STUDIES ON PANDU ROGA W.S.R. TO HYPOTHYROIDISM
Sukalyan Ray*1 & Kaushik Porel2
*1Assistant Professor, Department of Roga Nidan, Raghunath Ayurved Mahavidyalay & Hospital, Contai, Purba Medinipur, West Bengal
22nd year PGT, Department of Roga Nidan, Institute of Post Graduate Ayurvedic Education and Research, Shyamadas Vaidya Sastra Pith Hospital, Kolkata 700009, West Bengal

Abstract
In absence of clear description, a newly emerged pathological condition or a disease should be compared with any established disease as per Ayurvedic thought on the basis of similarities between their Nidan (causative factors), Samprapti (pathogenesis) & Lakshans (clinical features). This comparative study is very essential to determine the therapeutic and preventive aspect of any newly emerged disease. Hypothyroidism is one of the most important disorders of thyroid gland emerging now a days. In this disorder there is decreased synthesis of thyroid hormones like T3 & T4. In absence of any clear reference to this disorder in our ancient compendiums, hypothyroidism can be compared with Pandu Roga. Pandu Roga is one of the most important diseases described in the ancient Ayurvedic compendiums. This disease is occurred due to vitiation of Pitta Dosha, which afflicts Rasa, Rakta & Mamsa Dhatu. Pandu Roga and hypothyroidism are identical on the basis of their causative factors, pathogenesis & clinical features. Hypothyroidism can be occurred due to several causes among which iodine deficiency and autoimmune thyroiditis are the most common. Likewise, Pandu Roga has two different pathogenesis like Dhatukshaya (can be compared with iodine deficiency) and Avaran (can be compared with autoimmune reaction). Apart from these, several clinical features like Daurvalya (weakness), Shishiradweshi (aversion to cold), Avipaka (anorexia), Gatrasadan (muscle cramp) etc are also very identical between these two disorders. In this study, literary information regarding the similarities between Pandu Roga and hypothyroidism has been verified through clinical study. A comparative discussion has been carried out between the causative factors, pathogenesis and clinical features of Pandu Roga and hypothyroidism. This study has also been carried out to evaluate the efficacy of stipulated Pandu Rogahara Chikitsa management in 15 patients of hypothyroidism, comprising Virechan Karma by Trivrit Churna at a dose of 3 grams before lunch & dinner with warm water along with powder Punarnava Mandoor at a dose of 250 mg with honey after lunch and dinner. Both the therapeutic procedure was continued for 60 days. After 60 days the effect of the stipulated therapeutic procedure has been evaluated in 14 patients with 1 dropout, on the basis of subjective and objective parameters. All the findings have been statistically analyzed using paired ‘t’ test. The obtained results have been interpreted as – p <0.05 is significant & p <0.001 is highly significant. The results showed ‘p’ value < 0.001 after 60 days in most of the parameters (subjective and objective), which indicates that, the Pandu Rogahara Chikitsa which has been followed in this study is very efficacious to combat Pandu Roga and subsequently to combat hypothyroidism.
Introduction

According to the concept of Ayurvedic pathophysiology, any disease occurs due to three fundamental alteration in human body – Dosha Prakopan (vitiation of Dosha), Dhatu Pradushan (affliction of Dhatu) and Srota Dusti (vitiation of Srota). The fundamental cause behind all these three events is diminution of Agni, which is responsible for digestion (in form of Jatharagni), absorption (in form of Bhutagni) and metabolism (in form of Dhatwagni) (1). In accordance with Ayurvedic philosophy, diagnosis of any disease is based on the five component - Nidan (causative factor), Purva Rupa (prodromal features), Rupa (clinical features), Upashay (relieving factors) and Samprapti (pathological analysis), together known as Nidan Panchak(2). Whenever any disease, described in our ancient compendiums, is compared with any pathological condition as per concept of western science, should be compared on the basis of the aforesaid fundamental factors.

Pandu is a disease which has been described with great importance in all major and minor texts of Ayurveda. In fact it is one of the commonest pathological conditions encountered in hospital practice. Pandu is caused by diminution of Agni and vitiation of Pitta Dosha (mainly Sadhak Pitta) (3) due to intake of various Nidan. The principal Dushya in Pandu are Twak (represents Rasavaha Srota) (4), Rakta (represents Raktavaha Srota) and Mamsa (represents Mamsavaha Srota) (5). According to Acharya Charak, Pandu occurs in our body through two different pathways – one due to Dhatu Kshaya (depletion of body element) and another due to Avaran or Margavarodha (can be compared with impaired physiological pathway) (shown in Figure 1).

In both the pathways several clinical manifestations occur due to affliction of Dushya by vitiating Dosha. Each clinical manifestation is contributed by vitiating Dosha along with one or more afflicted Dushya i.e. Dhatu. The disease Pandu is generally compared with anaemia as per modern thoughts. But if we analyze Pandu through previously stated components of disease diagnosis, we come to the conclusion that the disease Pandu can be compared with several pathological conditions as per western medical scienceapart from anaemia. One of such pathological condition is hypo-function of thyroid gland, known as hypothyroidism.
The thyroid gland, which is the largest and one of the most important endocrine gland in human body, is located on the anterior side of the neck, right below the larynx. It has two lobes and is composed of many thin follicular cells with a type of epithelial tissue origin. These follicles store thyroid hormones in the form of thyroglobulin molecules until body requires them. Thyroid gland synthesizes and secretes two major hormones, known as 3,5,3’ – triiodothyronine (T3) and thyroxin, which can sometimes be referred to as 3,5,3’,5’ – tetraiodothyronine (T4). These hormones are necessary for thermo-genic and metabolic homeostasis in adult(6). Hormonal output from thyroid gland is mediated by thyroid stimulating hormone (also known as TSH or thyrotropin) secreted by anterior pituitary. The secretion of thyrotropin itself is mediated by thyrotrpin releasing hormone (TRH) secreted by hypothalamus. The thyroid axis is a classic example of an endocrine feedback loop. Hypothalamic TRH stimulates pituitary production of TSH, which in turn stimulates thyroid hormone synthesis and secretion. Thyroid hormones, acting predominantly through thyroid hormone receptor beta-2, feedback to inhibit TRH and TSH production. The ‘set point’ in this axis is established by TSH. TSH plays a pivotal role in control of the thyroid axis and serves as most useful physiologic marker of the thyroid hormone action(7). Iodine uptake is the critical first step in thyroid hormone synthesis. The most common disorders of thyroid gland include hyperthyroidism, hypothyroidism and thyroid nodules, which are generally benign thyroid neoplasm but may change to thyroid cancer (8). Iodine deficiency remains the most common cause of hypothyroidism worldwide. In areas of iodine sufficiency, autoimmune disease (Hashimoto’s thyroiditis) and iatrogenic causes (treatment of hyperthyroidism) are most common (9). Iodine deficiency is responsible for endemic goiter and cretinism but is an uncommon cause of adult hypothyroidism unless the iodine intake is very low or there are complicating factors, such as the consumption of thiocyanates in cassava or selenium deficiency (10). Autoimmune hypothyroidism may be associated with a goiter (Hashimoto’s, or goitrous thyroiditis) or, at the later stages of the disease, minimal residual thyroid tissue (atrophic thyroiditis)(11). The mean annual incidence rate of autoimmune hypothyroidism is up to 4 per 1000 women and 1 per 1000 men (12). The mean age at diagnosis is 60 years, and the prevalence of overt hypothyroidism increases with age. Subclinical hypothyroidism is found in 6–8% of women (10% over the age of 60) and 3% of men (13).

In the above context, the present study was carried out to evaluate –

1. Concept of Pandu Roga and its clinical diagnosis
2. Evaluation of hypothyroidism in accordance to pathology of Pandu Roga
3. To assess the efficacy of stipulated Panduhara Chikitsa in the management of hypothyroidism.

Material And Methods
The literary information regarding the similarities between Pandu Roga and hypothyroidism of the basis of causative factor, pathogenesis & clinical features have been verified through clinical study. Assessment of homologous features of Pandu and hypothyroidism were done on the basis of subjective and objective criteria. The study has been also carried out to evaluate the efficacy of stipulated Panduhara management, consisting Shodhan & Shaman therapy in the management of hypothyroidism. The subjective and objective criteria have been evaluated before and after treatment for assessment of the efficacy of administered therapy.

Selection of Patients
15 patients were selected from OPD of Institute of Post Graduate Ayurvedic Education & Research, at Shyamadas Vaidya Sastra Pith hospital, Kolkata -9, irrespective of their sex, occupation and religion. The patients having low serum thyroid hormone level (T3 & T4) with raised serum TSH level were selected for the study and subsequently the features of Pandu were evaluated on the basis of subjective and objective parameters. Prior to carry out the study the informed patient consent form was duly signed by the patients.

Inclusion Criteria
1. Patients above 20 years of age and below 60 years of age, irrespective of their occupation, sex and religion.
2. Patients who are willing to include themselves into the study.
3. Patients having the serum TSH level > 4.25 µIU/mL
4. Patients having the serum T3 level < 77 ng/dL & serum T4 level < 5.4 µg/dL
5. Primarily detected hypothyroidism patient, not taking any type of medication.
6. Primarily detected hypothyroidism patient without any other chronic and acute disease.

Exclusion Criteria
1. Patients below 20 years of age and above 60 years of age, irrespective of their occupation, sex and religion.
2. Patients who are not willing to include themselves into the study.
3. Patients having the serum TSH level less than 4.25 µIU/mL.
4. Patients having the serum T3 level greater than 77 ng/dL & serum T4 level greater than 5.4 µg/dL.
5. Primarily detected hypothyroidism patient, taking thyroxin medication.
6. Primarily detected hypothyroidism patient with any other chronic and systemic disease.

Subjective Parameter
The subjective parameters were selected considering the identical features between Pandu Roga and hypothyroidism. These are:
1. Daurvalya (tiredness, weakness)
2. Ruksha/Swedabhava (dry skin)
3. Shishirdweshi (feeling cold)
4. Kopana (irritability/mood alteration)
5. Aruchi/Hataanala (poor appetite)
6. Swas (dyspnea)
7. Alpavaaka (diminished voice)
8. Gatra Sadan/Gatra Shula (paresthesia/muscle cramp)
9. Karna Kheda (impaired hearing)
10. Shunashikutanana (periorbital oedema with puffy face)
11. Nidralu (sleepiness)
12. Bhrama (difficulty in concentration)

Objective Parameter
1. Estimation of serum TSH level
2. Estimation of serum T3 level
3. Estimation of serum T4 level

Adoption of Therapeutic Procedure
Pandu Rogais a disease which is caused chiefly by vitiated Pitta and Rakta. Virechan is a type of Samshodhan Chikitsa (bio purification therapy) which is indicated in all types of Pittaja & Raktaja Vikara as well as Pandu. Similarly Punarnava Mandoor is a well-known drug indicated as Shaman Chikitsa (pacifying management) in the management of Pandu. The stipulated drug has been prepared as per formulation given in CharakSamhita in the apothecary department of the study conducting institution. The above two therapy has been administered as:
1. Virechan Karma by root powder of Trivrit (Operculina turpethum)- 3 gm with warm water before lunch and dinner, along with 2. Powder Punarnava Mandoor - 250 mg with honey after lunch and dinner. Each of the therapy has been continued simultaneously for 60 days. After 60 days the effect of the stipulated therapeutic regimen has been evaluated.

Pathyapathya
Patients have been advised to avoid Simbi, Patrasak, Hing, Masa, Pinyak, Sarsap, Tambul, Sura, Mrid vaksana, Amla, Lavana, Vidahi and Guru dravya, Atimbupan, Dusta ambupan, Viruddha adhyasana, Vyama, maithuna, Vega dharan, Divaswapna and others Pitta-prokopa ahar Vihar. Along with these, they have been advised to intake Madhur–Tikta-Kashaya rasa enriched substances more as part of regular diet.
Study Protocol

Duration of study
The duration of the study was 60 days.

Assessment Criteria
Assessment has been done on the basis of subjective and objective criteria before and after treatment. For the statistical evaluation each of the subjective parameters has been arranged as per gradation.

Follow up of patients
All the patients were reviewed after 60 days from the date of administration of first dose. Any special information regarding the general health of the patient was recorded accordingly.

Study sample
Total 15 patients of hypothyroidism with features of Pandu Roga were included in the study.

Statistical analysis
The information gathered on the basis of observation made about various parameters has been subjected to statistical analysis in terms of Mean, Standard Deviation (SD) and Standard Error (SE). Paired ‘t’ test was carried out at P<0.05 and P<0.001. The obtained results were interpreted as -P<0.05 is significant & P<0.001 is highly significant.

Observations And Results
Among the 15 patients total 1 patient was dropped out during study course. Hence complete clinical survey was done in 14 patients. Distribution of subjective parameters of Pandu Roga among the 14 patients of hypothyroidism shows that, Daurvalya present in 14 patients (100%), Ruksha / Swedabhava present in 14 patients (100%), Shishirdweshi present in 12 patients (85.71%), Kopana present in 11 patient (78.57%), Aruchi / Hataanala present in 14 patient (100%), Swas present in 12 patient (85.71%), Alpavaaka present in 7 patient (50.00%), Gatra Sadan / Gatra Shula present in 13 patient (92.85%), Karna Kheda present in 6 patient (42.85%), Shunakshikutana present in 12 patient (85.71%), Nidralu present in 12 patient (85.71%) & Bhrama present in 13 patient (92.85%) [table no. 1].

Statistical analysis of subjective and objective parameters in 14 patients of hypothyroidism before and after 60 days of treatment shows that Shodhan therapy in terms of Virechan and Shaman therapy in terms of Punarnava Mandoor have significant efficacy on both the subjective and objective parameters with ‘p’ value <0.001 in most of the parameters after 60 days. [table no. 2].

Table 1 : Distribution of the subjective parameters in 14 patients of hypothyroidism

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Subjective Parameters</th>
<th>No. of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>01.</td>
<td>Daurvalya</td>
<td>14</td>
<td>100%</td>
</tr>
<tr>
<td>02.</td>
<td>Ruksha / Swedabhava</td>
<td>14</td>
<td>100%</td>
</tr>
<tr>
<td>03.</td>
<td>Shishirdweshi</td>
<td>12</td>
<td>85.71%</td>
</tr>
<tr>
<td>04.</td>
<td>Kopana</td>
<td>11</td>
<td>78.57%</td>
</tr>
<tr>
<td>05.</td>
<td>Aruchi / Hataanala</td>
<td>14</td>
<td>100%</td>
</tr>
<tr>
<td>06.</td>
<td>Swas</td>
<td>12</td>
<td>85.71%</td>
</tr>
<tr>
<td>07.</td>
<td>Alpavaaka</td>
<td>7</td>
<td>50.00%</td>
</tr>
<tr>
<td>08.</td>
<td>Gatra Sadan / Gatra Shula</td>
<td>13</td>
<td>92.85%</td>
</tr>
<tr>
<td>09.</td>
<td>Karna Kheda</td>
<td>6</td>
<td>42.85%</td>
</tr>
</tbody>
</table>
Hypothyroidism is such a pathological condition which has not been explicitly be given a stipulated name where there is less synthesis of thyroid hormone. Iodine deficiency remains the most common causative factor due to iodine deficiency causing hypothyroidism in a highly efficient manner. All the metabolic functions are regulated by Dhatwagni, as seen in Pandu, where due to impairment of Dhatwagni, there is less production of different tissue element like Rasa&Rakta.

Iodine deficiency remains the most common cause of hypothyroidism worldwide. Iodide uptake by thyroid gland cells is a critical first step for thyroid hormone synthesis. Thyroid gland extracts iodine from the circulation in a highly efficient manner. Deficiency of iodine as a part of diet will lead to hypothyroidism. This pathway of hypo secretion of thyroid hormones due to iodine deficiency can be compared with Dhatukshayajanya Pandu, where there is deficiency of Rasa Dhatu production which eventually leads to Rakta Dhatu Kshaya. The term Dhatu Kshaya can be interpreted as Dravyata Kshaya (loss of whole tissue element), Gunata Kshaya (diminished component of tissue).
In both of the above pathway of hypothyroidism, there is diminished secretion of thyroid hormones (T3 & T4) in one side and on the other side, hyper-secretion of TSH to maintain homeostasis. This phenomenon can be compared with ‘Eka Deshiya Vriddhi – Eka Deshiya Kshayaof Dosha Dushya’ hypothesis as described in various Ayurvedic compendiums in relation with pathogenesis of disease(25).

Although there is very little clinical evidence available regarding the role of stress in the pathogenesis of autoimmune hypothyroidism(26), but theoretically stress has very significant role in maintaining the ‘Hypothalamus-Pituitary-Thyroid’ Axis. The various psychological factors like Kama, Chinta, Bhaya, Krodha, Upahata Chetasa etc mentioned under the causative factors of Pandu Roga, can be compared with stress(27).

There are many similarities in between the clinical feature of hypothyroidism with Pandu Roga as described in various texts. Considering this, a comparative study between clinical features of hypothyroidism and Pandu Roga has been tabulated in Table 3.

Table 3 : Comparative study of clinical features found in hypothyroidism and Pandu Roga (28)

<table>
<thead>
<tr>
<th>Sl No.</th>
<th>Clinical Features</th>
<th>Hypothyroidism</th>
<th>Pandu Roga</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Tiredness, weakness ( Daurvalya / Arohana Ayasa)</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>2.</td>
<td>Dry skin ( Rukhatwa / Swedabhava)</td>
<td>++</td>
<td>++ *</td>
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<tr>
<td>3.</td>
<td>Feeling cold ( Shishiradweshi)</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>4.</td>
<td>Hair loss ( Shirna Loma)</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>5.</td>
<td>Impairment of concentration (Bhrama)</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>6.</td>
<td>Weight Gain ( Bhar Vriddhi)</td>
<td>++</td>
<td>--</td>
</tr>
<tr>
<td>7.</td>
<td>Poor appetite ( Hatanala / Aruchi)</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>8.</td>
<td>Dyspnea ( Swas)</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>9.</td>
<td>Hoarse voice (Alpa Vaaka / Vaaka Parushya)</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>10.</td>
<td>Oligomenorrhea / Amenorrhea (Krichrartav / Anartav)</td>
<td>++</td>
<td>++ **</td>
</tr>
<tr>
<td>11.</td>
<td>Paresthesia ( Kati Uru Pada Sadan)</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>12.</td>
<td>Muscle cramp ( Gatra shula / Pindikaudveshtan/ Mriditairiva Gatraischa Pitdonmasthitaairiva Cha)</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>13.</td>
<td>Impaired hearing ( Karna Ksheda)</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>14.</td>
<td>Peri orbital oedema &amp; Puffy face (Shunakshikuta)</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>15.</td>
<td>Irritability / Mood alteration ( Kopan)</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>16.</td>
<td>Drowsyness ( Nidralu)</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>

* Rukshyatwa found as prodromal feature in Pandu Roga. However, during complete manifestation of Pandu this symptom must be aggravated (29).
Hypothyroidism and Punarnava Mandoor against further as described Table 1 shows that most of the patients of hypothyroidism have subjective parameters of Pandu Roga present. This observation validates the concept that hypothyroidism can be compared with Pandu Roga in Ayurveda.

To further validate this concept, the possible patho-physiology behind each symptom of hypothyroidism has been explained below through Ayurvedic concept of Dosha (here Pitta Dosha), Dhatus (Rasa, Rakta&Mamsa), Srotas (here Rasavaha, Rakta Srota, Mamsavaha Srota), Oja&Agni in accordance with Sampapti (pathology) of Pandu Roga.

Weakness is caused by vitiation of Rasa Dhatu as well as depletion of Oja. Dry skin with decreased sweating is caused by vitiation of Raka Dhatu. Lack of concentration and mood alteration is caused due to vitiation of Sadhak Pitta, which is situated within the Hriday. Poor appetite is due to diminution of Agni, an essential phenomenon in any disease. Dyspnoea and hoarseness of voice are caused by vitiation of Rasavaha Srota, specifically Rasavaha Srota, because Hriday is the common root of this Srota along with Pranavaha Srota. Vitiation of Pranavaha Srota produces dyspnoea with hoarseness of voice. Oligomenorrhea and amenorrhea are cause by vitiation of Rasa Dhatu as well as depletion of Oja. Periorbital oedema and oedema in peripheral parts of the body is caused by vitiation of Twak (Rasa Dhatu), Shonita i.e. Rakta Dhatu&Mamsa Dhatu. Impaired hearing is due to vitiation of Rasa Dhatu. Hair loss is due to vitiation of Pitta along with Vata Doshas as well as vitiation of Rasa Dhatu. Cardiac arrhythmia is caused by vitiation of Rasa Dhatu. Drowsiness or sleepiness is caused due to vitiation of Rasavaha Srota along with depletion of Oja. Decreased libido in both sexes is caused by vitiation of Rasavaha Srota. In advanced stage of Pandu Roga, Shotha (oedema) manifests in various parts of the body. Oedema occurs due to retention of interstitial fluid. In hypothyroidism there is increase body weight. In contrast to popular perception, the weight gain is due mainly to fluid retention in the myxedematous tissues and not due to deposition of fat. This particular aspect of pathology of hypothyroidism is also identical with pathology of Pandu Roga.

Table 2 shows the statistical analysis of various subjective and objective parameters of 14 patients, before and after 60 days of treatment. Table 2 shows the ‘p’ value <0.001 in most of the parameters, which indicates that, the therapeutic procedure is significantly efficacious in the management of hypothyroidism after 60 days.

Virechan by Trivrit Churna eliminates vitiiated Pitta Dosha as well as it is helpful in the management of vitiation of Rasa, Rakta and Mamsa Dhatu. Punarnava Mandoor is a compound drug which is very effective in the management of Pandu Roga. This drug consists of Punarnava, Trivrit, Trikatu, Vidanga, Chitrak, Kustha, Haridra, Triphala, Danti, among others. Majority of the ingredients have Pittanashak property as well as active against Rakta and Pandu Roga. This drug is also effective against Shotha which is seen in the advanced stage of Pandu Roga. Virechan and Punarnava Mandoor probably reduce the inflammation of thyroid in autoimmune thyroiditis and thus help in regularize the secretion of thyroid hormone. However, actual pharmacodynamics of the above two therapeutic procedure in case of autoimmune hypothyroidism is a matter of further detailed scientific studies as per standards of modern biochemistry rather than only clinical observation.

Conclusion

In absence of categorical description of hypothyroidism in ancient Ayurvedic texts, this pathological condition should be studied in accordance with Pandu Roga. Hypothyroidism and Pandu Roga are identical on the basis of similarities between their causative factors, pathogenesis and clinical features. This comparative study of Pandu Roga w.r.t. to hypothyroidism is very helpful to determine the line of management of hypothyroidism. Thus management of Pandu Roga as described in our ancient compendiums in form of Shodhan Chikitsa like Virechan and Shaman Chikitsa like Punarnava Mandoor are also very effective to combat hypothyroidism.
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