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“SUGAR INDUCED HYPO-THYROIDISM IN AYURVEDA- A COMPARATIVE REVIEW STUDY”

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Abstract - Many of us have heard or read about artificial sweeteners affecting the thyroid that was a stunning example reported at first time in American Association of Clinical Endocrinologists (AACE), 22nd Annual Scientific & Clinical Congress. Hypothyroidism is posing a major challenge both in developing as well as developed countries. The use of sugar substitutes (artificial sweeteners or non-nutritive sweeteners) has increased dramatically in the past few decades. They have been used as a substitute for sucrose (table sugar) in various diet-related disorders. Their excessive use has been linked to hyperphagia and obesity-related disorders. Hashimoto's thyroiditis (chronic autoimmune thyroiditis) is a disease that involves the immune-mediated destruction of the thyroid gland gradually leading to its failure. Animal studies report that artificial sweeteners affect the immune system. Moreover, animal studies show that sucralose diminishes the thyroid axis activity.

Ayurveda from its existence into the modern world is facing a major challenge. Endocrine disorders are difficult to understand in Ayurveda. Though certain disorders like Diabetes mellitus are well described in various Ayurvedic texts but as far as diseases of thyroid gland are concerned they are not well understood. In Ayurveda, we correlate the disorders caused by thyroid gland as *Galganda*, *Gandmaala* etc but the concept of hormone overproduction or under secretion is somewhere missing. Hence, here is an attempt to get the understanding of disease autoimmune Hypothyroidism induced by sugar substitute through various ayurvedic principles.

Keywords - Hashimoto's thyroiditis, sugar substitutes, Ayurvedic Galgand, Autoimmune formaldehyde, samparpti.

Introduction –

Thyroid gland is an one of the most important gland of the endocrine system. It regulates metabolic, respiratory, cardiovascular, digestive, nervous and reproductive system either directly or indirectly. Thyroid hormone regulates the metabolic rate of the body. Lack of thyroid hormone or resistance of the body tissue to the thyroid hormone with respect to metabolic demand result in disorder called hypothyroidism. Deficiency of thyroid hormone caused due to various reasons like iodine deficiency, autoimmune disease, radiation therapy, drugs or thyroid surgery ^[1]. There is not any reference of Thyroid gland and Hypothyroidism in Ayurveda. However, a disease named *Galganda*, characterised by neck swelling is well known^{[2][3]}. Acharya Charaka included it under 20 *Shleshma Vikara* ^[4]. According to Acharya Charaka manifestation of multiple granthi around the neck is called *Gandmala* and single swelling in the *parshava* of the neck is *Galganda*. So *Galganda* and *Gandmala* can be co-related with hypothyroidism.

The whole world is aware about the importance of iodine in our body, so they will take sufficient iodine with diet and iodine related thyroid disorder felt less now. The most common cause of hypothyroidism is an autoimmune disorder known as Hashimoto's thyroiditis. Hashimoto's disease is an inflammation of the thyroid

gland with T lymphocytes and auto antibodies against specific thyroid antigens such as thyroid peroxidase, thyroglobulin and TSH receptor^[5]. Some type of thyroiditis are caused by an infection, but Hashimoto's is not an infection. Some type of disease characterized by infiltration of autoimmune disorders occur when your immune system produces antibodies that attack your own tissues. The immune system is designed to attack and remove harmful invaders from the body,

Such as bacteria, viruses and toxins^[6]. Sometimes this process involves your thyroid gland. Large amounts of damaged immune cells invade the thyroid gland, these immune cells are called lymphocytes^[7], Hashimoto's also known as chronic lymphocytic thyroiditis or chronic autoimmune thyroiditis. It is a disease characterized by the gradual failure of the thyroid gland due to an immune-mediated destruction and apoptosis of the gland. The two main types of Hashimoto thyroiditis include goitrous autoimmune thyroiditis and atrophic autoimmune thyroiditis. Both of these types have a common serological and pathological manifestation. These include lymphocytic infiltration and follicular destruction as well as high serum concentrations of antibodies to thyroid peroxidase (TPO) and thyroglobulin (TG)^[8].

Sugar substitutes are very low energy or zero energy substances that are used to replace sugar in the diet. They are mostly available in the market as "sugar-free or "no sugar" substances. In today's era sugar consumption is too much in a form of chocolate, cold drink, soft drink, junk food, artificial fruit juices etc. So gradually developing hypothyroidism induced by sugar in this time. 2500 years ago all text of Ayurveda has mentioned that excess of *madhur ras* (ie sugar) can cause neck swelling, Thyroid nodule, Thyroid goitre, Hypothyroidism and obesity^[9].

Sweetener is the substance used to sweeten food or drink, especially one other than sugar. It is a mainly two type.

1. **Natural sugar**- Exist or produced by, nature without added chemical or fancy machinery. The only sugars that are optimal to eat are wild, non - hybridized, seeded fruits, and the natural sugars and starches in living vegetables, trees, seeds, nuts and roots. Fruits and vegetables contain natural sugar in the form of fructose and in dairy products, such as milk and cheese, as lactose.
2. **Artificial or refined sugar** - which are also called sugar substitutes, alternative sweeteners, or non sugar sweeteners, these substances used to replace sugar in foods and beverages. They can be divided in to two large groups-
 - **Nutritive sweeteners** - which add some energy value (calories) in food.
 - **Non nutritive sweeteners** - which are also called high intensity sweeteners because they are used in very small quantities, adding no energy value in food.

In 2011 FDA grant only five artificial sweeteners to be used in food products -

- Saccharin
- Acesulfame
- Aspartame
- Neotame
- Sucralose.

But around 38 sweeteners available in market. The most commonly used ones include aspartame, sucralose, and saccharin. The sugar substitutes are attributed with a large number of health-related side effects in animal studies, ranging from obesity to various malignancies and we do not try to know before using any product, that the product is sweet and in what quantity. Sugar substitutes are much sweeter than sucrose^[10]. Aspartame is 200 times sweeter than sucrose whereas sucralose (a synthetic product of sucrose) generates 600 times more sweetness as compared to sucrose. This is because of the replacement of three hydroxyl groups in sucrose with three chlorine groups in sucralose^[11]. The use of sugar substitutes use is more prevalent in females^[12].

In 2017, sucralose was the most common sugar substitute used in the manufacture of foods and beverages

Material and Methods –

Facts for this study was obtained out by literature search and critical review. The pathogenesis of hypothyroidism was studied from modern medicine textbooks of various authors and by searching various online medical research databases like pubmed, Google scholar and other national research data bases. The study of various Ayurvedic texts were made critically and an effort is made to understand the complete pathogenesis of hypothyroidism in terms of *Ras, Dosha, Dushya, Agni, and Srotas*.

Mechanism- According to studies, artificial sweeteners reduce the number of beneficial bacteria in the gut significantly, which leads with an increase in pH. As the gut microbes constitute around 80% of the immune system, this inhibits the immune system and thus the thyroid^{[13],[14]}. According to a study done on rats that compared the effects of sucrose on the thyroid with those of sucralose, sucralose diminishes the thyroid axis activity as opposed to sucrose, which stimulates it. Sucralose diminishes thyroid peroxidase activity, leading to a decrease in TSH, as well as in the plasma levels of T3 and T4^[15]. Aspartame is composed of two amino acids, phenylalanine and aspartame, which are connected to methanol^[11]. Aspartame in the body further metabolizes to formaldehyde^[16]. Moreover, a study done on male albino rats showed that formaldehyde (a metabolite of aspartame) causes the regression of the follicular epithelial cells of the thyroid gland, which leads to decreased levels of T3 and T4, and increased TSH levels. There is a possibility that, initially, formaldehyde increases the stimulation of the thyroid follicles, which rapidly worsens the synthetic capacity of the gland. This ultimately leads to the failure of the thyroid gland^[17]. Formaldehyde, a metabolite of aspartame is reported to be associated with Type IV delayed hypersensitivity. Studies have shown that in the oral cavity of rats, mice, and human's sucralose and sucrose stimulate the same sweet taste of the G-protein coupled receptor complex T1R2/T1R3^[18]. Moreover, the pharmacokinetics of sucralose is similar in humans and rats^[19].

In Ayurveda the etiological factors related to *Kaphavataja Prakopaka*, *Agnimandya Janaya* and *Rasa pradoshaka Nidana* may be responsible for the genesis of hypothyroidism^[20]. due to Lifestyle factor and excessive intake of *madhur ras* the disease process begins in the gut with imbalanced digestive fire (*Agni*) and the production of undigested food waste (*Ama*).

Ama is a concept that can be understood as accumulated of unutilized, unmetabolized product due to hypofunctioning of digestive and metabolic enzymes. This untransformed food material accumulates in gastrointestinal level. *Ama* is a state of intermediately metabolism which are toxic in nature, hinders the absorption products of digestion increase or decrease the peristalsis and on absorption produces gastrointestinal disorders as well as extra gastrointestinal disorders. Sometimes due to extra gastrointestinal disorders or external negative influences or improper secretion of digestive juices by liver and pancreas. In the gut not all the food digested specially *madhur ras pradhan dravya* because gut villi does not absorb the proper amount of *madhur ras*, rest part of food is called *AMA*. In that half of it absorbed as nutrient and a half undigested, unmetabolized food product that circulates in the body as toxins. *Ama* lines the wall of the bowel, impeding absorption and assimilation of nutrients. This toxic material *ama* can be viewed as a foreign toxic substance by body and the immune system can react by forming antibodies to it, giving rise to antigen antibody complex and in immune disorders. During the physiology there is accumulation of impurities and toxins from inside the body come internal metabolic and cellular waste products, such as free radicals damaged cells and tissues and from outside come external impurities such as pesticides (from food and water), pollutants (from air) and toxins that occur naturally in foods. All these are collectively referred to as *ama*.

This progresses from the level of plasma (*rasa*) and *Rasadhatu* plays a major role in pathogenesis as *Rasaja Vikaras* mentioned in Charak samhita are similar to the clinical features of hypothyroidism. *Rasadhatvagni-mandhya* leads to *Rasaja Vridhi* and over production of *Mala of Rasadhatu* i.e. *Mala Kapha Vridhi*. *Dhatvagnimandhya* is also the major features of the disease and continues up the chain, inhibiting the formation of strong and healthy tissues until *Ojas* is affected^[21]. Once the quality of *Ojas* is disturbed (caused by the presence of *Pitta dosha* in the form of heat then the immune system begins to act improperly, attacking the thyroid gland and the full blown autoimmune condition develops^[22]. Whether the autoimmune condition manifests as Graves or Hashimoto's depends upon the specific *doshas* imbalance involved.

Discussion –

Here, we report the first case of autoimmune thyroiditis with hypothyroidism induced by sugar substitutes in American Association of Clinical Endocrinologists (AACE) 22nd Annual Scientific & Clinical Congress – Creating an Oasis of Quality of Care in the Desert, May 1-5, 2013, in Phoenix, AZ. (Abstract #1083) presenting a case of Hashimoto's hypothyroidism induced by high intake of beverages containing

sugar-substitutes, which resolved completely with the elimination of these products from diet. This case emphasizes that in all patients diagnosed with Hashimoto's Thyroiditis, intake of sugar-substitutes should be inquired. If found positive, discontinuation of intake and close follow-up of thyroid function test should be done.

Five years later, Clinical Hospital of new York presented once again a case on Autoimmune Thyroiditis with Hypothyroidism Induced by Sugar Substitutes, it is based on 2013 case report According to the case association between Hashimoto's thyroiditis and the excessive consumption of sugar substitutes is shown by the quick return of thyroid stimulating hormone and antibody levels to normal after eliminating the use of sugar substitutes making them culprit in the development of Hashimoto's thyroiditis. The long lag time between the use of artificial sweeteners and the clinical presentation of Hashimoto's thyroiditis might be a limiting factor, so large control studies should be done to confirm this association.

According to 1973 research published in "The American Journal of Clinical Nutrition", sugars in all forms (glucose, fructose, and sucrose) can impair immune system function, hurting the ability of white blood cells to do battle against threats. It's best to minimize sugar consumption and to try to keep sugar at around five percent of your dietary makeup.

In Ayurveda, Acharyas had told many thousands of years ago that too much of the *madhur ras* is due to this disease. Accordingly Acharya Charaka the main causes of Thyroid goiter is excessive intake of *madhur ras*. It is observed that excessive intake of *madhur ras* further aggravates the symptoms of Hypothyroidism. *Nidana Parivarjana* is the basic treatment of any disease in Ayurveda. The *Nidana Parivarjana* of Thyroid goiter gives symptomatic relief and restrains further advancement of disease. The *Deepana – Pachana* therapy of *Ama Dosha* strengthens *Jatharagni* and in turn regularizes *Bhootagni* and *Dhatvagni*. Thus the Ayurveda therapy not only gives symptomatic relief but also metabolism at the cellular level is kept into check. So it can be concluded that avoid the *madhur ras* can be useful in Hypothyroidism.

Conclusion –

Thus, we can conclude from this study that hypothyroidism is caused by excessive intake of *madhur ras*, and Ayurveda Acharyas was well known of this disease and causes.

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