex, published in the last 10 years using DeCs and MeSH terms Alternatives Theapeutics AND Hypothyroidism AND Levothyroxine, in addition to the different AND booleans.

**Expected results:** It is expected to describe the use of alternative treatment as an adjunct to Levothyroxine therapy in hypothyroidism, in addition, it is desired to list the main alternative treatments used in hypothyroidism, describing their risks and benefits; to detail whether the use of alternative treatment adjuvant to Levothyroxine therapy provides better benefits in a comprehensive manner in patients with hypothyroidism.

**Conclusion:** It has been demonstrated through an exhaustive search that Levothyroxine as the only treatment to combat all the symptoms caused by Hypothyroidism, especially with the discomfort caused at the emotional level in terms of anxiety and stress has been shown that supplementation with selenium has brought new favorable results in these areas.

**Key words:** Acupuncture, hypothyroidism, Chinese medicine, T4.

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## INTRODUCTION

Hypothyroidism is a condition linked to deficiency of "*thyroid hormones*", represents one of the pathologies with more incidence in the health consultation, primarily affecting the female population, increasing its incidence in relation to the progression of the age of people, the percentage of cases is increased due to arbitrary management with Levothyroxine.

The diagnosis of Hypothyroidism is mainly made with anamnesis, physical examination, the gold standard is to identify the level of thyroid hormones as to "*Thyroid Stimulating Hormone (TSH)*", the value is Triiodothyronine "*(T3)*" and Tiroxin "*(T4)*"; These will be evaluated according to age, iodine intake.

The alternative treatment focused mainly on the use of (acupuncture and medicinal herbs) provides better results in terms of maintaining normal thyroid hormone levels managing stress and the neurohumoral state of patients, evidence has been presented on the persistence of symptoms despite using pharmacological therapy with Levothyroxine at optimal doses (1,2).

This poor adherence of the drug causes the patient to continue with the deterioration in mood, triggering hormonal alterations that affect this pathology through the following Systematic Review if it is feasible to perform a combination of alternative treatment with Levothyroxine in individuals suffering from Hypothyroidism (3,4).

It is for these reasons that we seek through this research to make a comparison on the comprehensive benefit of patients with hypothyroidism (mood, hormone levels, stress, quality of life) between alternative therapy (acupuncture, herbal medicines, etc.) and the gold standard; in order to establish a better therapy that comprehensively covers the improvement of the patient (3,5).

It has been described in some research that Levothyroxine is very effective in regulating hormone levels of TSH, T3 and T4; Therefore, it is essential to treat patients with hypothyroidism, but it has been described that people continue to have discomforts such as stress, anxiety, in the neurohumoral state; that despite having an adequate regimen in the taking of the medication do not present improvement in terms of their integral well-being (6,7).

By providing accessible, organized and more understandable information to the public so that the entire population, regardless of the culture to which they belong or the degree of education, can make use of it, and that serves as a guide to reinforce the future knowledge of the new medical generations, constituting a fundamental component on which This method can be supported and incorporated as a new therapeutic regimen in endocrine diseases, including hypothyroidism (1,8).

By comparing the risks and benefits of both medications, it will be possible to verify the weak points of each of them and, if possible, they can be complemented to provide an overall improvement to patients and having fewer side effects that usually cause a lot of discomfort to people and even lead to non-compliance in taking the drug (9,10).

## **METHODOLOGY**

Respecting the standards established by "*PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)*" 33, a systematic review was carried out using the OVI technique in order to find all articles and types in Spanish and English from reliable scientific journals, whose publications must be from January 2013 to December 2023. this research was carried out in databases such as "*Medline/PubMed, Scielo, Web of Science*", Latindex and used the descriptors DeCs, MeSH in combination c on the words claves.

### **Inclusion Criteria**

Articles in Spanish and English were included, studies that provide us with relevant information on new therapeutic regimens in hypothyroidism in both humans and animals. These articles should be publications from January 2013 to December 2022.

### **Exclusion Criteria**

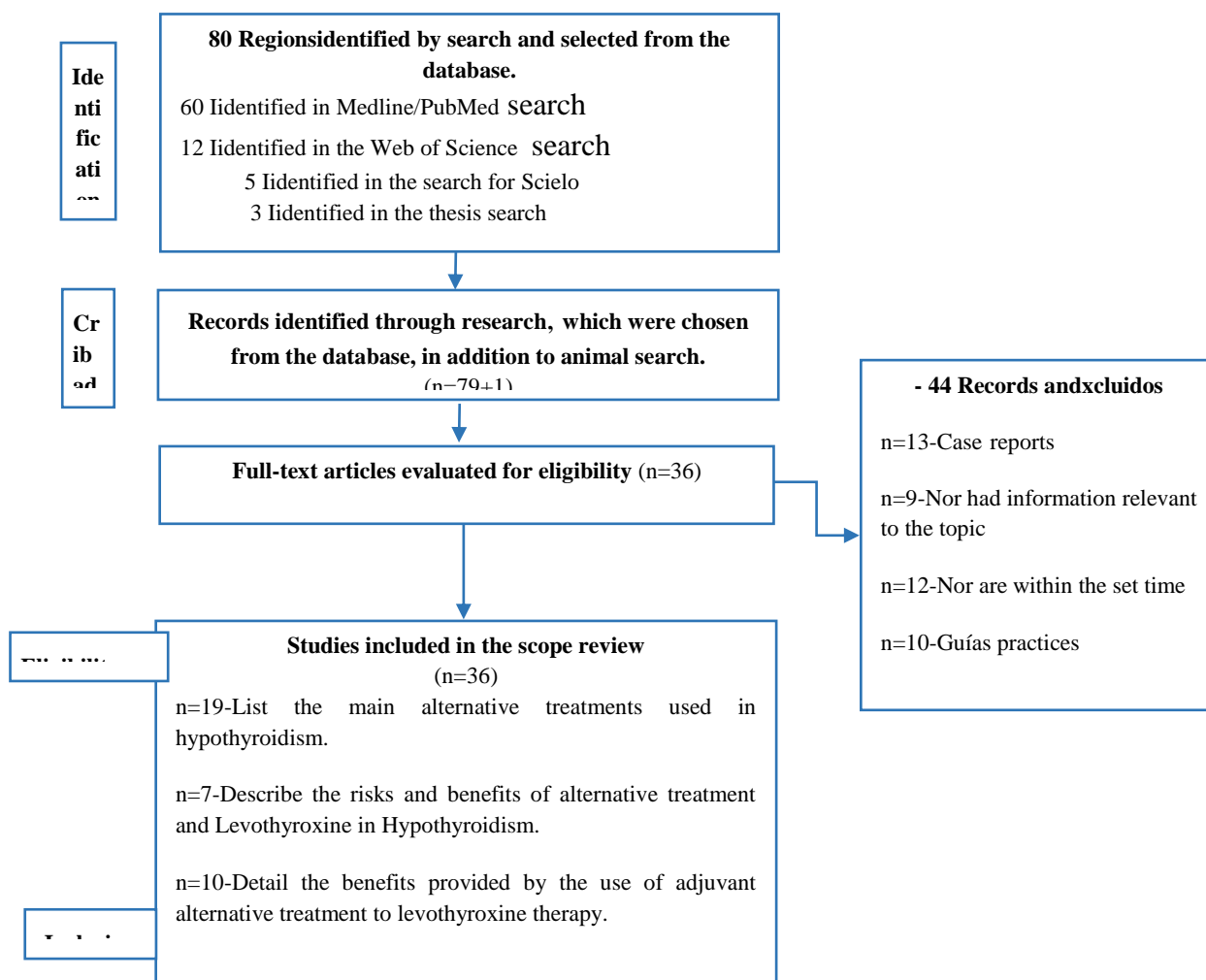
Duplicate articles, whose information was inaccessible, which are not related to topic, to the objectives of the research, letters, theses, case reports, guides, were excluded .

### **Data extraction**

The complete reading of studies that meet all the aforementioned criteria was carried out and data were extracted such as title, author, year of publication, country, objective, method, design, number of participants, results, limitations of the study in reference to the use of alternative treatment as an adjunct to therapy with Levothyroxine in hypothyroidism.

## RESULTS

In the first instance, 80 articles were obtained, of which 33 systematic review articles were chosen, doctoral theses, of which the most current were considered and those that complied with the exclusion and inclusion parameters implemented in this review. The same ones described in the following figure.



Among the investigations are cohort studies, original articles, thesis, randomized controlled study.

The articles reflect in a concrete and coherent way what are the adverse effects caused by the administration of Levothyroxine, and which are the areas that can not yet be covered in

full, it is clearly stated that this drug does not help maintain a balance in the mood of the people studied, so it is feasible to conduct more research on the impact of acupuncture treatments on this nature.

In the study conducted by Li F, Qi Z, et al./2020, called The efficacy of acupuncture for the treatment and the fertility improvement in child-bearing period female with Hashimoto Disease, it was determined that acupuncture was beneficial to stop or delay the progression of HT and improve fertility in the female fertile period.

In another research conducted by Perros P, Van Der Feltz-Cornelis C, et al./ 2021, it was determined that despite orally administering  $l_t4$  and  $l_t3$ , some symptoms such as asthenia, weight gain and mood alteration persisted.

In the doctoral thesis of Jonathan Aguilar Manzo/2020 entitled The effect of selenium on regulatory T cells; it was evidenced that this mineral is able to reestablish the Treg cell population thanks to the positive regulation of Foxp3 expression through DNA methylation.

In the research of Fung Kei Cheng / 2018, An overview of the contribution of acupuncture to thyroid disorders, it was observed that after 20 or 30 minutes of acupuncture sessions, 20 affected patients achieved a considerable reduction in the values of TSH and thyroid peroxidase antibody (TPOAb), in addition to which it can regulate the neuroimmunoendocrinological system, resulting in significant positive changes in thyroid hormone levels.

In the research carried out by Chiovato L, Magri F, Carlé A./ 2019, Hypothyroidism in Context: Where We've Been and Where We're Going, it is visualized that the use of levothyroxine is aimed at preventing the progression to overt hypothyroidism, reducing the appearance of coronary artery disease and improving neuropsychiatric and musculoskeletal symptoms although these do not subside under the treatment used.

Table 1: List the main alternative treatments used in hypothyroidism.

<b>TITLE</b>	<b>AUTHOR/YEAR</b>	<b>TYPE OF STUDY</b>	<b>TYPE OF TREATMENT</b>
The efficacy of acupuncture for the treatment and the fertility improvement in child-bearing period female with Hashimoto Disease.	Li F, Qi Z, et al./2020	Randomized controlled study	Acupuncture
Acupuncture for Hashimoto thyroiditis: study protocol for a randomized controlled trial	Shanze Wang, Jiping Zhao et al./2021	Original Article	Acupuncture for 16 weeks

The effect of selenium on regulatory T cells	Jonathan Aguilar Beef/2020	Dissertation	Selenium
Pharmacological Uses of the Plants Belonging to the Genus Commiphora	Latha S, Selvamani P, et al./2021	I am a student analytic	Plants of Commiphora species
Myo-inositol in autoimmune Thyroiditis, and hypothyroidism	Poupak Fallahi, Silvia Martina Ferrari et al./2018	Revision	Myo-inositol + Selenium (Se)
The Role of Inositol in Thyroid Physiology and in Subclinical Hypothyroidism Management	Benvenga S, Nordio M, et al./ 2021	Clinical trial	Mioinositol
An overview of the contribution of acupuncture to thyroid disorders.	Fung Kei Cheng/2018	Revision Narrative	Acupuncture
The efficiency and safety of methimazole And propylthiouracil In hyperthyroidism: A meta analysis of randomized	Tan S, Chen L, et al./ 2021	Metanálisis	Metimazol
Profile of Levothyroxine Replacement Therapy in Graves' Disease Patients with Hypothyroidism Post-Radioactive Iodine Ablation: Focus on Different WeightBased Regimens.	Saravut Mathiphanit, Nalin Yenseung, and al./2022	Revision Hindsight	Radioactive iodine

Table 2: Describe the risks and benefits of alternative treatment and levothyroxine in hypothyroidism.

TITLE	AUTHOR /YEAR	TYPE OF STUDY	TYPE OF TREATMENT	PROCEEDS	RISKS
The enigma of persistent symptoms in hypothyroid patients	Perros P, Van Der Feltz-Cornelis C, and al./ 2021	Revision Narrative	Levothyroxine	Don't solve the riddle of symptoms Persistent.	Symptoms persist, include fatigue, increased Weight and changes of humor.

treated with levothyroxine					
Diagnosis and treatment of hypothyroidism in the elderly	Leonidas H. Duntas, Paul Michael Yen/2019	Revision Narrative	LT4	Achieving Euthyroidism to Improve patient survival.	
Hypothyroidism in Context: Where We've Been and Where We're Going	Chiovato L, Magri F, Carlé A./2019	Search for Literature	Levothyroxine	Prevent progression to hypothyroidism manifest, as well as reduce the occurrence of coronary artery disease and improve neuropsychiatric symptoms and musculoskeletal associated with hypothyroidism.	Side effects Cardiovascular neuropsychiatric and Musculoskeletal
Appropriate dose of levothyroxine replacement therapy for hypothyroid obese patients	Ratanapornsompong G, Sriphrapradang C./2021	Revision hindsight	Levothyroxine		Higher doses of LT4 in individuals severely obese could be attributed to an increase in mass lean body.
Hypothyroidism	Torres Barrea, M.Cayón	Revision Narrative	Levothyroxine	Maintain a serum concentration	

	Blanco			constant of T4 and T3 once it has been Stability achieved.	
Hypothyroidism	Trifu DS, GilFournier Left N, et al./2020	Revision Narrative	Levothyroxine (T4)	At 6 weeks there will be a balance complete between T4L and effects levothyroxine biologics.	In excessive doses levothyroxine Causes a loss Accelerated mass bone in patients Postmenopausal It also increases the wall thickness cardiac and its contractility and, in Patients elderly, increases the risk of fibrillation auricular
Liothyronine and desiccated thyroid extract in the treatment of Hypothyroidism	Idrees T, Palmer S, et al./2020	I am a student Observational	Levothyroxine	Improve symptoms such as fatigue, fall of hair, nausea	Have not been associated with reactions adverse to medicament
Treatment with levothyroxine in patients elderly with hypothyroidism	Grigoris Efraimidis, Torquil Watt, et al./2021	Revision Narrative	Levothyroxine	Treatment with levothyroxine improves quality of life (including symptoms) in patients with hypothyroidism. However,	



				since the symptoms and, therefore, manifestations of hypothyroidism experienced by patients are more Vague among the elderly, the effects observed in the most Young people cannot, without a doubt, extrapolate to the elderly.	
Use of thyroid hormone in hypothyroid patients and euthyroid subjects in	Spain: A John C. Galofré, Roberto Attanasio, et al./2022	Article Original	LT4	A minority (2.6%) thought that the LT4 combination with liothyronine was the Treatment of Choice from the home, while the 97.4% stated that LT4 is the therapy of First line for hypothyroidism.	The indications for treatment with LT4 in the euthyroidism were infertility in women with positive antithyroid studies (48.5%) and simple goiter (21.2%).
Approach to the hypothyroidism subclinical	Macedo Silva S, Carvalho A, et al./ 2020	Revision Bibliographic	Levothyroxine		Treatment with T4 exogenous must considered due

in the adult					to an increase of risk of heart failure and death from causes Cardiovascular
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TITLE	AUTHOR/YEAR	TYPE OF STUDY	TYPE OF TREATMENT	PROCEEDS	RISKS
The efficacy of acupuncture for the treatment and the fertility improvement in child-bearing period female with Hashimoto Disease.	Li F, Qi Z, et al./2020	I am a student controlled Randomized	Acupuncture	Acupuncture in stopping or delaying HT progression and improve fertility in the female fertile period	Hematoma in the acupuncture point, bleeding, fainting, severe pain infection, needles stuck and needles Routes.
Acupuncture for Hashimoto thyroiditis: study protocol for a randomized controlled trial	Shanze Wang, Jiping Zhao et al./2021	Article Original	Acupuncture for 16 Weeks		Sangrado, bruising, fainting and severe pain
The effect of selenium on T cells Regulatory	Jonathan Aguilar Beef/2020	Dissertation	Selenium	Selenium is able to restore Treg cell population thanks to the positive regulation of the expression of Foxp3 through methylation in	

				DNA.	
Uses of the Plants Belonging to the Genus Commip	Latha S, Selvamani P, et al./2021	I am a student analytic	Plants of the species of Commiphora	They possess pharmacological properties, antiarthritic and anti-inflammatory, antiatherogenic, antibacterial, anticoagulants, antichroeliasis, antiepilépticas, antifascioliasis, antifúngicas, antiheterofidiasis, antihipercolesterolémico, antihiperlipidémico, antihipotiroidismo, antiobesity, antiosteoarthritic, antiosteoclastogenesis, antioxidant, antiparasitic, antipyretic, antischistosomiasis, antiseptic, antitrombótico, antiulceroso, cardioprotective, enzyme inhibitor COX, cytotoxic/anticancer/anticancer, DNA cleavage, hypotensive,	

				<p>inhibits lipid peroxidation, inhibits production of NO and NO synthase, insecticide, anesthetic local, molluscicide, muscle relaxant smooth.</p>	
<p>Myo-inositol in autoimmune Thyroiditis, and hypothyroidism</p>	<p>Poupak Fallahi, Silvia Martina Ferrari et al./2018</p>	<p>Revision</p>	<p>Myo-inositol + Selenium (Se)</p>	<p>In a double randomized controlled trial blind by Nordio et al, it was observed that in the group treated with Myo-inositol + Selenium changes in TSH levels were observed (<math>4.4 \pm 0.9</math> vs. <math>3.1 \pm 0.6</math> <math>\mu</math>IU/ml, with a ratio of <math>P &lt; 0.01</math>). In another study by Morgante et al. Herself showed a significant decrease in TSH, levels of AbTPO and AbTg, and also to a Improvement</p>	

				of thyroid hormones and personal well-being.	
The Role of Inositol in Thyroid Physiology and in Subclinical Hypothyroidism Management	Benveng a S, Nordio M, et al./ 2021	Clinical trial	Mioinositol	Regulates TSH iodization in the process HT biosynthesis, physiological levels of MYO correlate with a condition euthyroid and are considered as possible markers of thyroid malignancy.	
An overview of the contribution of acupuncture to thyroid disorders.	Fung Kei Cheng/2018	Revision Narrative	Acupuncture	Reduce symptoms and improve Relevant biomarkers, in a study performed on 20 patients affected by Autoimmune thyroid disease observed that after 20 or 30 minutes acupuncture sessions, 20 patients affected reached a significant decrease in the levels of TSH and thyroid peroxidase	In a study performed at 20 People don't There were changes in thyroid hormone free (fT4) or in the antibodies antitiroglobulina (TGAb).

				antibody (TPOAb). It was evidenced acupuncture can regulate the neuroimmunoenocrinological system, resulting in positive changes significant hormone levels Thyroid.	
The efficiency and safety of methimazole and propylthiouracil in hyperthyroidism: A meta-analysis Of randomized controlled trials.	Tan S, Chen L, et al./ 2021	Metanálisis	Metimazol	Reduction of levels of T3, T4, FT3 and FT4, decreasing the risk of damage to liver function and increasing the level of TSH.	Daily administration 10 mg MMI Caused hypothyroidism spontaneous in 2 patients with goiter diffuse.
Profile of Levothyroxine Replacement Therapy in Graves' Disease Patients with Hypothyroidism Post-Radioactive Iodine Ablation:	Saravut Mathiphanit, Nalin Yenseung, and al./2022	Revision Hindsight	Radioactive iodine	At the end of follow-up, 62.4% of patients reached hormone levels thyroid stimulant (TSH) within the reference interval, and 22.1% had TSH levels	From the study carried out 15.5% had TSH levels by above.

Focus on Different WeightBased Regimens.				below the range of reference.	
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Table 3: Detail the benefits provided by the use of adjunctive alternative treatment to levothyroxine therapy.

TITLE	AUTHOR/YEAR	TYPE OF STUDY	TYPE OF TREATMENT	PROCEEDS
TRACE ELEMENTS AND THEIR ASSOCIATION WITH PRIMARY AND SUBCLINICAL HYPOTHYROIDISM	Vargas PSG, Nieto JMO, Casadiego JPP, Navarro IVT/2021	Review of revisions	Selenium and iodine	Selenium supplementation at TPOAb levels, TgAb. It was also shown that following supplementation with iodine decreased TSH levels and thyroglobulin (12), however, another review included three trials in which a group of pregnant women with iodine and showed that there are no differences regarding the risk of presenting hypothyroidism during pregnancy and postpartum, in addition, to have the same probability of being diagnosed with

				hypothyroidism
Adult hypothyroidism in a basic health zone	López-Macías I, Hidalgo-Requena A, Pérez-Membrive E, González-Rodríguez ME, Bellido-Moyano C, Pérula-de Torres /2018	Observational, descriptive and cross-sectional study	Levothyroxine Radactive iodine	It is determined that the The vast majority of patients with hypothyroidism subclinical are being treated with levothyroxine (OR 21,58; IC 95% 2,89-161,05; p=0.003) and that a part of the patients who presented in their day hypothyroidism primary after receiving iodine treatment radioactive present currently hypothyroidism subclínico (OR 10,84; IC 95% 2,25-52,21).
Get better treatment for the patient with hypothyroidism	Amoros ALI, Zayas AC del A, Llivisaca DMD, Manzanares JEG, Tristá SET /2023	Review of revisions	Levothyroxine and triiodothyronine	There is no significant difference

## DISCUSSION

According to Fangyuan, Zhang, et al. It is said that to date there are no specific treatments to adequately reduce the predominant symptoms in Hashimoto's Thyroiditis, as acupuncture is a safe and economical therapeutic alternative, it has been seen after conducting some studies that it is an adequate practice to reduce the symptoms and level the parameters of the biomarkers. Instead, an emerging technique called MOK pharmacopuncture can



stabilize levels of Th1/Th2 cytokines by helping to eradicate autoimmune responses; while Shanze, Jiping, et al, with a sample of 60 people, certain points were used to verify the effectiveness of acupuncture as an alternative for the treatment of hypothyroidism especially subclinical for it were used three points San Jian (LI3) which corresponds to radial depression, He Gu (LI4) radial to the midpoint of the second metacarpal and Qu Chi (LI11) lateral face of the elbow, After performing the procedure was observed changes in the levels of serum antithyroperoxidase antibodies (TPOAb), serum antithyroglobulin antibodies (TgAb) and thyroid hormone values such as Total thyroxine (FT4), free thyroxine (FT3), thyroid stimulating hormone (TSH), however no treatments have been found that can lower pressure in the neck, fatigue, changes in mood.

According to Petros, Van Der Feltz, et al, it is recommended to administer to all people with hypothyroidism a combination of LT4 + LT3 because the single use of LT4 has not been shown to reduce symptoms in patients, while in two systematic reviews it was obtained that the administration of LT4 + LT3 and dried thyroid extract (DTE) did not have significant improvements in terms of quality of life, neurocognitive function and somatic symptoms. On the other hand, Aguilar, when focusing on an investigation study carried out *"in mice to which 0.3 mg / kg of sodium selenite was applied, an increase in Treg cells and expression of Foxp 3 mRNA was subsequently observed, this characteristic may be due to the fact that selenium is able to reestablish the population of these cells due to a regulation of the expression of Foxp3 through DNA methylation."* In contrast to Orihuela, who in his master's thesis details that facial acupuncture Dien Cham being an innocuous and minimally invasive process does not produce adverse effects, there was improvement in (25 patients) in terms of asthenia, (20 patients) anopathies and (17 patients) sensation of cold, in (18 patients) improved hair loss, in (16 patients) the alteration of memory (17 patients) improved the estremiento according to Rome III Criteria II, in (7 patients) dry skin and in (19 patients) generalized oedema.

According to Vargas, in his pharmacological thesis he describes that some plants such as Commiphora Mukul exerts a direct action on the hypothalamic-pituitary axis or directly on the thyroid gland, in studies carried out in rat thyroid cultures the inhibitory effect of melatonin on thyroid function was verified, decreasing the uptake of iodine, triiodothyronine by resin and free thyroxine, Therefore it is concluded that it directly stimulates thyroid function. On the other hand, Costa mentions that hypothyroidism during pregnancy needs immediate treatment based on LT4 since according to the statements of The American Endocrine Society (TES) the benefits outweigh the risks, it is also recommended to treat patients before and during the first trimester of pregnancy with Levothyroxine if the TSH figures exceed 2.5 MIU / L, presenting adverse effects such as palpitations, tremor, anxiety, weight loss.

In contrast to Carrión, who argues that synthetic levothyroxine (T4) is the main treatment for hypothyroidism which is administered orally in a single dose, because in the peripheral

organs it is fractionated to T3 binding to thyroxine-binding globulin (TGB), in a study conducted with 30 participants it was observed that 63% presented adverse reactions to the taking of Levothyroxine constituted by Abulia presented in 16% of participants were followed by sweating 14% and tachycardia 13%.

On the other hand, Malo, Karol, in his pharmacological thesis describes that algae having a direct effect on the thyroid gland by having iodine as one of its compounds can increase catabolic processes and help lose weight, while Madurga, Sánchez, called that the interaction between Levothyroxine and soy can trigger a lower absorption at the intestinal level of the drug impairing its desired effect, So it is essential to couple the dosage of the same at the beginning or at the end of the phase in which the individual is administered "*soy supplements*". According to Calderón some medicinal plants used for the treatment of hypothyroidism have an adequate compound of andodor among them stand out garlic, almond, hazelnut, being able to solve the iodine deficit presented by certain patients with dysfunction of the thyroid gland, instead cinnamon, hyssop, fennel are thyroid stimulants, the characteristics of these plants is that they contain essential oils, Vitamins and antioxidants, for patients who have hypothyroidism together with overweight is recommended vegetables (spinach, garlic), cereals (oats), as there is no scientific information that evaluates their results as a treatment for hypothyroidism are reegadas in traditional medicine.

## CONCLUSIONS

It has been demonstrated through an exhaustive search that Levothyroxine as the only treatment to combat all the symptoms caused by Hypothyroidism, especially with the discomfort caused at an emotional level in terms of anxiety and stress has been shown that supplementation with selenium has brought new favorable results in these areas.

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## GLOSSARY

**Acupuncture:** Place needles directly on the skin in so-called acupoints. To "*control symptoms such as pain, nausea, vomiting*".

**Levothyroxine:** Also known as L-thyroxine, it is a manufactured form of the thyroid hormone thyroxine. It is used to treat thyroid hormone deficiency, including a severe form known as myxedema coma. It may also be used to treat and prevent certain types of thyroid tumors. It is not indicated for weight loss.

**Thiamazole:** Also known as methimazole, it is a medication used to treat hyperthyroidism. This includes "*Graves' disease, toxic multinodular goiter*" and thyrotoxic crisis. It is taken by mouth. Full effects may take a few weeks to occur.

**Radioactive iodine:** associated with nuclear energy, medical diagnostic and treatment procedures, and natural gas production.