IJPSR (2021), Volume 12, Issue 6 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 08 June 2020; received in revised form, 09 October 2020; accepted, 03 May 2021; published 01 June 2021

INCREASED ENZYMATIC ACTIVITY OF THYROID PEROXIDASE-TREATMENT FOR CONGENITAL HYPOTHYROIDISM

P. J. Sujitha [1] and S. Arunkumar [* 2]

Department of Pharmacology [1], Vinayaka Mission College of Pharmacy, Salem - 636008, Tamil Nadu, India.
Department of Pharmacy Practice [2], J.K.K. Nattraja College of Pharmacy, Kumarapalayam - 638183, Tamil Nadu, India.

Keywords:

Congenital Hypothyroidism, Thyroid Peroxidase, Genetics, Thyroid peroxidase antibodies test, Gene and stem cell therapy

Correspondence to Author:
Mr. S. Arunkumar

Student,
Department of Pharmacy Practice,
J.K.K. Nattraja College of Pharmacy,
Kumarapalayam - 638183, Tamil Nadu, India.

E-mail: arunkumar.s@jkkn.ac.in

ABSTRACT: Congenital Hypothyroidism may be defined as a heterogeneous group of disorders characterized by goiter or cretinism due to an absolute or relative deficit of the enzyme Thyroid Peroxidase (TPO), and it is action. Chronic hypothyroidism also leads to goiter and cretinism associated with end gland damage, dysfunction, cancer, and failure, including the retina, kidney, nervous system, heart, and vascular tissue damage. The screening for Congenital Hypothyroidism (CH) may either be in the form of a thyroid function test or via thyroid peroxidase antibodies test, as recently recommended by the Thyroid Federation Association (TFA). Unto now, the treatment of goiter and cretinism is levothyroxine supplement and gland surgery removal. This review will establish the effectiveness of the enzymatic drug (TPO) and its indication for the treatment of PCH when compared to other therapies. This review also highlights the enzyme thyroid peroxidase (TPO) role and current treatment strategies on Congenital Hypothyroidism (CH).

INTRODUCTION: The thyroid gland is an endocrine gland in the neck, which consists of two lobes connected by an isthmus. The thyroid gland secretes three hormones, thyroxine (T4), tri-iodothyronine (T3), and calcitonin [1]. The hormones thyroxine has important functions related to energy metabolism, control of body temperature, bone development, and maturation of the CNS, among other metabolic processes throughout the body. Thyroid diseases are arguably among the common endocrine disorder worldwide.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.12(6).3316-19

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.12(6).3316-19

Common causes of hypothyroidism in children were thyroid Dysgenesis, Dyshormonogenesis, and Thyroiditis [2]. Congenital hypothyroidism is defined as mild iodine deficiency during pregnancy which may affect the neurodevelopment of the offspring, and it occurs due to deficiency of TPO or another factor including concomitant drug therapy such as corticosteroids [3].

India to no exception, according to the projections from various studies on the thyroid. Studies from Mumbai have suggested that congenital hypothyroidism is common in India, the disease occurring in 1 out of 2640 neonates when compared with the worldwide average value of 1 in 3800 subjects. In childhood, too, hypothyroidism can occur; in the clinical-based study also found that, out of 800 children with thyroid disease, 79% had hypothyroidism [4].

This article makes an attempt to revisit the importance of recent advances in treating Congenital Hypothyroidism.

Factor Affecting Thyroid Peroxidase:

The Risk Factor, Sign and Symptom of Congenital Hypothyroidism: The Risk Factor of Congenital Hypothyroidism include gender (Female are more prone to CH than Male) [5], anti-thyroid cancer treatment, manic depression, thyroid surgery, elderly generation, autoimmune disorders like diabetes or rheumatoid arthritis. Sign and symptoms of Congenital Hypothyroidism are experience weakness, sleepiness, slowness of speech, constipation, weight gain, edema of larynx, hearing loss, dry skin and coarse hair, puffy, depression, dysarthria, cold intolerance [6, 7, 8, 9].

Complication of Primary Congenital Hypo-thyroidism are myxedema coma, diabetes, left ventricle hypertrophy, acute heart failure, hypositis, retroperitoneal fibrosis, pituitary hyperplasia, postdate delivery, macrosomia, bowel syndrome, supraseller chordoid glioma [10, 11, 12, 13, 14, 15].

Dietary Factors: The factors affecting thyroid Peroxidase include *Myrcia uniflora* flavonoids, aqueous extract of kalanchoe brasilensis, usage of leucomalachite green products likes dyes [16, 17, 18]. Also anti-thyroid, cough medicine, sulfonamides, lithium, phenylbutazone, soybeans, millet, cassava, cabbage, root vegetables, flower vegetables, leafy vegetables, fruity vegetables, legumes, seafood, phenolic contaminates like chocolate, cookies, cakes, bonbons, salami, canned meat, sausages, eggs, bacon, cedevita (powder based vitamin juice), fruits juices, refreshing non-alcoholic drink bran bread, white bread full-fat cheese, cottage cheese, butter [19, 20, 21]. As well hard cheese, sour cream venison, animal fats, lamb, pork mushrooms, canned and pickled vegetables, potato, muesli dried fruits nuts, hard liquor, vegetables juices, powder, soups, tea, olive oil, milk, coffee, yoghurt, fresh fruits, chicken, turkey, beef, veal macaroni or rice, jam, vegan diet, and marmalade fruit compote plant oil, TPO is inhibited by the thioamide drugs, such as propylthiouracil and methimazole [22, 23, 24, 25]. In diagnostic immunohistochemistry, the expression of TPO is lost in papillary thyroid carcinoma [26]. Initially, dietary factors are increase secretion TPO, long-term intake causes decrease TPO secretion.

Current Therapy of Primary Congenital Hypothyrodism:

Levothyroxine: Levothyroxine is used to treat an underactive thyroid gland by it replaces low thyroid hormone level produced by your thyroid gland to help to maintain normal body homeostasis. Initial dosing ranging from 50 mcg/day in case of primary congenital hypothyroidism [27]. It is a prolonged therapy to maintain the body thyroxine level. Due to long-term use, they have common side effects like nervousness, insomnia, pyrexia, convulsions, acute psychosis, thyroid storm, tachycardia, arrhythmia [28]. I also have some drug interactions like iron, calcium, proton pump inhibitors like omeprazole, statins, and oestrogen [29].

Removal Gland Surgery: Gland Removal Surgery helps to avoid complications like pain and to bleed in the respiratory tract and disturb body homeostasis [30, 31, 32]. This surgery has several complications like hemorrhage, respiratory obstruction like hematoma, bilateral recurrent nerve palsy, laryngeal edema, leukocytosis, tachycardia seroma, recurrent laryngeal nerve injury, thyroid storm, destruct the parathyroid gland, recurrent thyrotoxiocosis, hypertrophic SCAR/KELOID, rarely pneumothorax [33, 34, 35, 36, 37].

Genetic: Congenital Hypothyroidism involves autosomal recessive/dominant genes characterized by the inability to utilize iodine in thyroid. Biallelic non–functional TPO mutation produces iodine organification defect; monoallelic mutation carrier will have normal thyroid function. The coordination between clinical phenotype and TPO genotype is mentioned in **Table 1** [38, 39, 40, 41].

TABLE 1: THE CO-ORDINATION BETWEEN CLINICAL PHENOTYPE AND TPO GENOTYPE

S. no.	Percentage	Classification	Description	Represenatative TPO genotype
1	50%	Monoalleic mutation carriers	Normal TSH – Normal Thyroid Size	Cys808fs; WT[1]
2	30%	Mild TPO	Subtile elevated of TSH marked	Gly387Arg; Trp527Cys;
3	<30%	Deficiency	Goiter high T_3 to T_4 molar ratio, High Tg	Trp527Cys; Asp224del;c.839-3A>G; Gly553C; Asp574, Leu527Cys;
4	15%	Severe	Subtile elevated of TSH Marked	Gly387Arg; Trp527Cys;

Recent Development in Congenital Hypo-thyroidism Therapy:

Gene Therapy: The Potential to extract functional thyroid follicular cells from the principle, recombinant technology. A Full-length cDNA clone for human thyroid peroxidase(TPO), which was inoculated into the mammalian cell as vector pECE was stably transfected into Chinese hamster ovary(CHO) cells. These clones assayed by human TPO mRNA, TPO protein, and TPO enzyme activity was seen, then it is further moved to culture [42]. In this technique have several advantages like avoiding surgery complications as mention above and also avoid ADR caused by levothyroxine [it is permanent therapy for treating hypothyroidism] [43]. It also indicated dyslipidemia, toxic adenoma, thyroiditis, and some non-thyroidal illness, like some autoimmune diseases [44, 45, 46].

Stem Cell Therapy: The Potential to extract functional thyroid follicular cells from embryonic stem cells (ESC's) or induced pluripotent stem cells (iPSC's) would have potentially directed for congenital or post-surgical hypothyroidism patients. The thyroid follicular cells were developed by the creation of two models that have allowed for the save of hypothyroid mouse recipients through the transplantation of thyroid follicular cells derived from mouse ESC's. It is a preferred alternative to long-term pharmacologic therapy. Indeed, regenerative therapy would provide physiologic replacement of both T4 and T3 without reliance on an external source [47, 48].

CONCLUSION: It is a major threat to over global. Unto now, the most effective method to treat this disease is levothyroxine supplement and gland surgery removal. Thus, it is meaningful to establish an effective and economical protocol for the enzyme thyroid peroxidase production, which helps in congenital hypothyroidism. The development of regenerative therapy based on stem cell technology helps to the development of Enzymatic drugs.

Our review concludes that an increase in the production of enzyme thyroid peroxidase by using the recent technology will be a solution for Congenital Hypothyroidism.

ACKNOWLEDGEMENT: I would like to thank the management and Principal of JKK Nattraja College of Pharmacy, Kumarpalayam, College, for providing all the facilities required to carry out my work.

CONFLICTS OF INTEREST: All authors declare no conflicts of interest.

REFERENCES:

1. Kirsten D: The thyroid gland: physiology and pathophysiology. Neonatal Netw 2000; 19(8): 11-26.
2. Jeffery GH, Bassett J, Mandham J and Denny RC: Vogel's text book of quantitative chemical analysis. Longman Scientific and Technical Pub. U.K. 1994.
3. Liu YC, Yeh CT and Lin KH: Molecular functions of thyroid hormone signaling in regulation of cancer progression and anti-apoptosis. Int J Mol Sci 2019; 20(20): 4986.
4. Cherella CE and Wassner AJ: Update on congenital hypothyroidism. Current Opinion in Endocrinology, Diabetes and Obesity 2020; 27(1): 63-69.
5. Kim H, Moon SY and Han K: Treatment of hypothyroidism using Korean medicine: 2 case reports. Medicine (Baltimore) 2020; 99(18): e19737.
6. Kim J, Gosnell JE and Roman SA: Geographic influences in the global rise of thyroid cancer. Nature Reviews Endocrinology 2020; 16(1): 17-29.
7. Minuto MN, Ansaldo GL and Santori G: Possible role of low magnesium levels in the onset of postoperative hypoparathyroidism following thyroidectomy. Minerva Chirurgica 2019; 74(6): 445-51.
8. Sweep CG, Meer MJ and Ross HA: Chronic infusion of TNF-alpha reduces plasma T4 binding without affecting pituitary-thyroid activity in rats. The American Journal of Physiology 1992; 263(6): E1099-E1105.
9. Louro P, Duraes J and Oliveira D: Woodhouse-Sakati Syndrome: First report of a Portuguese case. American Journal of Medical Genetics 2019; 179(11): 2237-40.
10. Gupta V, Singh A and Khadgawat R: The spectrum of clinical and subclinical endocrinopathies in treatment-native patients with celiac disease. Indian Journal of Gastroenterology 2019; 38(6):518-526.
11. Hayakawa N, Sato Y and Nagasaka A: High levels of DNA polymerase β mRNA corresponding with the high activity in Graves' thyroid tissue. Journal of Endo-crinological Investigation 2017; 40(4): 385-89.
12. Dratman MB and Martin JV: The many faces of thyroxine. AIMS Neuroscience 2020; 7(1): 17-29.
13. Laugesen D, Malmstroem S and Ebbehoj E: Effect of 9 months of vitamin D supplementation on arterial stiffness and blood pressure in Graves' disease: a randomized clinical trial. Endocrine 2019; 66(2): 386-97.
14. Le SN, Porebski BT and McCoey J: Modelling of Thyroid Peroxidase Reveals Insights into Its Enzyme Function and Autoantigenicity: PLOS One 2015; 10(12): e0142615.
15. Levie D, Korevaar TIM and Bath SC: Association of maternal iodine status with child IQ: a meta-analysis of individual participant data. The Journal of Clinical Endocrinology and Metabolism 2019; 104(12): 5957-67.
16. Little AS, Kelly DF and White WL: Results of a prospective multicenter controlled study comparing surgical outcomes of microscopic versus fully endoscopic transsphenoidal surgery for nonfunctioning pituitary adenomas: the Transphenoidal Extent of Resection (TRANSSPHER) Study. J of Neurosurgery 2019; 1-11.

17. Zhou J, Luo J and Lin J: Perinatal risk factors for congenital hypothyroidism: A retrospective cohort study performed at a tertiary hospital in China. Medicine (Baltimore) 2020; 99(26): e20838.
18. Tirado-Caballero J, Rivero-Garvía M and Gonzalez-Pombo M: Fully Endoscopic Transforaminal-Transchoroidal Approach for Tectal Area Tumor Removal. World neurosurgery 2020; 137: 164-72.
19. Ferreira AC and Silva CM: Rich inhibition of TPO by *Myrcia uniflora* flavoinoids. Chemical Research in Toxicology 2006; 19: 351-55.
20. Goncalves CFL, de Freitas ML and Ferreira ACF: Flavonoids, Thyroid Iodide Uptake and Thyroid Cancer-A Review. Int Journal of Mole Sciences 2017; 18(6): 124.
21. Gebreslassie YT: Equilibrium, Kinetics, and Thermo-dynamic Studies of Malachite Green Adsorption onto Fig (*Ficus cartia*) Leaves. Journal of Analytical Methods in Chemistry 2020; 7384675.
22. Yang Y, Chen Q and Yu WY: Herbal Active Ingredients: An Emerging Potential for the Prevention and Treatment of Papillary Thyroid Carcinoma. Bio Med Research International 2020; 2020: 1340153.
23. Xie QP and Xiang C: The patterns and treatment of postoperative hemorrhage and hematoma in total thyroidtomy via breast approach: Experience of 1932 cases. Endocrine. 2019; 63: 422-29.
24. Matana A, Torlak V and Brdar D: Dietary factors associated with plasma thyroid peroxidase and thyroglobulin antibodies. Nutrients 2017; 9(11): 1186.
25. Huser S, Guth S and Joost HG: Effects of isoflavones on breast tissue and the thyroid hormone system in humans: a comprehensive safety evaluation. Archives of Toxicology 2018; 92(9): 2703-48.
26. Delitala AP, Capobianco G and Cherchi PL: Thyroid function and thyroid disorders during pregnancy: a review and care pathway. Archives of Gynecology and Obstetrics 2019; 299(2): 327-38.
27. Ma C, Xie J and Wang H: Radioiodine therapy versus antithyroid medications for Graves' disease. The Cochrane Database of Systematic Reviews 2016; 2: CD010094.
28. Subhi O, Schulten HJ and Bagatian N: Genetic relationship between Hashimoto`s thyroiditis and papillary thyroid carcinoma with coexisting Hashimoto`s thyroiditis. PLOS One 2020; 15(6): e0234566.
29. Aleksander PE, Brückner-Spieler M and Stoehr AM: Mean High-Dose l-Thyroxine Treatment Is Efficient and Safe to Achieve a Normal IQ in Young Adult Patients With Congenital Hypothyroidism. The Journal of Clinical Endocrinology and Metabolism 2018; 103(4): 1459-69.
30. Xue J, Zhang L and Qin Z: No obvious sympathetic excitation after massive levothyroxine overdose: A case report. Medicine (Baltimore) 2018; 97(23): e10909.
31. Irving SA, Vadiveloo T and Leese GP: Drugs that interact with levothyroxine: an observational study from the thyroid epidemiology, adult and research study (TEARS). J of Cli Endocri and Metabol 2015; 82: 136-77.
32. Li L, Liu W and Tao H: Efficacy and safety of negative pressure versus natural drainage after thyroid surgery: A systematic review and meta-analysis. Medicine (Baltimore) 2018; 97(31): e11576.
33. Parate LH and Pujari V: Post thyroidectomy haematoma causing servere supraglottic oedema and pulmonary oedema – a case report. Journal of Clinical Diagnostic Research 2014; 8(8): 01-02.
34. Materazzi G, Ambrosini CE and Fregoli L: Prevention and management of bleeding in thyroid surgery. Gland surgery, 2017; 6(5): 510-15.
35. Shah SR: Idiopatic thyroid storm mimicking SIRS in a patient with hypothyroidism-a dignositic dilemma. Journal of Community Hospital Internal Medi 2018; 8: 368-69.
36. Castagna MG, Dentice M and Cantara S: DIO2 Thr92Ala Reduces Deiodinase-2 Activity and Serum-T3 Levels in Thyroid-Deficient Patients. The Journal of Clinical Endocrinology and Metabolism 2017; 102(5): 1623-30.
37. Techer R, Houde M and Verreault J: Associations between organohalogen concentrations and transcription of thyroid-related genes in a highly contaminated gull population. The Science of the total environment 2016; 545: 289-98.
38. Hirano T, Yamad M and Sato K: Invasive pulmonary mycormycosis with pulmonary rare in with pulmonary esonophlia. BMC J of Pulmonary Medi 2017; 17: 76-78.
39. Valko M, Leibfritz D and Moncol J: Free radicals and antioxidants in normal physiological functions and human disease. Int J of Biochem and Cell Bio 2007; 39(1): 44-84.
40. Zarogoulidis P and Kioumis L: Pneumonthorax: form definition to diagnosis and treatment. Journal of Thoracic Disease. 2014; 6: 372-76.
41. Abramowixz MJ and Targovnik HM: Identification of a mutation in the coding sequence of the human thyroid peroxidase gene causing congenital goiter. Journal of Clinical Investigations 1992; 90(4): 1200-04.
42. Lee C and Harun F: Variable clinical phenotypes in a family with homozygous c.1159G>A mutation in the thyroid peroxidase. Gene Hoirm Res Paaediatr 2014; 8(2): 241-45.
43. Kotani T and Umeki KA: Novel mutation in the human thyroid peroxidase gene resulting in a total iodide organification defect. J of Endocri 1999; 160(2): 267-73.
44. Brunt LH and Skinner REH: Different effects of altered patterns of movement and stains on joint cell behavior and skeletal morphogenesis, cell behavior and skeletal morphogenesis. Osteoarthritis Carti 2006; 24(11): 41-42.
45. Chovanova M, Zorkocy G and Struhananska E: Production strategies of thyroid peroxidase form Branochiostoma belcheri, in *E. coli*. Journal of Biotechnology and Biomaker 2018; 8: 16-17.
46. Srivastava VK and Singh H: Association of thyroid peroxidase antibody and dyslipidema in subclinical hypothyroidism. Journal of Family Medicine and Primary Care 2017; 6: 63-68.
47. Tagoe CE and Sheth T: Rheumatic associations of autoimmune thyroid disease: a systematic review. Journal of Clinical Rheumatology 2019; 38: 1808-09.
48. Hollenberg AN and Choi J: Regenerative therapy for Hypothyroidism: mechanisms and possibilities. Journal of Molecular Cell Endocrinology 2017; 445: 35-41.

How to cite this article:
Sujitha PJ and Arunkumar S: Increased enzymatic activity of thyroid peroxidase-treatment for congenital hypothyroidism. Int J Pharm Sci & Res 2021; 12(6): 3316-19. doi: 10.13040/IJPSR.0975-8232.12(6).3316-19.