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Research Article

EFFECT OF ESCITALOPRAM ON THYROID FUNCTION IN PATIENTS WITH DEPRESSION- A HOSPITAL BASED STUDY

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ABSTRACT

Introduction: Depression is a common, recurrent, clinically and biologically heterogeneous disorder. Depression is commonly associated with several endocrine disorders and patients should be routinely investigated for endocrine disorders. Mood and anxiety disorders are higher with thyroid dysfunction. This association is attributed to the hypothalamic-pituitary-thyroid (HPT) axis regulation. In hypothyroid patients the prevalence of depression was found 33.0% to 43.0% and for anxiety 20.0% to 33.0%. In case of hyperthyroidism it is even higher with 53.0% to 69.0% for anxiety and 30.0% to 70.0% for depression. **Materials and Methods:** The study was conducted in the department of Psychiatry Sher-I- Kashmir Institute of Medical Sciences (SKIMS) Medical College and Hospital.The study sample comprised of 200 patients diagnosed with first episode depression (Major depressive disorder) attending psychiatric outpatient department by using DSM 5criterion. Patients with major depression entering a treatment with escitalopram were assessed with the Structured Clinical Interview for DSM-5 and were rated on the Hamilton depression rating scale (HAM-D). Blood samples were taken for TSH, thyroxine (T4) and triiodothyronine (T3) measurement. Patients were then assigned to receive escitalopram for 6 weeks, After 6 weeks the thyroid hormone assessment was repeated and HAM-D was again applied. Mean concentrations of TSH, were slightly raised which were statistically significant, T3 and T4 were within reference ranges. Patients who showed no or minimum clinical response were administered increased dose of escitalopram and patients in whom TSH showed a subclinical response were treated with venlafaxine and after 12 weeks, TSH decreased with improvement in HAM-D score.
Results: Majority of the participants were males, predominantly belonging to age group of 18-29 years, mostly having education up to middle school, working in semi-skilled or unskilled group and married. Clinical profile revealed that most of the patients had mild to moderate form of depression, a few also reported severe form of depression. Some of them had given family history of thyroid disorder and psychiatric illness. The Hamilton Depression Rating Scale-(HAM-D) analysis pointed towards presence of depression with mean score of 13.34 before start of treatment and 11.24 and 9.96 respectively after6 and 12 weeks of treatment. Most of the patients had no or negligible change in thyroid indices, some of them had changes within euthyroid range and some of them had changes within sub-clinical range, which were statistically significant. **Conclusion:** Escitalopram was not associated with clinically significant changes in thyroid hormone levels in euthyroid patients suffering from depression. However, results suggest that patients with normal thyroid function, who were treated with escitalopram, are susceptible to minor insignificant changes which also demonstrate the safety of administering escitalopram in euthyroid patients with depression. Although, the patients on treatment with escitalopram do not need strict monitoring of thyroid hormone levels. However, regular and periodic assessments of thyroid function should be carried out in patients with depression.

INTRODUCTION

Mental disorders affect people all over the world, of all ages, women and men, the rich and the poor, from urban and rural environments. Depressionas one of the major mental disorder and third leading cause of global disease burden, accounting for 4.3% of total disability-adjusted life years. Depression is a common, recurrent, clinically and biologically heterogeneous disorder. It affects the mental and emotional wellbeing of a person. [1-3] Mental health survey indicated that 10-15% of population in their lifetime experience major depression. [4] In India a survey reported an overall prevalence of 15.9% for depression.[5]Depression is commonly associated with several endocrine disorders and patients should be routinely investigated for endocrine disorders.[6,7]On the other hand behavioral disturbances are also associated in patients with major endocrine disorders.[8]

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All thyroid states are associated with psychiatric manifestation, be it hypothyroid or hyperthyroid. Subclinical hypothyroidism is a condition when patients with normal peripheral thyroid hormones namely free T_3 (FT_3) and free T_4 (FT_4), with a slightly elevated (typically<10mIU/L) serum level of thyroid-stimulating hormone (TSH, thyrotropin), with or without physical features of hypothyroidism may have psychological and emotional impairment.[9-11] Mood and anxiety disorders are higher with thyroid dysfunction. This association is attributed to the hypothalamic-pituitary-thyroid (HPT) axis regulation. In hypothyroid patients the prevalence of depression was found 33.0% to 43.0% and for anxiety 20.0% to 33.0%. In case of hyperthyroidism it is even higher with 53.0% to 69.0% for anxiety and 30.0% to 70.0% for depression. [12]

The treatment option for depression as per the W.H.O consists of basic psychosocial support combined with antidepressant medication & psychotherapy.[13]Patients with mild depression, treatment may entail psychological support, problem solving, exercise, informal counselling, or formal psychosocial interventions. For moderate and severe depression, anti-depressant medication (in combination with psychotherapy) is the mainstay of treatment. In view of less adverse effects, superior safety profile, less drug-drug interactions, cost effectiveness and overall efficacy selective serotonin reuptake inhibitors (SSRIs) are common initial choice to treat depression. Escitalopram is preferred among SSRIs in patients because of low propensity to cause drug interactions. Generally, it is advisable to start at a lower dose and increase gradually (start low, go slow), however patients must be given adequate dose of SSRI to ensure a remission of symptoms. Medication usually takes 4-6 weeks for improvement in clinical symptoms.[14,15]

Manystudies have evaluated both the predictive value of baseline thyroid indices and subsequent response to antidepressant treatment, as well as the change in these indices with treatment.[16-19] Up to 10% of individuals with depression may present with elevated levels of thyroid-stimulating hormone (TSH) and normal thyroxine (T4) and triiodothyronine (T3) levels (subclinical hypothyroidism). The most common change in thyroid hormones with antidepressant treatmentt is decrease in T4 and free T4 without a significant reduction in TSH, these changes are generally within the euthyroid range of values.[20]

Hence it has been seen that there is an association between SSRI treatment and thyroid function. In this study, we explored these two areas, first the effect of escitalopram on thyroid hormones and second, the relation of thyroid function and depression.

Aims and objectives

- ✓ To study the effect of optimal antidepressant dose of Escitalopram i.e 10-20 mg on thyroid stimulating hormone, thyroxine, and triiodothyronine in patients with first episode of depression.(major depressive episode)
- ✓ To study the affect of:
- ✓ Gender on thyroid stimulating hormone, thyroxine, and triiodothyronine in patients with first episode of depression on optimal antidepressant dose of escitalopram i.e 10-20 mg.
- ✓ Age on thyroid stimulating hormone, thyroxine, and triiodothyronine in patients with first episode of depression on optimal antidepressant dose of escitalopram i.e 10-20 mg.

METHODOLOGY

Study Area: The study was conducted in the department of Psychiatry Sher-I- Kashmir Institute of Medical Sciences (SKIMS) Medical College and Hospital, Bemina, Jammu and Kashmir.The study was approved by the SKIMS Ethical Committee. The study sample comprised of200 patients diagnosed with first episode depression (Major depressive disorder)attending psychiatric outpatient department by using DSM 5criterion. The severity of the depression was assessed by HAM-D scale. Patients attending psychiatric outpatient department during the study period of 18 months were screened and those satisfying the inclusion and exclusion criteria and who agreed to have their peripheral thyroid hormones assayed before and after treatment with the escitalopram, gave written informed consent were enrolled in the study.

Inclusion Criteria

1. Patients above 18 years of age.
2. Patients with depression (MDD).
3. Those able to understand and answer proforma questionnaire verbally.
4. Those willing to participate and give informed consent.

Exclusion Criteria

1. Patients <18 years of age.
2. Patients with depression with psychotic features.
3. Patients with pregnancy and lactation.
4. Any patient with suicidal attempts.
5. Bipolar and related disorders.
6. Family history of Bipolar and related disorders.
7. Current or recent treatment with an antidepressant.
8. History of thyroid disease or current treatment with thyroid hormones.
9. History of treatment with lithium.
10. Any comorbid general medical conditions.
11. History of substance abuse or dependence.
12. Patients unable to understand and answer proforma questionnaire verbally
13. Those not willing to participate or give informed consent.

After written informed consent each patient was individually interviewed along with the proforma prepared for the study. The details about medical and psychiatric complaints and other aspects of clinical profile were taken. A general physical examination and investigations was advised if needed to rule out any comorbid medical condition. The rating scale HAM -D was administered to assess the severity.

Instruments

Semi-structured proforma: Proformawas prepared for the study which included social-demographic profile, Clinical profile (including history of present complaints medical and psychiatric, Family and Personal history and clinical examination and diagnosis).

DSM-5: Diagnostic and Statistical Manual of Mental Disorders Fifth Edition was used for the diagnosis of depression. DSM-5 diagnostic criteria has been used for

diagnosing the patients having depression.[21] DSM-5 diagnostic criterion is a tool for collecting and communicating accurate public health statistics on mental disorders. DSM-5 is designed better to fill the need of clinicians, patients, families, and researchers for a clear and concise description of each mental disorder organized by explicit diagnostic criteria supplemented. Diagnosis was formulated under the supervision of the consultant in the department.

***Hamilton Depression Rating Scale- Ham-D*:** Hamilton Depression Rating scale (HAM-D) has been used for assessing the severity of depression. The Ham-D is the most widely used clinician-administered depression assessment scale. A score of 0–7 is generally accepted to be within the normal range, 8-13-mild depression, 14-18-moderate depression,19-22-severe depression.[22]

Thyroid Profile Test: Venous blood samples were drawn for measurements of serum TSH, thyroxin (T4) and triiodothyronine (T3) among other routine laboratory tests Serum TSH, T4, and T3 levels were analyzed by Ultrasensitive Sandwich Chemiluminesence Immunoassay. Normal ranges were defined as 0.50-6.50 uIU/ml for serum TSH, 0.70-2.50 ng/ml for T3, and 4-13 ug/dl for T4.

Drug Administration

Escitalopram is the **S**-isomer of the racemic compound citalopram, a selective serotonin reuptake inhibitor (SSRI) that is widely used in both psychiatric and primary care practices for the treatment of depression. Escitalopram 10 mg/day is optimum dose for treatment of mild to moderate MDD while escitalopram 20 mg/day is an effective dose in patients with moderate to severe depression**.** As our study is purely for patients with unipolar depression

Subjects were then treated with escitalopram 5 mg daily for first 7 days and then medication dose increased to 10 mg. Nine subjects did not complete the posttreatment thyroid measurements and were considered as drop out from the study**.** Our sample, therefore, includes 191 subjects at baseline. Subjects were again assessed after every two weeks for side effects.

At baseline, thyroid indices were measured using standard venepuncture techniques: At the end of the study, the same thyroid indices were measured again. At 6 weeks follow up, subjects were assessed again and HAM-D scale was applied, and thyroid tests were performed. Subjects 54.5% (n=104) with a HAM-D score less than previous scores were continued with same 10 mg dose of escitalopram, and those subjects 30.4% (n=58) in whom there was no improvement or slight change on HAM-D score, their dose of escitalopram was increased to 20 mg daily and 15.2% (n=29) in whom TSH were in subclinicalrange were changed to venlafaxine. At 12 weeks follow up, subjects were assessed, HAM –D scale and Thyroid tests were performed again. Response to treatment was measured by the change in HAM-D scores before and after treatment, with positive values reflecting improvement in HAM-D symptoms. A stepwise regression analysis was used to predict improvement in Ham-D scores, with baseline values for TSH, T3, and T4 as the independent variables.

Sample Size Calculations: The sample size calculations were performed by Statistical Software G Power (3.0.10). Based on 5% alpha error and 80% power of study, atleast 183 patients were required to carry out the study. Assuming a 10% non-response rate, 200 patients were included in the study.

Statistical Analysis: All data thus collected was tabulated and analysed statistically using SSPS software version 20.0 under guidance of a statistician and conclusions were drawn.

RESULTS

Age distribution of studied patients

Age (years)	No. of Patients	Percentage %
18-29	81	42.4
30-39	42	22.0
40-49	26	13.6
50-59	38	19.9
≥60	4	2.1
Mean±SD=35.3±13.56		

Gender distribution of patients

Gender	No. of Patients	Percentage %
Male	106	55.5
Female	85	44.5
Total	191	100

HAMD Score in patients before and after treatment

HAMD Score	Mean	SD	Paired Samples test		
			Comparison	Paired Difference	P-value$
Pre Treatment (I)	13.34	3.080	I vs II	2.1	<0.001*
After 6 weeks (II)	11.24	2.742	I vs III	3.38	<0.001*
After 12 weeks (III)	9.96	2.335	II vs III	1.28	<0.001*

*Statistically Significant Difference (P-value <0.05), $P-value by Paired t-test

Mean TSH in patients before and after treatment

TSH	Mean	SD	Paired Samples test		
			Comparison	Paired Difference	P-value
Pre Treatment (I)	3.45	1.526	I vs II	-1.1	<0.001*
After 6 weeks (II)	4.55	1.697	I vs III	-1.08	<0.001*
After 12 weeks (III)	4.53	1.596	II vs III	0.02	0.791

*Statistically Significant Difference (P-value <0.05), $P-value by Paired t-test

Table 11 Showing mean T3 in patients before and after treatment

T3	Mean	SD	Paired Samples test		
			Comparison	Paired Difference	P-value
Pre Treatment (I)	1.05	0.399	I vs II	-0.02	0.005*
After 6 weeks (II)	1.07	0.419	I vs III	-0.02	0.038*
After 12 weeks (III)	1.07	0.404	II vs III	0.00	0.791

Table 12 Showing mean T4 in patients before and after treatment

T4	Mean	SD	Paired Samples test		
			Comparison	Paired Difference	P-value
Pre Treatment (I)	5.79	1.438	I vs II	-0.01	0.861
After 6 weeks (II)	5.8	1.466	I vs III	0.05	0.293
After 12 weeks (III)	5.74	1.509	II vs III	0.06	0.300

Thyroid changes in patients at 6 week and 12 week treatment

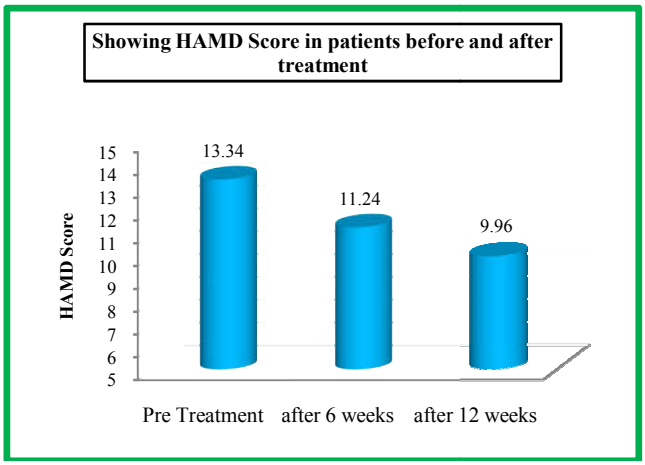
Thyroid Changes	After 6 weeks		After 12 weeks	
	No. of Patients	Percentage (%)	No. of Patients	Percentage (%)
Negligible or No change (<0.1 uIU/ml)	104	54.5	103	53.9
Change within Euthyroid range (0.1-6.50 uIU/ml)	58	30.4	86	45.0
Change Within Sub-clinical range((6.50-10 uIU/ml)	29	15.2	2	1.0

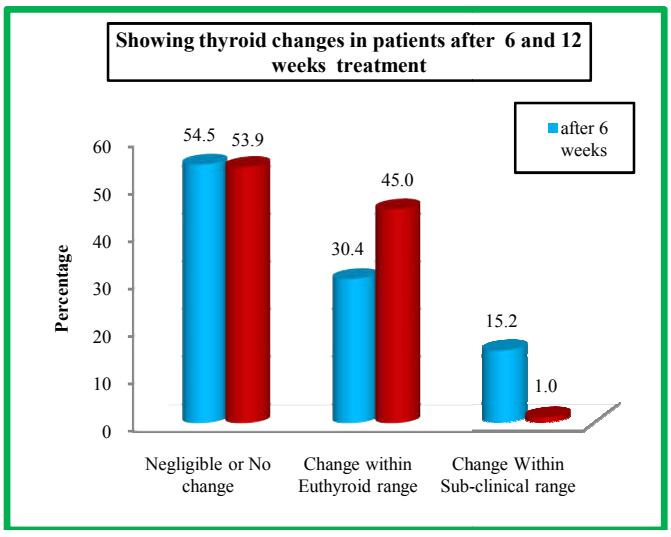
Association of thyroid changes with gender in studied patients

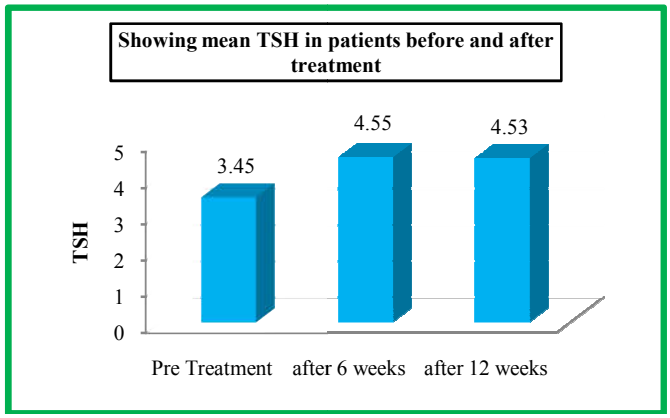
Thyroid changes		Male		Female		P-value
		No.	%age	No.	%age	
After 6 weeks	Negligible or No change	51	48.1	53	62.4	0.065
	Change within Euthyroid range	36	34.0	22	25.9	
	Change Within Sub-clinical range	19	17.9	10	11.8	
After 12 weeks	Negligible or No change	50	47.2	53	62.4	0.139
	Change within Euthyroid range	54	50.9	32	37.6	
	Change Within Sub-clinical range	2	1.9	0	0.0	

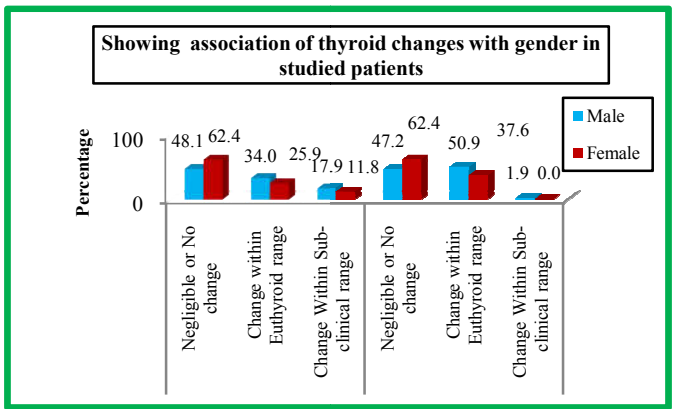
Association of thyroid changes with age in studied patients

Thyroid changes		Age (years)					P-value
		18-29 N=81	30-39 N=42	40-49 N=26	50-59 N=38	≥ 60 N=4	
After 6 weeks	Negligible or No change	42 (51.9%)	26 (61.9%)	12 (46.2%)	22 (57.9%)	2 (50%)	0.761
	Change within Euthyroid range	23 (28.4%)	12 (28.6%)	11 (42.3%)	11 (28.9%)	1 (25%)	
	Change Within Sub-clinical range	16 (19.8%)	4 (9.5%)	3 (11.5%)	5 (13.2%)	1 (25%)	
After 12 weeks	Negligible or No change	41 (50.6%)	26 (61.9%)	12 (46.2%)	22 (57.9%)	2 (50%)	0.852
	Change within Euthyroid range	39 (48.1%)	15 (35.7%)	14 (53.8%)	16 (42.1%)	2 (50%)	
	Change Within Sub-clinical range	1 (1.2%)	1 (2.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	









In our study Majority of our patients 81 (42.4%) were aged between 18-29 years, 42 (22.0%) were 30-39 years of age, 26 (13.6%) were aged between 40-49, 38 (19.9) were aged between 50-59, and only 4 (2.1%) patients were more than 60 years. The mean age was 35.3±13.56. Males constituted 106 (55.5%) while as there were 85 (44.5%) females out of a total of 191 patients. As far as the residence of the studied population is concerned, there were 101 (52.9%) patients who belonged to rural areas and 90 (47.1%) were from urban areas and 98 (51.3%) were uneducated, 8 (4.2%) patients were primary pass, 16 (8.4%) were middle pass, 29 (15.2%) were matriculates, 32 (16.8%) were graduates, and 8 (4.2%) were postgraduates. Table 5 shows that in our studied population 97 (50.8%) were unemployed, 79 (41.4%) were employed and 15 (7.9%) were students. Therewere 104 (54.5%) married men and women in our study, 73 (38.2%) were unmarried, 7 (3.7%) each were widowed and divorcee. Inour study belonged to middle socioeconomic class, 57 (29.8%) patients were from lower class and 15 (7.9%) patients were belonging to upper socio-economic class. Therewere only 38 (19.9%) patients in our study who had family history of psychiatric illness while as 153 (80.1%) were not having any family history of psychiatric illnesses. Only 22 (11.5%) patients in our study had family history of thyroid disorder while as 169 (88.5%) were not having any family history of thyroid disorder. The mean pre-treatment HAM-D score in patients was 13.34, after 6 weeks the mean HAM-D score was 11.24 and after 12 weeks the HAM-D score was 9.96. the mean pre-treatment TSH level in patients was 3.45, After 6 weeks, the mean TSH level was 4.55 and after 12 weeks, the mean TSH level was 4.53 andmean pre-treatment T3 level in patients was 1.05, After 6 weeks the mean T3 level was 1.07 and after 12 weeks &the mean T3 level was 1.07 and the mean pre-treatment T4 level in patients was 5.79, After 6 weeks the mean T4 level was 5.8 and after 12 weeks the mean T4 level was 5.74.There was no

or negligible change in thyroid hormone levels of 104 (54.5%) patients after 6 weeks, After 12 weeks 103 (53.9%) patients observed no or negligible change in their thyroid hormone levels. 58 (30.4%) patients had changes in thyroid hormone levels within euthyroid range After 6 weeks, while as 86 (45.0%) patients observed changes in thyroid hormone levels within euthyroid range after 12 weeks 29 (15.2%) patients had changes in thyroid hormone levels within sub-clinical range after 6 weeks, while as only 2 (1.0%) patients observed changes in thyroid hormone levels within sub-clinical range after 12 weeks. After6 weeks there was no or negligible changes in thyroid hormone levels in 51 (48.1%) male patients and 53 (62.4%) female patients, 36 (34.0%) male patients and 22 (25.9%) females patients observed changes in thyroid hormone levels within euthyroid range and 19 (17.9%) males and 10 (11.8%) females had change in thyroid hormone levels within sub-clinical range.After 12 weeks there was no or negligible change in thyroid hormone levels in 50 (47.2%) male patients and 53 (62.4%) female patients, 54 (50.9%) male patients and 32 (37.6%) females patients observed change within euthyroid range and 2 (1.9%) males and 0 (0.0%) females had changes within sub-clinical range.After6 weeks there was no or negligible change in thyroid hormone levels in 42 (51.9%) patients aged 18-29 years, 26 (61.9%) patients aged 30-39 years, 12 (46.2%) patients aged 40-49 years, 22 (57.9%) aged between 50-59 and 2 (50%) patients aged > 60 years. There were 23 (28.4%) patients aged 18-29 years, 12 (28.6%) patients aged 30-39 years, 11 (42.3%) patients aged 40-49 years, 11 (28.9%) patients aged 50-59 years and only 1 (25%) patient aged > 60 years with thyroid hormone level changes within euthyroid range. 16 (19.8%) patients in our study aged 18-29 years, 4 (9.5%) aged 30-39 years, 3 (11.5%) aged 40-49 years, 5 (13.1%) aged 50-59 years and only 1 (25%) patient aged > 60 years had thyroid changes within sub-clinical range. After 12 weeks there was no or negligible change in thyroid hormone indices in 41 (50.6%) patients aged 18-29 years, 26 (61.9%) patients aged 30-39 years, 12 (46.2%) patients aged 40-49 years, 22 (57.9%) patients aged 50-59 years and 2 (50%) patients aged > 60 years. There were 39 (48.1%) patients aged 18-29 years, 15 (35.7%) patients aged 30-39 years, 14 (53.8%) patients aged 40-49 years, 16 (42.1%) patients aged 50-59 years and 2 (50%) patient aged > 60 years with thyroid changes within euthyroid range. 1 (1.2%) patients in our study aged 18-29 years, 1 (2.4%) aged 30-39 years, had thyroid changes within sub-clinical range and none of the patients with sub-clinical range change in thyroid were 40-60 years of age.after 6 weeks there was no or negligible change in thyroid hormone levels in 24 (63.2%) patients with family history of psychiatric illness, 80 (52.3%) patients with no family history psychiatric illness. There were 6 (15.8%) patients with family history psychiatric illnesses and 52 (34.0%) patients with no family history of psychiatric illness with thyroid changes within euthyroid range. 8 (21.1%) patients in our study had family history of psychiatric illnesses and 21 (13.7%) did not had any family history of psychiatric illnesses with thyroid changes within sub-clinical range.

After 12 weeks there was no or negligible change in thyroid hormone levels in 24 (63.2%) patients with family history psychiatric illness, 79 (51.6%) patients with no family history of psychiatric illness. There were 14 (36.8%) patients with family history of psychiatric illnesses and 72 (47.1%) patients with no family history of psychiatric illness with thyroid changes within euthyroid range. None of the patients in our study had family history of psychiatric illnesses while as 2 (1.3%) did not had any family history psychiatric illnesses with thyroid changes within sub-clinical range. After6 weeks there was no or negligible change in thyroid hormone levels of 10 (45.5%) patients with family history of thyroid disorders and 94 (55.6%) patients with no family history of thyroid disorders. Among our studied patients who had thyroid changes within euthyroid range 5 (22.7%) patients had family history of thyroid disorder and 53 (31.4%) patients had no family history of thyroid disorder. Out of patients with thyroid changes within sub-clinical range in our study 7 (31.8%) patients had family history of thyroid disorders and 22 (13.0%) did not had any family history of thyroid disorders. After 12 weeks there was no or negligible change in thyroid hormone levels in 10 (45.5%) patients with family history of thyroid disorders and 93 (55.0%) patients had no family history of thyroid disorders. Among patients with thyroid changes within euthyroid range 11 were (50.0%) patients had family history of thyroid disorders and 75 (44.4%) patients had no family history thyroid disorders. out of 2 patients with thyroid changes within sub-clinical range only 1 (4.5%) of the patients in our study had family history of thyroid disorders and 1 (0.6%) did not had any family history of thyroid disorders.

DISCUSSION

In our study, mean age was 35.3±13.56 yrs and majority of our patients 81 (42.4%) were aged 18-29 years, Similar age distribution was observed by Rajiv *et al*.[23] and Gitlin *et al*.[24]In our study, out of 191 patients, males constituted 106 (55.5%) while as 85 (44.5%) were females, Our results were similar to the study conducted by Rajiv *et al*.[23] in which males were 50.4% and females were 49.3%.

In our study there were 38 (19.9%) patients who had family history of psychiatric illness (panic disorder, generalized anxiety disorder, phobia) while as 153 (80.1%) were not having any family history of psychiatric illness. There were only 22 (11.5%) patients in our study who had family history of thyroid disorder while as 169 (88.5%) were not having any family history of thyroid disorder. In a study by Thapa *et al*.[25] majority of the subjects i.e. 93.3% (56) had no family history of thyroid disorders and in remaining 6.7% (4) of the cases, there was a positive family history of hypothyroidism. About 83.3% (50) did not have family history of mental disorder.In our study the mean pre-treatment HAM-D score was 13.34±3.08 (P<0.001) and mean HAM-D score after treatment with escitalopram 10 mg after 6 weeks was 11.24±2.74 (p<0.001) and after 12 weeks was 9.96±2.33 (p<0.001), which was statistically significant. Escitalopram 10 mg/day is optimum dose for treatment of moderate MDD while escitalopram 20 mg/day is an effective dose in patients with moderate to severe depression.[26]

Decrease in HAM-D score reflects improvement in symptoms with medication (escitalopram). Gitlin *et al*. in their study also observed the mean HAM-D score before treatment was 20.7 (SD 1, range 14–31) and after treatment, the mean HAM-D score was 7.8 (SD 1.4, range 0-18). Zhou *et al*. in their study revealed that the 8 week escitalopram treatment decreased the HAMD scores.[27]

In our study the mean pre-treatment TSH was 3.45±1.526 and after 6 weeks treatment with escitalopram the mean TSH was 4.55±1.697 (P<0.001) which was statistically significant and after 12 weeks it was 4.53±1.596 (P<0.791). So in our study

there was increase in TSH after 6 weeks of treatment. Salih *et al*.[28] also observed an increase in TSH values after treatment with sertraline. Hoflich *et al*.[29] also reported in their study an increase in TSH values with fluvoxamine. ***Gitlin et al.[24] in their study***, observed TSH (mU/L) before treatment 1.23 ±0.17 and after treatment 1.51 ±0.29, P<0.14, so there was a slight increase in TSH levels. However, some other studies observed no changes in TSH values after the treatment with SSRI's.[30] In our study mean pre-treatment T3 in patients was 1.05±0.399 (<0.005) and after 6 weeks treatment with escitalopram was 1.07± 0.419 (p<0.038), which was statistically significant and after 12 weeks was 1.07±0.404 (P<0.791). Shelton *et al*.[31] found no significant changes in TSH or total T4 with fluoxetine treatment but found an association between the decline in T3 levels and response to fluoxetine. Reduced or unchanged levels of serum tri-iodothyronine (T3) have been reported in patients treated with antidepressants. In our study the mean pre-treatment T4 in patients was 5.79±1.438 (p<0.861) and after 6 weeks treatment with escitalopram was 5.8±1.466 (p<0.293) which was not statistically significant and after 12 weeks was 5.74±1.509 (P<0.300). Slight increase in T4 with treatment after 6 weeks was observed with slight decrease in T4 values after 12 weeks. Gitlin *et al*.[24] in their study observed that there was a slight decrease in T4 after treatment. These differences were statistically significant. In their study T3 before and after treatment was 1.58 ±0.10 and 1.41 ±0.07 (P< 0.05) T4 before and after treatment was 95.88 ±7.34 and 78.50 ±5.28 (P<0.02) and Free T4 before and after treatment was 19.18 ±0.90, 16.99 ±0.77 (P<0.09). However, unaltered T4 level is also reported.[32]

This can be apprehensible when considering the mechanisms of action of escitalopram on monoaminergic neurotransmitters that may influence the secretion of thyroid hormones. The relationships between HPT axis and monoaminergic neurotransmitters have been investigated by many studies [33] suggested that the alterations in the HPT axis in depression might be associated with the deficiency in serotonin and/or noradrenalin levels. Given the relationship between serotonergic activity and HPT axis, the effects of serotonergic activity on the central regulation of TRH secretion is believed to be predominantly inhibitory.[34] It has been hypothesized that reduced serotonergic input could increase TRH secretion which may lead to the downregulation of pituitary TRH receptors in euthyroid depressed patients.[35]

In our study the significant change was seen in the TSH levels as compared to T3 and T4 levels. one group comprising of 104 (54.5%) patients showed no or negligible change (<0.1 uIU/ml) in their thyroid stimulating hormone levels after 6 and 12 weeks, though minor change was seen in 1 patient after 12 week follow up.

Another group comprising of 29 (15.2%) patients had changes in thyroid stimulating hormones within sub-clinical range (6.50-10 uIU/ml) after 6 weeks treatment with escitalopram and after 12 weeks follow up they showed levels in euthyroid range after changing their treatment except in 2 (1.0%) patients which remained in sub clinical range.

Third group comprising of 58 (30.4%) patients which were in euthyroid range (0.1-6.50 uIU/ml) after 6 weeks, showed same levels after 12 weeks follow up. Due to the decreased TSH levels in patients from other two groups 28 patients had change in thyroid levels within euthyroid range after 12 weeks follow up which showed that 86 (45.0%) patients remained in euthyroid range after 12 weeks follow up.

Those patients who had no or negligible change in thyroid hormone within euthyroid range were continued on medication (escitalopram) and these patients were responding to treatment as seen by decreased HAM-D score. ***Patients who had change in their thyroid hormones within subclinical range and had no decrease in their symptoms were substituted with other antidepressant venlafaxine which has no*** significant alterations in any thyroid indices.[28] After 12 weeks patients who were substituted with venlafaxine had improvement in symptoms and TSH levels decreased within euthyroid range.
In our study, after 6 and 12 weeks follow up, no or negligible change in thyroid hormone levels in relation to gender, age and with family history of psychiatric or thyroid disease was observed.

A number of reports suggest that treatment with antidepressant drugs leads to changes in thyroid function tests: either decreased peripheral thyroid hormone levels and/or increased TSH levels.[36] However, these results have not always been confirmed,[37] owing in part to methodological limitations, eg, small sample sizes, variable definitions of depression, hospitalization status, and technical factors, such as differences in the sensitivity of the assays used inthe measurement of thyroid hormones and TSH. Furthermore, it remains unclear whether changes in thyroid function are a direct effect of an antidepressant on the thyroid axis or a correlate of clinical improvement. Studies suggest that chronic antidepressant treatment decreases thyroid function.[38] However, there are studies which support the notion that tricyclic antidepressants have no consistent effect on TSH secretion.[39]

Most studies have shown that antidepressant treatment with SSRIs does not induce significant changes in TSH levels in depressed patients. However it has been reported that response to tricyclic antidepressants is associated with (i) higher pre-treatment T4 levels; and (ii) decreased measures (within the normal range) of T4 and free thyroxine (FT4) without changes in triiodothyronine (T3) or TSH levels.[40]Thus, although this is not supported by all studies, changes in thyroid function appear to be related to clinical recovery rather than to a direct effect of the antidepressant drug.

This is further supported by the fact that normalization of the TSH test is related to clinical recovery, while, irrespective of outcome, TSH values are not significantly changed by 6 weeks of treatment with escitalopram or venlafaxine,

SUMMARY AND CONCLUSION

Patients with major depression entering a treatment with escitalopram were assessed with the Structured Clinical Interview for DSM-5 and were rated on the Hamilton depression rating scale (HAM-D). Blood samples were taken for TSH, thyroxine (T4) and triiodothyronine (T3) measurement. Patients were then assigned to receive escitalopram for 6 weeks, After 6 weeks the thyroid hormone assessment was repeated and HAM-D was again applied. Mean concentrations of TSH, were slightly raised which were statistically significant, T3 and T4 were within reference ranges. Patients who showed no or minimum clinical response were administered increased dose of escitalopram and patients in whom TSH showed a subclinical response were treated with venlafaxine and after 12 weeks, TSH decreased with improvement in HAM-D score.

Following conclusions can be drawn from the data analysis

Majority of the participants were males, predominantly belonging to age group of 18-29 years, mostly having education up to middle school, working in semi-skilled or unskilled group and married.Clinical profile revealed that most of the patients had mild to moderate form of depression, a few also reported severe form of depression. Some of them had given family history of thyroid disorder and psychiatric illness. The Hamilton Depression Rating Scale-(HAM-D) analysis pointed towards presence of depression with mean score of 13.34 before start of treatment and 11.24 and 9.96 respectively after6 and 12 weeks of treatment.Most of the patients had no or negligible change in thyroid indices, some of them had changes within euthyroid range and some of them had changes within sub-clinical range, which were statistically significant. When the demographic factors were correlated with thyroid profile, the factors of age educational level, gender and family history of psychiatric and family history of thyroid disorder did not have any significant correlation. When the HAMD scores were compared across the treatment with escitalopram 10mg, most of the patients had lower scores.

Treatment of patients with escitalopram decreases HAM-D score, which reflects improvement in symptoms with medication. Significant increase in TSH values has been seen in patients after 6 weeks, while no significant change was observed after 12 weeks.

Escitalopram was not associated with clinically significant changes in thyroid hormone levels in euthyroid patients suffering from depression. However, results suggest that patients with normal thyroid function, who were treated with escitalopram, are susceptible to minor insignificant changes which also demonstrate the safety of administering escitalopram in euthyroid patients with depression.Although, the patients on treatment with escitalopram do not need strict monitoring of thyroid hormone levels. However, regular and periodic assessments of thyroid function should be carried out in patients with depression.

Implications

- ✓ Careful diagnosis of depression can help in early starting of treatment so that it can greatly decrease morbidity in patients.
- ✓ Early intervention for psychiatric and thyroid symptoms in depressive patients can help them to comply with on-going treatment in a better way and thus enhance the treatment outcome.

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