Study Protocol

Evaluation of Vamana and Virechana Karma in the Treatment of Hypothyroidism – A Study Protocol

Abstract-
Background: Hypothyroidism can be understood and assessed on the basis of Agni, Doshas, Dushyas, Sthanas and Srotasas. In Ayurveda Vamana and Virechana Karma is considering as best line of purification procedures for the removal of toxin materials from the human body. Hypothyroidism occurs because of hypo functioning of thyroid gland which is located in neck region and even most of the signs and symptoms prove the involvement of Kapha Sthana and Kapha Dosha. So, in the present clinical research, Vamana and Virechana karma of Panchkarama will be selected as clinical tool to check its impact on Hypothyroidism (Galaganda). Aim and Objectives: To explore Vamana & Virechana Karma regarding their Clinical Importance. To validate Vamana & Virechana Karma as an effective mode of treatment in the management of Hypothyroidism. Methodology: 90 (45 in each group) patients will be selected by randomized reference standard controlled single blind double arm clinical trial, and third party will assign and enlist the patient. In Group A (Control) – Standard/ Control Group treated with Thyroxin and Group B (Experimental) – Intervention Group treated with Vamana and Virechana Karma. The evaluation will be recorded on 0 30, 60, 90, 120, 150, 180 days. Results: Changes will be observed in objective outcomes. Conclusion: Vamana and Virechana will be effective in Hypothyroidism.

Key Words: Vamana, Virechana, Thyroid Profile, Hypothyroidism

Introduction:
Thyroid related disorders is one of the commonest disorders of Endocrine. As per the report by World Health Assembly, in more than 110 countries about 1.5 billion persons are vulnerable to thyroid disorders. ‘World Health Organization (WHO) appraise that about 200 million people are suffering from goiter, although most of the goiters are small and subclinical’ [1, 2]. Thyroid hormones (TH) are vital for growth and development and have an important role in energy homeostasis by maintaining the proper metabolism in body. The decease or increase in the production of thyroid hormones resulted in various conditions which are characterized as hyper function (hyperthyroidism), hypo function (hypothyroidism), or inflammation (thyroiditis) of thyroid glands which can be benign or cancerous. Hypothyroidism is one of the disorders of the endocrine system in which the needed thyroid hormone is not being produced by thyroid gland. Due to which number of symptoms occur, such as deprived ability to tolerate cold, tiredness, constipation, depression, and weight gain. In pregnancy if hypothyroidism remains untreated it may lead to delays in growth and intellectual development in the baby or cretinism. It is also observed that hypothyroidism is more prevalent in older woman than man.

Subclinical hypothyroidism (SCH) defined as a condition which is asymptomatic or presenting few to various full blown symptoms of overt hypothyroidism. Subclinical thyroid dysfunction is demarcated as an abnormal serum TSH level (reference range: 0.30 to 6.50 µIU/L) and FT4 and FT3 levels within their reference range. The prevalence of SCH in general population is 3% to 8% in United States of America. Prevalence of SCH is relatively high among elderly women. In an elderly population, Iodine treatment and medication play a vital role in the progression of subclinical thyroid disorder compared to other causes of thyroid dysfunction.
In Ayurveda no any description of any disease condition similar to Hypothyroidism is found yet, several scattered references may be seen in various texts. On the basis of various hormonal disorders, Nindita Purushas [3] and Avaranas [4] can be described. Looking at the pathogenesis of hypothyroidism, this disorder can be said to be caused due to hypo functioning of the Agni as per the principles of Ayurveda.

Treatment of hypothyroidism with the allopathic medicines brings the value of Thyroid Stimulating Hormone (TSH) and thyroxin (T4) to normal range but continuous medication make the patient drug dependent until death. So, a better, safer and long lasting therapy is needed for the patients such type of ailment can be done through the heritage of Ayurveda. Hence, long term cohort study is required to claim that Vamana & Virechana karma is efficacious and helpful in the discontinuation of modern medicine.

The population prevalence is about 10%, mounting to 18%–22% in the elderly, of hypothyroidism [5, 6]. 5.0% of individuals (out of 2779 persons) older than 18 years were reported of hypothyroidism, defined as having a TSH > 6 mU/L, in the classic Whickham study conducted in the United Kingdom in 1977 [7]. The hypothyroidism diagnosis is mainly based on a TSH value, which has been refined over the last 25 years, getting ever greater sensitivity and reliability in measuring very low as well as high levels of TSH levels [8].

Notably, TSH measurement represents the most powerful interpreter for the outcome of spontaneous hypothyroidism in patients over 55 years, as these subjects reveal a low incidence of overt hypothyroidism (OH), who present with low serum TSH [9].

‘The prevalence of SCH in India, as gathered from various clinical and epidemiological studies ranges from 6 to 15%.’ [10].

A study in 2016 regarding assessment of ‘prevalence of hypothyroidism in pregnancy with TSH, conducted in nine states of India, found 13.13% of pregnant women to be hypothyroid. As per the guidelines of FOCSI, ITS & NRHM – Trimester-specific Thyroid Stimulating Hormone (TSH) cut offs of 2.5 mIU/L for the first trimester and 3.0 mIU/L for the second and third trimester, prevalence was found to be 44.3 per cent, 32.0 per cent, and 34 per cent in the first, second, and third trimester respectively’. There is considerable regional disparity in prevalence. It is more common in females than males (2-8 times higher) with reports of prevalence [11].

‘There is most prevalence of SCH compared to subclinical hyperthyroidism because in general population prevalence for SCH is 4% to 10% while for subclinical hyperthyroidism it is about 2% of general population’. The severity of the disease develops with the age and common in an elderly population. It is more mutual than anyone would believe and millions of people are presently hypothyroid & do not recognize it. In owed course of time, untreated hypothyroidism may lead to number of health glitches such as obesity, arthritis, heart disease, infertility etc.

Ayurveda has from time to time described the common thyroid-connected problem known as the simple goiter (Galaganda) [11], a state of hypothyroidism. The non-production of appropriate thyroid hormones leads to hypothyroidism. Ayurveda (Galaganda) is the most common hypothyroid form of the enlarged thyroid gland. [12], can now be correlated with goiter. According to Ayurvedic literature, impairment of vayu, kapha, and meda leads to the enlargement of the thyroid gland [13].

According to modern science, metabolic action of the body is controlled by thyroid hormones and as per Ayurveda, metabolic procedures of the body are under the control of Agni. The reason of hypothyroidism is modification in metabolic activity which, agreeing to Ayurveda, relates to vitiation of Dhatvagni and leading to dhatwagni mandya. The regular and irregular roles of Agni and Thyroid gland are alike. Even the signs of Agnimandya and Hypothyroidism are nearly same.
Hyperthyroidism is the byproduct of thyroid hormone production and is often referred to as thyrotoxicity in the peripheral tissues. Which include genetic susceptibility, a major hyperthyroidism factors seem to be the immunologic increase in IgG antibodies or thyroid stimulants [14]. Enhancing thyroid hormone secretion, this result in increased metabolism and waste of energy. Reportedly, hyperthyroidism – thyrotoxic, exophthalmic goiter or Graves, thyroid carcinoma, adenoma, etc are the following diseases: thyroidism.

Two related hormones Thyroxine (T4) and Triiodothyronine secrete thyroid gland (T3). These hormones play a vital role during development in cell differentiation and help maintain thermogenic and metabolic homeostasis in the body. Hypothyroidism is termed deficiency of these hormones and the Basal Metabolic rate of the body lowers [BMR]. Subclinical hypothyroidism or mild thyroid failure is a most common endocrine disorder, affecting quality of life or health concern, with ‘the prevalence of 3 to 8% in the general population of without known thyroid disorders, worldwide. The prevalence varies with age, gender and geographic location’.

SCH is documented to be associated with various co morbidities like elevated LDL cholesterol and triglyceride levels, increased prevalence of coronary heart disease and related mortality, increased residual myocardial ischemia, increased peripheral neuropathies, muscular weakness, and reduced exercise capacity [15-18]. SCH is also found to be common in certain neuropsychiatric disorders like bipolar mood disorders, impaired cognitive functions in young,[19] Moreover, it has been found that treatment of SCH reduces the bad cholesterol levels and attenuates the likelihood of atherosclerosis[20].

Objectives:
• To explore Vamana & Virechana Karma regarding their Clinical Importance.
• To validate Vamana & Virechana Karma as an effective mode of treatment in the management of Hypothyroidism.

Research Question:
• In patients with Subclinical/ Primary Hypothyroidism, does Vamana and Virechana Karma decrease TSH level?

Hypothesis:
Research Hypothesis:
– Vamana and Virechana Karma are effective in decreasing the TSH level.
– Vamana and Virechana Karma is effective tool to improve the general wellbeing of patient with subclinical / Primary Hypothyroidism.

Null Hypothesis:
– Vamana and Virechana Karma have no role in decreasing the TSH level.
– Vamana and Virechana Karma have role in improving the general wellbeing of patients with subclinical/Primary hypothyroidism.

Materials and Methods:
Trial Design: Randomized Reference Standard Controlled Single Blind Double Arm Clinical Trial
Study Design: Patients attending OPD & IPD of Department of Panchakarma, Mahatma Gandhi Ayurved College & Research Center, Wardha and Shri Krishna Govt. Ayurvedic College, Kurukshetra will be selected for the study.

Grouping & Interventions:
– Two groups, parallel line
  • Group A:- Standard/ Control Group treated with Thyroxin.
  • Group B:- Intervention Group treated with Vamana and Virechana Karma.
**Composition of Trial Drugs:** All herbs will be purchased from an authentic pharmacy. Composition of trial drug is as follows –

Table 1. Composition of Trial Drugs

| S.No. | Sanskrit Name | Botanical Name | Parts Used | Quantity |
|-------|---------------|----------------|------------|----------|
| For Snehana | | | | |
| 1. | Go Ghrita | Cow’s Ghee | Whole | As per Patient Need |
| For Vamana | | | | |
| 1. | Madana Phala | Randia dumetorum | Fruit | 5 Part |
| 2. | Saindhava Lavana | Rock Salt | Whole | 1 Part |
| 3. | Madhu | Honey | Whole | 10 Part |
| For Virechana | | | | |
| 1. | Draksha Churna | Vitis vinifera | Fruit | 2 Part |
| 2. | Aragwadha Churna | Cassia fistula | Fruit | 2 Part |
| 3. | Haritiki Churna | Terminalia chebula | Fruit | 2 Part |
| 4. | Kutaki Churna | Picrorhiza kurroa | Fruit | 1 Part |
| 5. | Erund Tailam | Ricinus communis | Whole | 4 Part |

**Inclusion Criteria:**
Patients between the age of 20 to 50yrs, who are ready to give informed consent, having T3 Level < 100 ng/dL, T4 Level < 0.8 ng/dL, TSH > 4 mU/L, and are yogya for Vamana and Virechana Karma.

**Exclusion Criteria:**
Patients ayogya for Vamana and Virechana, Pregnancy or lactation, Congenital / diffuse Goitre (ICD-10 = E03.3), Chronic obstructive lung disease - already diagnosed, Iodine deficiency Goiter (ICD-10 = E00-02), Thyrotoxicosis (ICD-10 = E05) and of Thyroiditis (ICD-10 = E06).

**Interventions:**
Table 2. Total duration of intervention will be same for both the groups as follows –

| | Group A | Group B |
|---|---------|---------|
| Sample size | 45 | 45 |
| Intervention | Tab. Thyroxin | Vamana & Virechana Karma |
| Duration of treatment | 30 days | 30 days* |
| Follow up period | 180 days (Day – 30, 60, 90, 120, 150, 180) | 180 days (Day – 30, 60, 90, 120, 150, 180) |
| Approximate Total duration | 180 days | 180 days |

Table 3. Schedule of Duration of Treatment
| Days | Group B |
|------|---------|
| 1. | **Snehapana**  
* (Go-Ghrita 30 ml morning at 07:00 am empty stomach) |
| 2. | **Snehapana** |
| 3. | **Snehapana**  
* (Go-Ghrita increasing the dose by 30-50ml in Arohankramam (acc.to kosta, agni, and rogibala)) |
| 4. | daily morning at 07:00 am empty stomach |
| 5. | Till 7th day |
| 6. | **Abhyanga** (with Til Tailam) & **Nadi Sweda** |
| 7. | **Abhyanga** (with Til Tailam) & **Nadi Sweda** |
| 8. | **Abhyanga** (with Til Tailam) & **Nadi Sweda** |
| 9. | **Abhyanga** (with Til Tailam) & **Nadi Sweda**  
**Vamana Karma**  
In Morning  
* (Madan-Phal Pippali Churna – 5 gm + Saindhava Lavana – 1 gm + Honey – 10 gm)  
**Samsarjana Krama**  
(Evening – *Peya*) |
| 10. | **Samsarjana Krama**  
(Morning – *Peya*  
Evening – *Peya*) |
| 11. | **Samsarjana Krama**  
(Morning – *Vilepi*  
Evening – *Vilepi*) |
| 12. | **Samsarjana Krama**  
(Morning – *Vilepi*  
Evening – *Akrita Yusha*) |
| 13. | **Samsarjana Krama**  
(Morning – *Akrita Yusha*  
Evening – *Akrita Yusha*) |
| 14. | **Samsarjana Krama**  
(Morning – *Krita Yusha*  
Evening – *Krita Yusha*) |
| 15. | **Samsarjana Krama**  
(Morning – *Krita Yusha*  
Evening – Normal Diet) |
| 16. | Rest Day |
| 17. | Rest Day |
| 18. | **Snehapana**  
* (Go-Ghrita morning at 07:00 am empty stomach) equal to 1/3rd of Day 7 dose |
| 19. | **Snehapana**  
* (Go-Ghrita morning at 07:00 am empty stomach) equal to 2/3rd of Day 7 dose |
| 20. | **Snehapana**  
* (Go-Ghrita morning at 07:00 am empty stomach) equal to Day 7 dose  
**Abhyanga** (with Til Tailam) & **Nadi Sweda** |
| 21. | **Abhyanga** (with Til Tailam) & **Nadi Sweda** |
| 22. | **Abhyanga** (with Til Tailam) & **Nadi Sweda** |
| 23. | **Abhyanga** (with Til Tailam) & **Nadi Sweda** |
| 24. | **Abhyanga** (with Til Tailam) & **Nadi Sweda**  
**Virechana Karma** |
|   |   |
|---|---|
|   | Kwath made from Draksha Churna 20 gm + Aragwadha Churna 20 gm + Haritiki Churna 20 gm + Kutaki Churna 10 gm in 500 ml of water reducing it to 60 ml with Erand Tailam 40 ml |
| 25. | **Samsarjana Krama**  
(Morning – Peya  
Evening – Peya) |
| 26. | **Samsarjana Krama**  
(Morning – Vilepi  
Evening – Vilepi) |
| 27. | **Samsarjana Krama**  
(Morning – Vilepi  
Evening – Akrita Yusha) |
| 28. | **Samsarjana Krama**  
(Morning – Akrita Yusha  
Evening – Akrita Yusha) |
| 29. | **Samsarjana Krama**  
(Morning – Krita Yusha  
Evening – Krita Yusha) |
| 30. | **Samsarjana Krama**  
(Morning – Krita Yusha  
Evening – Normal Diet) |

**Criteria for discontinuing or modifying allocated interventions:**
If any untoward incidence, features of drug sensitivity or any other disease or problem arises, the subject will be withdrawn from the study and will be offered free treatment till the problem subsides.

**Follow up:** On 30th, 60th, 90th, 120th, 150th and 180th day.

**Primary Outcomes:** To evaluate Vamana & Virechana Karma in correcting the values of Thyroid Profile.

**Secondary Outcomes:**
- To evaluate Vamana & Virechana Karma in lowering the requirement of Thyroxin.
- To correlate the biochemical changes with improvement in the general wellbeing of patients of Hypothyroidism.

**Statistical Analysis:**
The progressions from the pattern will be dissected by utilizing Paired and Unpaired ‘t’ Test for target standards.

**Time duration till following up:** The patient will be followed up during treatment 180 days

**Follow up period:** 0, 30th, 60th, 90th, 120th, 150th and 180th day

**Recruitment:** 90 (45 in each group) patients will be selected by randomized reference standard controlled single blind double arm clinical trial, and third party will assign and enlist the patient.

**Methods:** Data collection, management, and analysis

**Data collection methods:** Assessment criteria

**Objective Parameters**
Prakruti Pariksha (Analysis), Height and Weight (Body Mass Index) and Serum concentration of T3, T4 and TSH. All parameters will be assessed before and after the
treatment except Prakruti Pariksha (Analysis). Prakruti Pariksha (Analysis) will be done only before the start of the treatment.

Data management: the information passage coding will be finished by the third party.

Ethics and dissemination: Research ethics approval; approval from the research ethics committee has taken. No- Ref. No. MGACHRC/IEC/Aug-2020/99

Consent or assent: The made consent will be taken from the patient before starting the assessment. During the investigation, the classification of every patient will be kept up.

Dissemination policy: The information will be dispersed by paper distribution. Creation qualification rules and any proposed utilization of expert scholars.

Informed consent materials: With all the data model assent structure and other related documentation will be given to members.

Discussion:
Hypothyroidism can be understood and assessed on the basis of Agni, Dosha, Dushya, Sthana and Srotas. In Ayurveda Vamana and Virechana Karma is considering as best line of purification procedures for the removal of toxin materials from the human body. Hypothyroidism occurs due to hypo functioning of thyroid gland which is located in neck region and even most of the signs and symptoms prove the involvement of Kapha Sthana and Kapha Dosha. So, in the present clinical research, Vamana and Virechana karma of Panchkarma will be selected as clinical tool to check its impact on Hypothyroidism (Galaganda).

Vamana and Virechana karma are traditional and deep-rooted Panchkarma procedures which induces wellness. Vamana and Virechana Karma mean induction of emesis and purgation which helps to remove toxins from the body especially through the intestine. Generally depending upon intensity of procedure this Karma are classified into three categories; Mridu (mild) Madhya (intermediate) and Tikshna (strong). As like other Karmas, these Karma also carried out in three steps; Poorvakarma, Pradhanakarma and Pashchatakarma. Sneha Pana, fomentation and oil massage are suggested before performing this Karma to liquefy Dosha and toxins. Seeing the Kapha and Pitta dosha prevalence, sroto shodhaka, Agnivardhaka and dosha pratyanika chikitsa these are best measures for the treatment of hypothyroidism.

Here in this regard a study is proposed to study the hormonal disorders influences and body mass index on the body with reference to Vamana and Virechana Karma in Hypothyroidism. Presently available managements are not capable of bringing TSH to normal level as no particular type of treatment is available to make these thyroid glands to secrete hormones to normal level. In this study we plan to find out the association of hormonal disorders and hypothyroidism to offer a remedy through Vamana and Virechana procedures of Panchkarma.

In this thesis an attempt is made to review the related literature of hypothyroidism and hormonal disorders interrelationships and Vamana and Virechana Karma in detail. The observed data of influence of Prakriti on hypothyroidism, precipitating role of hormonal disorders and relief in respect to subjective and objective parameters are studied. All the parameters are well studied under the limelight of statistics and fair conclusions are drawn. The major conclusions are to make the use of Vamana and Virechana Karma in controlling TSH and relieving various symptoms of Hypothyroidism. A number of related studies were reviewed. Kombe et. al. assessed effect of kanchanar guggul in sub-clinical hypothyroidism with respect to agnimandya[21]. Kolli et. al. reflected on correlation of thyroid disorders with abnormal uterine bleeding[22]. Acharya et. al. reported on Early Manifestation of Impending Thyroid Storm[23]. Other related studies by Talwar et. al. [24], Neema et. al. [25], and Dixit et. al. [26] were reviewed.
In this study the diagnosed cases of Hypothyroidism will be taken as mentioned in the inclusion criteria and effect of Vamana and Virechana will be assessed.

**Strengths:** In case these procedures work on Hypothyroidism then this will be a boon for the patients to get rid of daily medication and as secondary outcome these procedures will help the individuals in the regularization of other systems of the body.

**Limitations:** No such limitations are being seen in current scenario as these procedures are in use of even healthy individuals since centuries.

**Conclusion:**
These procedures are very effective not only in many disorders but also in healthy individuals. That is why these are selected to be conducted on the patients of Hypothyroidism. As not much study of their role in this disorder has been found hence with the expectation of high significant change this study is planned.

**NOTE:**

The study highlights the efficacy of "Ayurveda" which is an ancient tradition, used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable.

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