Treatment of Hashimoto's thyroiditis with herbal medication

Norakant Neupane, Manpreet Kaur, Pranav Kumar Prabhakar

Department of Paramedical Sciences, Lovely Professional University, Phagwara, Punjab, India

Abstract

Hashimoto's thyroiditis (HT) is an autoimmune thyroid disorder, an organ-specific disease, which is characterized by diffused goiter with lymphocytic infiltration, which leads to destruction of thyroid gland causing hypothyroidism. This is a condition where the thyroid gland does not release enough of thyroid hormone called thyroxin due to the insufficient amount of iodine. Some common sign and symptoms of Hashimoto's disease and hypothyroidism are weight gain, depression, and constipation, irregular and heavy menstrual period. However, herbal treatment is effective and enhances thyroid function. There are some natural-occurring herbs such as gum guggul (*Commiphora mukul*), Blue flag root (*Iris versicolor*), bladder wrack (*Fucus vesiculosus*), and seaweeds which are commonly used to treat this disorder. These herbs have different mechanism of action in HT and hypothyroidism disorder. Bladder wrack upregulate the production of iodine processing hormone, whereas gum guggul increases the conversion of tetraiodothyronine into triiodothyronine, and blue flag root is a detoxifying agent. This review article summarizes the herbal treatments which are commonly used and also their mechanism of action.

Key words: Bladderwrack, guggul, hyperthyroidism, hypothyroidism, iodine, thyroxine

INTRODUCTION

ashimoto's thyroiditis (HT) is an autoimmune disorder in which the immune system turns against the body's own tissue and its show their features as diffuse goiter, lymphocytic infiltration in the presence of autoantibody, which leads to destruction of follicular cell of thyroid grand and cause hypothyroidism. Hypothyroidism is a condition in which thyroid gland does not make enough thyroxin and triiodothyronine (T3) hormone according to the body needs.[1] Both the genetic factor and the environmental factor are responsible to cause HT.[2] HT is the most frequent cause of hypothyroidism recorded in 4-9.5% of the adult population and leads to affects the central nervous system, growth and development, cardiovascular system (CVS), skeletal system, gastrointestinal tract (GIT), and reproductive activity.[3] Various biochemical diagnostic tests are available for the diagnosis of HT such as the thyroid-stimulating hormone (TSH) test, antithyroid antibodies tests, and the free tetraiodothyronine (T4) hormone test. [4] The HT can be managed by various medicinal systems such as allopathic and herbal drugs. [5] These medications help to regulate the function of thyroid gland with its action of mechanism that will further discuss in detail.

ETIOLOGY AND COMPLICATIONS OF HT

The HT disorder is caused by multistep process which includes genetic, immunological, and environmental factors. The normal thyroid cells leads to production of antibodies directed against thyroid tissue in case of loss of immune tolerance which causes the destruction if it is thyroid grand. It is believed that thyroid tissue produce thyroglobulin which plays a central role in the pathogenesis of HT.^[6] It is reported that thyroglobulin proteins have approximately 40 different type of epitope, which has an involvement in the pathogenesis of HT.^[7]

Some genetic factors also play role in pathogenesis of this disease as well as other autoimmune disorder such as major histocompatibility complex, cytotoxic T-lymphocyte association (CTLA-4), and human leukocyte antigen genes.^[8] Normally, CTLA-4 plays a vital role in upregulating

Address for correspondence:

Prabhakar Pranav Kumar, Department of Paramedical Sciences, Lovely Professional University,

Phagwara - 144 411, Punjab, India.

Phone: +91-7696527883.

E-mail: prabhakar.iitm@gmail.com

Received: 15-10-2016 **Revised:** 24-03-2017 **Accepted:** 05-08-2017 the immunological self-tolerance in body, and its downregulation is believed to be the first step of the causes of HT.^[9] Genetic susceptibility also associated with the deregulation of the regular destruction mechanism in thyroid gland.^[10] Thyrotrophs affected with HT, when compare with the normal thyroid cells, are capable of producing more Fas ligand protein leading to increase apoptosis.^[11] The common environmental factors which act as triggers for the HT are infection, cytokine, selenium, and iodine intake.^[12] Some study shows that hypothyroidism in patient with HT is caused by smoking also.^[13]

Hypothyroidism affects all the major body system such as CVS, nervous system, GIT system, reproductive system, renal function, plasma volume, and effect on hemopoietic and coagulation system.[3] Most of these pathologic changes can be reversed by the thyroid hormone replacement therapy.^[14,15] The general neurological manifestation of hypothyroidism is headache, tinnitus, psychiatric disorder, visual disturbances, other sensory disorders such as numbness, tingling, and paresthesias are frequently reported.[16] In the case of digestive system, HT results in achlorhydia and decreased peristaltic movement.[17] It also causes pernicious anemia with autoimmune thyroid disease.[18] In the case of female, HT is associated with the menstrual dysregulation and infertility,[19] whereas in males, it is associated with the abnormalities of gonadal function, disruption of gonadotropin secretion, and steroidogeneses.[20] Hypothyroidism is basically associated with anemia but few changes also occur in other cellular elements. Anemia is reported in 25-50% of hypothyroid patient and characterised by low metabolic rate, decreased oxygen consumption, and drop in erythropoietin levels.^[21] Such anemia is mostly normochromic and normocytic and these patients have normal iron stores normal red cell differentiation.[22]

SIGN AND SYMPTOMS

Thyroid hormone is produced in the glycoprotein thyroglobulin of thyroid gland consisting of follicles cells, which is synthesized through iodination of tyrosine residues.[23] The primary role of thyroid hormone is to regulate the basal metabolic rate. Main symptoms of HT are destruction of thyroid tissue result in less secretion of thyroid hormones as a result slowdown the metabolic process.[24] At the initial stage of disease, the TSH level not showing fluctuations very much. A number of other organ systems are also adversely affected due to the less secretion of thyroid hormones. Some of them are bradycardia, which is dysfunction of CVS, delayed reflexes and slowed speech as dysfunction of nervous system, constipation, increased bile reflexed, and acites are some gastrointestinal symptoms.[25] Decreased metabolism and result of fluid retention increased the body weight. Hypoglycemia, altered sensorium, and severe bradycardia result in myxedema which trigger, infection, surgery, and traumatic injuries are main characteristic of myxedema.

In some cases, rheumatic disease and autoimmune disease also affect with HT. Moreover, occasionally depression, irritability, fatigue, and confusion have been recognized as initial symptoms in patient after the diagnosis of HT.^[26]

DIAGNOSIS

Diagnosis of HT is based on the metabolic status of patient and type of lesion present in the patient. Diagnosis of HT is performed by the examination of antithyroid antibodies and ultrasonographic examinations.^[27] The measurement of thyroid hormone level indicates the glandular function. To evaluate the function level of thyroid gland commonly laboratory studies of T3, T4, and TSH level.^[4] Although the autoimmune disease is due to the presence of antithyroid antibody, there are no significant symptoms of hypothyroidism. In circumstances, follicular carcinomas lead to the false diagnosis due to the excess number of hyperplastic follicular cells. In contrast, there could be missing diagnosed as HT due to large number of Hurthle cell tumors.

Next modality is radioactive iodine uptake which is generally used in diagnosis thyroid discarders for the diagnosis of HT by Raid has been deliberate for many years. [2] Heterogeneous and hypoechoic pattern, thyroid function ultrasonography (USG) shows focal or diffuse glandular enlargement course for the chronic thyroiditis. USG is strongly recommended due to the presence of discrete hypoechoic micronodules (1-6 mm); fine exogenic fibrous septa may produce pseudolobulated appearance extensive hypervascularity indicating color. Benign and malignant nodules may coexist in the surroundings of diffuse thyroiditis. [28-30]

TREATMENT

Herbal treatment of hypothyroidism

There are a number of medicinal plant which is commonly used for the management of the HT. some of such plants are bladder wrack guggul, *Iris versicolor, Leonurus cardiac, Commiphora mukul, Melissa officinalis, Vitex agnus-castus,* and *Curcuma longa*.

Bladder wracks

Bladder wrack (*Fucus vesiculosus*), a member of the Fucaceae family, is a genus of brown algae found intertidal, especially in the Pacific Ocean. *F. vesiculosus* contain the flavonoid flucoxanthin^[31] and it is reported that *Fucus* contain highest antioxidant activity of the edible seaweeds. *Fucus* is a rich source of iodine and also having high bioavailability. It is also a rich in numerous minerals, that is, calcium, potassium, and contain moderate amount of phosphorous, selenium, magnesium, and zinc also. It also contains sufficient quantity

Table 1: Herbal treatment for hypothyroidism			
Herbal drug	Extract	Action on body	Dosage
Bladder wrack (F. vesiculosus)	Seaweed	Regulate hypothyroidism, anti-inflammatory, converting T4 into T3 antibacterial	4-8 drops, ×3/days
Gum guggul (<i>C. mukul</i>)	Dubbed guggulipid	Enhance T3 production, cholesterol lowering agent	25 mg, ×3/days
Blue flag root (I. versicolor)	Liquid of fresh rhizome	Detoxifying agent anti-inflammatory	1-2 ml, ×3/days

F. vesiculosus: Fucus vesiculosus, C. mukul: Commiphora mukul, I. versicolor: Iris versicolor, T3: Triiodothyronine, T4: Tetraiodothyronine

of Vitamins A, D, E, K, B2, B3, and B6. *Fucuses* contain these all vitamins and minerals that help to enhance the thyroid function when consumed in appropriate amount.^[30] The fresh cutted blade of *Fucus* and dried in low sunlight contains more amount of iodine.^[32] It also helps to decrease the trans-sialidase activity in blood, an enzyme that deals with cholesterol accumulation.^[33] This may helpful for hypothyroidism patients as decrease metabolism is associated with hyperlipidemia. In the 12 species tested, iodine levels varied from 16 μg/g in nori (*Porphyra tenera*) to 8165 μg/g in processed kelp granules made from *Laminaria digitata*.

Fucus also has the ability to decrease trans-sialidase activity in the blood, an enzyme associated with cholesterol accumulation. This may benefit patients with low thyroid function as decreased metabolism is associated with hyperlipidemia [Table 1].

Guggul

Guggul is also known as C. mukul that supports thyroid function. C. mukul (belongs to family burseraceae) contain its content of aromatic gummy resins that have many medicinal uses.[34] Guggul or Commiphora is reported as that it helpful to increase the iodine uptake by thyroid gland and also elevated the activity of thyroid peroxidase enzyme. [35] By the more production of T3 with healthy alteration in the ratio of T3 to T4 indicate a thyroid support effect.[35] Guggul may also lower lipid levels by supporting the thyroid basic metabolic function. [36] Guggul contain sterols, which is called as guggulsterones, which act on bile acid receptor to process lipids and also contribute to its hypolipidemic effects.[37] Guggul inhibits low-density lipoprotein (LDL) oxidation, which is mechanism of atherosclerosis.[38] It is also helpful to change the level of LDL with Guggul supplementation. It may also decreases the total lipid content through the thyroid function which has been documented with the animal studies.

The phytoconstituents of Commiphora is oleoresin which increases the iodine uptake by the thyroid glands and also increases the thyroperoxidase activity.

I. versicolor

I. versicolor also called blue flag, it is a small wild *Iris* found in the marshy area of North America. *I. versicolor* is also

helps to promote the function of thyroid gland with more production of T3. It is a detoxifying agent and specific for the treatment of thyroid enlargement and goiter. It is also used to treat hepatomegaly and splenomegaly.^[38] This plant contains volatile oils, resins, alkaloids, and oleoresin iridin. This medicinal plants was used since ancient time as an oral supplement or topically or both. This has special effect on the enlargement of thyroid and goiter.

Increasing the production of T3 by herbal medication

- Bladder wrack produces iodine and selenium.
- Guggul helps to increase the uptake of iodine.
- Blue flag is detoxifying the thyroid gland.
- Selenium helps to convert T4 into T3.
- Iodine uses in production of T3 and T4.

CONCLUSIONS

The optimum function of thyroid requires sufficient amount of iodine to synthesize and releases sufficient hormones. Iodine deficiency can cause number of negative health consequences along with hypothyroidism. HT is an autoimmune disorder caused by various environmental and genetic factors. Till date, no specific drug is available commercially to treat HT. Although hormone replacement therapy is one of the available options for the management of HT and hypothyroidism. Certain herbal and allopathic drugs are available to increase immune system and provide exogenous thyroid hormone which acts on all the body system. All these medicines should be taken under the prescription of doctor.

REFERENCES

- Akamizu T, Amino N, de Groot LJ. Hashimoto's thyroiditis. In: Thyroid Disease Manager. Available from: http://www.thyroidmanager.org/chapter/hashimotosthyroiditis1. [Last accessed on 2017 Jul 18].
- Fisher DA, Oddie TH, Johnson DE, Nelson JC. The diagnosis of Hashimoto's thyroiditis. J Clin Endocrinol Metab 1975;40:795-801.
- 3. Bello F, Bakari AG. Hypothyroidism in adults: A review

- and recent advances in management. J Diabetes Endocrinol 2012;3:57-69.
- Kasagi K, Kousaka T, Higuchi K, Iida Y, Misaki T, Alam MS, et al. Clinical significance of measurements of anti-thyroid antibodies in the diagnosis of Hashimoto's thyroiditis: Comparison with histological findings. Thyroid 1996;6:445-50.
- 5. Saikia UK, Saikia M. Drug-induced thyroid disorders. J Indian Med Assoc 2006;104:583, 585-7, 600.
- Champion BR, Page KR, Parish N, Rayner DC, Dawe K, Biswas-Hughes G, et al. Identification of a thyroxinecontaining self-epitope of thyroglobulin which triggers thyroid autoreactive T cells. J Exp Med 1991;174:363-70.
- 7. Male DK, Champion BR, Pryce G, Matthews H, Shepherd P. Antigenic determinants of human thyroglobulin differentiated using antigen fragments. Immunology 1985;54:419-27.
- Gebe JA, Swanson E, Kwok WW. HLA class II peptide-binding and autoimmunity. Tissue Antigens 2002;59:78-87.
- 9. Chistiakov DA, Turakulov RI. CTLA-4 and its role in autoimmune thyroid disease. J Mol Endocrinol 2003;31:21-36.
- 10. Giordano C, Richiusa P, Bagnasco M, Pizzolanti G, Di Blasi F, Sbriglia MS, et al. Differential regulation of Fasmediated apoptosis in both thyrocyte and lymphocyte cellular compartments correlates with opposite phenotypic manifestations of autoimmune thyroid disease. Thyroid 2001;11:233-44.
- 11. Limachi F, Basso S. Apoptosis: Life though planned cellular death regulating mechanisms, control systems and relations with thyroid disease. Thyroid 2002;12:27-34.
- 12. Boukis MA, Koutras DA, Souvatzoglou A, Evangepolau K, Vrontakis M, Moulapoulaos SD. Thyroid hormone and immunologic studies in endemic goiter. J Clin Endocrinol Metab 1983;57:859-62.
- 13. Fukata S, Kuma K, Sugawara M. Relationship between cigarette smoking and hypothyroidism in patients with Hashimoto's thyroiditis. J Endocrinol Invest 1996;19:607-12.
- 14. Polikar R, Burger AG, Scherrer U, Nicod P. The thyroid and the heart. Circulation 1993;87:1435-41.
- 15. Kabadi UM, Kumar SP. Pericardial effusion in primary hypothyroidism. Am Heart J 1990;120:1393-5.
- Ober KP. Acanthosis nigricans and insulin resistance associated with hypothyroidism. Arch Dermatol 1985;121:229-31.
- 17. Allain TJ, McGregor AM. Thyroid hormones and bone. J Endocrinol 1993;139:9-18.
- 18. Kogawa K. Parietal cell antibodies. Part I. Clinical and pathological studies of parietal cell antibodies. Gastroenterol Jpn 1975;10:35-51.
- 19. Joshi JV, Bhandarkar SD, Chadha M, Balaiah D, Shah R. Menstrual irregularities and lactation failure may precede thyroid dysfunction or goitre. J Postgrad Med 1993;39:137-41.

- 20. Stathatos N, Wartofsky L. Perioperative management of patients with hypothyroidism. Endocrinol Metab Clin North Am 2003;32:503-18.
- 21. Green ST, Ng JP. Hypothyroidism and anaemia. Biomed Pharmacother 1986;40:326-31.
- 22. Axelrod AR, Berman L. The bone marrow in hyperthyroidism and hypothyroidism. Blood 1951;6:436-53.
- 23. Zimmermann MB. Iodine deficiency. Endoor Rev 2009;14:347-408.
- Becker KL, Ferguson RH, McCohaney WM. The connective tissue diseases and symptoms associated with Hashimoto's thyroiditis. New Eng J Med 1963;263:277-80.
- 25. Baker BA, Gharib H, Markowitz H. Correlation of thyroid antibodies and cytologic features in suspected autoimmune thyroid disease. Am J Med 1983;74:941-4.
- 26. Hall RC, Popkin MK, DeVaul R, Hall AK, Gardner ER, Beresford TP. Psychiatric manifestations of Hashimoto's thyroiditis. Psychosomatics 1982;23:337-42.
- 27. Ceylan I, Yener S, Bayraktar F, Secil M. Roles of ultrasound and power Doppler ultrasound for diagnosis of Hashimoto thyroiditis in anti-thyroid marker-positive euthyroid subjects. Quant Imaging Med Surg 2014;4:232-8.
- 28. Yoshida H, Amino N, Yagawa K, Uemura K, Satoh M, Miyai K, *et al.* Association of serum anti-thyroid antibodies with lymphocytic infiltration of the thyroid gland: Studies of seventy autopsied cases. J Clin Endocrinol Metab 1978;46:859-62.
- 29. Zhang L, Li H, Ji QH, Zhu YX, Wang ZY, Wang Y, et al. The clinical features of papillary thyroid cancer in Hashimoto's thyroiditis patients from an area with a high prevalence of Hashimoto's disease. BMC Cancer 2012;12:610.
- 30. Yan X, Chuda Y, Suzuki M, Nagata T. Fucoxanthin as the major antioxidant in Hijikia fusiformis, a common edible seaweed. Biosci Biotechnol Biochem 1999;63:605-7.
- 31. Jimenez-Escrig A, Jimenez-Jimenez I, Pulido R, Saura-Calixto F. Antioxidant activity of fresh and processed edible seaweeds. J Sci Food Agric 2001;81:530-4.
- 32. Noge K, Becerra JX. Germacrene D, a common sesquiterpene in the genus *Bursera* (*Burseraceae*). Molecules 2009;14:5289-97.
- 33. Tripathi YB, Malhotra OP, Tripathi SN. Thyroid stimulating action of Z-guggulsterone obtained from *Commiphora mukul*. Planta Med 1984;50:78-80.
- 34. Panda S, Kar A. Gugulu (*Commiphora mukul*) induces triiodothyronine production: Possible involvement of lipid peroxidation. Life Sci 1999;65:PL137-41.
- 35. Wu J, Xia C, Meier J, Li S, Hu X, Lala DS. The hypolipidemic natural product guggulsterone acts as an antagonist of the bile acid receptor. Mol Endocrinol 2002;16:1590-7.
- 36. Stansbury J, Saunders P, Winton D. Promoting health thyroid function with iodine, bladderwrack, guggal and Iris. J Restorative Med 2012;1:83-90.

Norakant, et al.: Management of Hashimoto thyroiditis

- 37. Takasu N, Yamada T, Takasu M, Komiya I, Nagasawa Y, Asawa T, *et al.* Disappearance of thyrotropin-blocking antibodies and spontaneous recovery from hypothyroidism in autoim-mune thyroiditis. N Engl J Med 1992;326:513-8.
- 38. Devdhar M, Ousman YH, Burman KD. Hypothyroidism. Endocrinol Metab Clin North Am 2007;36:595-615, v.

Source of Support: Nil. Conflict of Interest: None declared.