

Study of Therapeutic Response on Variable Levothyroxine Supplementation in Hypothyroidism

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Abstract: Hypothyroidism is increasing worldwide and female predominate male i.e. - 1 out of 50 female and 1 out of 1000 male. TSH (thyroid stimulating Hormone, a secretion of pituitary gland) level is adjudged as an index of diagnosis of thyroid function. Hypothyroid status needs L thyroxin supplementation but its variable schedule poses metabolic dysfunction

Objective of Study:

To adjudge clinical effect of early morning fixed time intake of L thyroxin verses unscheduled administration in bioregulation of TSH level and metabolic process

Material & Methods:

1000 patients presenting with features suggestive of thyroid hypo function attending at Centre For Endocrinal & Metabolic research, Aarogyam Punarjeevan, Ram Bhawan, Ara Garden, Patna 14 and Institute of applied Endocrinology, National Institute of Health & Research, Warisaliganj (Nawada) Bihar 805130 were selected for the proposed study. For the comparative study patients were classified in two groups comprising equal number of patients and one group is administered L thyroxin early morning at fixed time as first intake while other group at varied time. Both group were recommended L thyroxin and other adjuvant as per their need

Result:

Present study of Levothyroxine supplementation at fixed schedule at early morning prior to onset of body biokinetics ensured excellent therapeutic outcome with TSH bioregulation and better quality of life and sustained and progressive therapeutic response without any adversity.

Conclusion:

Early morning intake of L thyroxin at fixed time as first intake is worth practicing for optimal thyro regulation and clinical outcome.

Keywords: L-thyroxine, biokinetics, fixed schedule

1. INTRODUCTION

Hypothyroidism progressively increasing globally in spite of W.H.O caution and measures to restrict Iodine deficiency and estimates burden of 42 millions population in India which is considered due to increasing dietary non nutrients and changed life style. Dietary non nutrients alter iodination of tyrosine and C cells of thyroid suppressing calcium metabolism resulting in deficiency of ionic form of calcium, accumulation of free radicals, thus presents with manifestations of thyroid hypofunction and hypocalcaemia. ¹⁻⁵

Thus patients of hypothyroidism, L- thyroxine supplementation is a prime need and its administration schedule poses varied clinical outcome, as in cases though TSH level gets declined but clinical presentation become worse thus patients taking Levothyroxine supplementation been evaluated to adjudge the clinical outcome and quality of life with fixed time early morning dose and varied time schedule .⁶⁻⁷

Alteration in thyroid function is common among female and hypothyroidism a common presentation among women these days. Hypothyroidism suppresses BMR through its effect on decline in gonadal hormone specially estrogenic and testosterone which causes sub cutaneous accumulation of mucin and retention of water and electrolyte and presents with - myxoedema, asthenia, leg cramps, exertional dyspnoea constipation etc, in addition also suppress sexual function and menses. ⁸⁻⁹

The most common parameters of ascertaining is assessment of serum thyroxin(T4) and thyroid stimulating hormone (TSH)and therapeutic supplement used is Levothyroxine but unawareness or incomplete education regarding schedule of levothyroxine supplementation, patients consume this supplements with variability ¹⁰⁻¹⁷ i.e.-

- Early in the morning at fixed time as first oral intake
- In the morning after natural routine practice
- Daily after breakfast
- Daily as per convenience

Though TSH gets improved with thyroxin level but patients present with varied presentations i.e.-

- Increase in body weight
- Fatiguability
- Asthenia
- Sleepy
- Abnormal muscular growth

Thus considering the above presentation a clinical assessment of these patients been planned to asses the rationale and significance of early morning fixed time as first consumption of levothyroxine been assessed.

Design of the Study: Comparative clinical study

Objective of the Study: Clinical evaluation of Levothyroxine administration in early morning at fixed time as first consumption verses other dose schedule in securing cure and ensure safety and better quality of life

2. MATERIAL AND METHODS

2.1. Material

1000 patients of hypothyroidism attending RA. Hospital & Resaearch Centre Warisaliganj and AArogyam punarjeev, Patna 14 been selected for the proposed study to adjudge the clinical significance and quality of life.

2.2. Methods

Selected patients irrespective of their disease status were interrogated for their disease duration, type of therapeutic consumption, their clinical effect, present status, history of consumption of Levothyroxine suppliments, their dose. After clinical examination patients were assessed for their thyroid profile, body weight, blood pressure, blood sugar, hepatic, hematological and renal profile, lipid profile, serum calcium, vitamin D3 and ECG. In patients of hypertension, history of convulsion or unconsciousness.

Based on the clinical presentation and thyroid profile patients were classified as ¹⁸⁻²¹ –

Mild	Patients presenting with heaviness in the body, exertional dyspnoea, lassitude, asthenia, swelling of the body, weight gain, constipation, menstrual irregularity TSH level >5.5-20.5
Moderate	Above presentation, leg cramps, uneasiness, vertigo, bodyache, joint pain TSH >20.5-40.5
Severe	With above presentation, obese, unable to walk, recurrent unconsciousness Involuntary movement TSH >40.5- 60.5
Malignant	Above presentation TSH > 60.5, decreased Vitamin D3 (Cholecalciferol), Decreased Serum Calcium, Raised blood sugar

For ease of study patients were categorised in two groups and administered i.e.-

Group A: those who were taking levothyroxine supplementation in early morning at fixed time

Group B: Those who were taking levo thyroxin supplementation at variable time daily

Starting dose of L thyroxin:

Following facts must be considered during recommendation of L thyroxin dose, i.e.-

- Patient's age (In elderly patient start with low dose and titrate the dose slowly)
- Body weight (1.5ug/Kg IBW)
- Cardiovascular status (In patients with coronary insufficiency start with very low dose)
- General health
- Concomittent medication
- Severity and duration of hypothyroidism

Patients were clinically evaluated for weight loss, improvement in vigor and vitality, regression in edema and muscle stiffness, relief in leg cramps and asthenia, serum TSH level.

Patients were investigated for basic bio parameters and based on clinical improvement, quality of life and thyroid profile, therapeutic outcome been classified as –

Excellent :	Complete reversal of clinical presentation with attainment of ideal body weight and TSH bioregulation within normal range.
Marked	improvement in clinical presentation, decline in body weight and TSH level
Poor	Only decline in TSH level without clinical relief and decline in body weight

3. OBSERVATION

Majority 297 (29.7%) were of age group 25-30 years while 68(6.8%) and 37(3.7%) were of age group 15-20 years and 45-50 years respectively (T-1)

Out of all 5% cases were male and 95% female (Pie diagram showing male: female composition)

Out of all 131(13.1%) patients were with TSH > 50.5 while 27(2.7%) were with TSH 5.5-10.5 (T-2)

Among the selected patients 199 were of mild, 427 moderate, 243 severe and 131 malignant grade of severity (Bar diagram)

Considering the body weight 239(23.9%) were with body weight 75-80 Kg (>IBW) while 105(10.5%) were having body weight >100 kg and 212(21.2%) with body weight 70-75 kg (T-3)

Among selected patients 66.2% patients were with haemoglobin >10gm %, 5% were with SGOT and SGPT >30 IU, 99.9% posses normal renal profile though 2.4% shows presence of albumin, 0.2%

presence of RBC and 64.2% presence of calcium oxalate sand in urine, 99.6% were with normal serum cholesterol, 37.6% with low Vitamin D3 and 39% with low serum calcium.

Out of all patients taking L- thyroxin supplementation at early morning at fixed time (group A) were 467 and 533 were taking L- thyroxin supplementation at unscheduled manner daily (group B). Group A constitutes no male patients.

Patients of group A shows sustained and progressive decline in TSH level in all while patients of group B shows variable and mild decline in TSH level.

97.6% patients of group A had marked relief in clinical presentation while only 63.4% of group B, 99.6% of group A patients had progressive decline in body weight and attended Ideal body weight without any discomfort while only 21.2% of group B had declined in body weight but non attended ideal body weight for the age and height and 35.8% patients of group B had abnormal muscle mass growth.

87.6% patients of group A had blood pressure bioregulation while 62.7% patients of group B remained with low blood pressure. 81.8% of group A had relief of constipation while 20.4 of group B, menses and libido marked improved in 84.8% and 92.8% respectively of group A contrary to 5.2% and 27.4% respectively of group B.

Conclusively 97.6% of group A achieved grade I therapeutic outcome as against 7% of group B (T-)

4. DISCUSSION

Thyroid secretes hormone to bio regulate body metabolism and its under activity is termed as hypothyroidism i.e.- persons suffering with hypothyroidism presents with manifestation of slow metabolism. Approximately one in 50 women and 1 in 1000 men suffers with hypothyroidism in their life and TSH (Thyroid stimulating Hormone, secreted by Pituitary gland) level is a most sensitive index, as elevated TSH level always suggest under activity of thyroid.²²⁻²⁸

Though various dose schedule been clinically evaluated but early morning fixed time consumption through out life remain worth as it ensure sustained and progressive decline in TSH level, marked relief of clinical presentation, decline in body weight, normotensive state and grade I clinical out come with improved quality of life in 97% patient while other schedules fail to ensure even symptomatic relief though causes decline in TSH level. This clinical supremacy can be explained as –

Early morning fixed time consumption of Laevo thyroxin acted by oral saliva and salivary amylase effect gets pronounced while consumption after oral ingestion or water intake oral saliva gets washed off or diluted thus administered L thyroxin fails to potentiate salivary amylase and restricted conversion of T4 to T3, hence early morning consumption not only causes decline in TSH but also ensure clinical improvement²⁹⁻³¹.

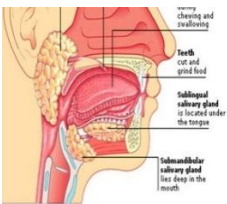
L Thyroxin	As first intake ----- Potentiate Salivary amylase , increased $T_4 \rightarrow T_3$
	
	Increases metabolism of Subcutaneous mucin
After water intake	Decreases body weight , improve clinical outcome
dilute saliva	
fails to act on L thyroxin	
decreased conversion of T4-T3	
Slows metabolic process	
Fails to relieve presentation	
(Schematic presentation of L thyroxin effect)	

Table1. Distribution of patients as per age and sex

Age group (In years)	Number of patients		
	Male	Female	Total
15-20	02	66	68
20-25	07	208	215
25-30	09	288	297
30-35	11	220	231
35-40	06	72	78
40-45	07	67	74
45-50	08	29	37

Pie diagram showing Male-Female Composition

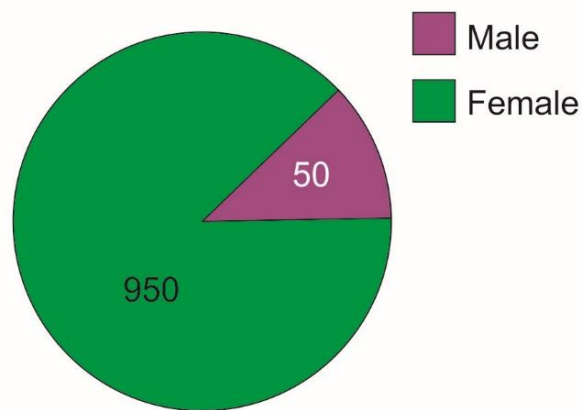
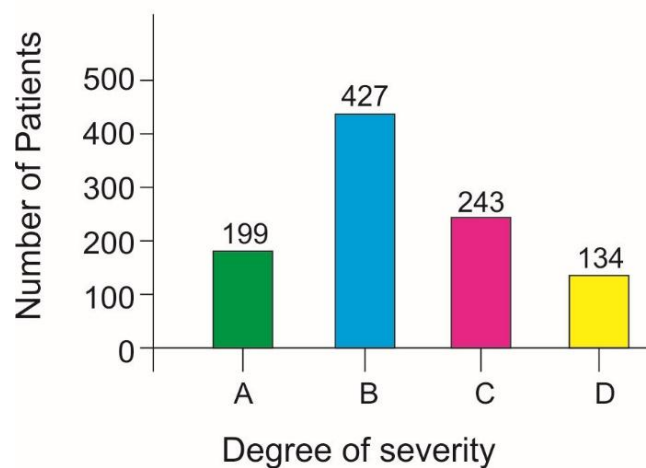


Table2. Distribution of patients as per TSH level

TSH Level (in μ IU/dl)	Number of patients
5.5-10.5	27
10.5-15.5	68
15.5-20.5	104
20.5-25.5	98
25.5-30.5	129
30.5-35.5	84
35.5-40.5	116
40.5-45.5	139
45.5-50.5	104
>50.5	131

Bar diagram showing degree of Severity



(Key: A= Mild; B= moderate; C= severe and D= malignant)

Table3. Distribution of patients as per body weight

Body weight (in Kg)	Number of patients
70-75	212
75-80	239
80-85	121
85-90	111
90-95	104
95-100	108
>100	105

Table4. Distribution of patients as per basic bio parameters

Particulars	Number of patients
Haematological : Haemoglobin : < 10 gm % >10 gm%	338 662
Hepatic profile : SGOT : <30 IU >30 IU	950 50
SGPT : <30 IU >30 IU	950 50
Renal profile : <1.5 mg >1.5 mg	999 01
Blood Urea <26mg >26mg	999 01
Urine : Albumin Present Absent RBC Absent Present Oxalate crystal Present Absent	24 976 02 998 642 358
Lipid profile Total Serum Cholestrol <200mg >200mg	996 04
Vitamin D3 (Chole calciferol) <20 >20	376 624
Serum Calcium : <8.8mg% >10mg%	390 610

Graph showing comparative decline in serum TSH level

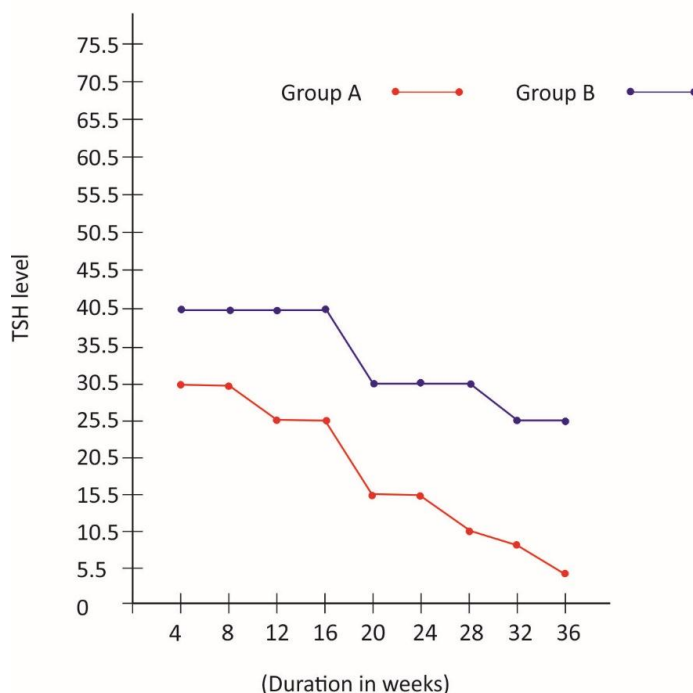


Table 5. Shows outcome of therapy

Particulars	Number of patients	
	Group A	Group B
Relief of clinical presentation	488 (97.6%)	317 (63.4%)
Body weight:		
Decline	498 (99.6%)	106 (21.2%)
Unaltered	02	215 (43%)
Abnormal body weight	-	179 (35.8%)
Blood Pressure:		
Normal	438 (87.6%)	89 (17.8%)
Low	62	411 (62.2%)
Constipation		
Relieved	409 (81.8%)	102
Unaltered	91	398 (79.6%)
Menses		
Bioregulated	424 (84.8%)	31
Unchanged	51	444 (88.8%)
Libido		
Decreased	36	313 (62.6%)
Unchanged	464 (92.8%)	187 (27.2%)
Therapeutic outcome		
Grade I	97.6%	7%
Grade II	2.4%	76%
Grade III	-	17%

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