



The Effect of Escitalopram on Thyroid Function in Patients with Depression: An experience from Government Medical College Srinagar and Associated Hospitals

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ABSTRACT

Background: All thyroid states are associated with psychiatric manifestation, be it hypothyroid, hyperthyroid or euthyroid state. Depression is more severe in hypothyroidism. **Aims and objectives:** The study was conducted to evaluate the effect of adequate antidepressant dose of escitalopram on thyroid function in patients with depression of euthyroid state over a period of six weeks and the relationship between thyroid function and depression. **Material and methods:** The study was conducted at Government Medical College Srinagar and associated hospitals from May 2013 to April 2016. The study sample comprised of 191 patients diagnosed with first episode depression. The evaluation of patients was done by using pro-forma to gather information on parameters pertaining to mental health/illness also physical indices. DSM-5 diagnostic criteria have been used for diagnosing the patients having depression. Diagnosis was confirmed by the consultant in the department. Hamilton Depression Rating scale (HAM-D) has been used for assessing the severity of depression. Baseline thyroid function test was performed in these patients and these patients were given approved/adequate dose of escitalopram. **Results:** The mean age was 35.3 years and males were 55.5%. Only 19.9% have family history with psychiatric illness and 11.5% have family history of thyroid disorder. HAMD score before treatment was 13.34 ± 3.080 ($p < 0.001$) and after first follow up 11.24 ± 2.742 ($p < 0.001$) and after second follow up was 9.96 ± 2.33 ($p < 0.001$) and TSH before treatment 3.45 ± 1.52 ($p < 0.001$) and after first follow up 4.55 ± 1.69 ($p < 0.001$), and after second follow up 4.53 ± 1.59 ($p = 0.791$). The thyroid changes in first and second follow up was negligible 54.5% and 53.9% and changes within thyroid range 30.4% and 45% and changes within subclinical range was 15.2% and 1% respectively. **Conclusion:** It is concluded that escitalopram was not associated with clinically significant changes in thyroid function in normal thyroid function patients with depression. However, results suggest that patients with normal thyroid function, who were treated with escitalopram, are more susceptible to minor changes.

Keywords: Depression, Escitalopram, Hypothyroidism

INTRODUCTION

Mental health survey indicated that 10-15% people in their lifetime experience major depression [1]. In India large sample survey reported an overall prevalence of 15.9% for depression [2]. In a study the prevalence of depression in Kashmir was reported approximately 55.72% [3]. All thyroid states are associated with psychiatric manifestation, be it hypothyroid, hyperthyroid or euthyroid state. Psychiatric manifestations ranging from mild affective disorders, emotional lability, anxiety disorders and even psychosis may be frequently associated with primary hyper and hypothyroidism [4-6]. Depression is more severe in hypothyroidism.

Patients with mild or sub threshold depression, treatment may entail psychological support, problem solving, exercise, informal counselling, or formal psychosocial interventions. For moderate 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 with multiple other medications/medical illnesses 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. Medications usually takes 4-6 weeks for improvement in clinical symptoms [7,8].

Aims and objectives

The study was conducted to determine:

- The effect of adequate antidepressant dose of Escitalopram on thyroid function in patients with depression of euthyroid state over a period of six weeks.
- The relationship between thyroid function and depression.

PATIENTS AND METHODS

The study was conducted at Government Medical College Srinagar and associated hospitals. Government Medical College Srinagar is a general hospital and has associated hospitals including psychiatry hospital which runs out-patient services whole week and has facility for in-patients. This hospital is located at the centre of city. The study sample comprised of 191 patients diagnosed with first episode depression (Major depressive disorder). The evaluation of patients attending OPD was done by using pro-forma which seeks to gather information on parameters pertaining to mental health/illness also physical indices viz, namely general appearance, body weight, height, pulse, blood pressure, and baseline investigation which includes ECG, chest X-Ray, CBC, blood sugar, and kidney function tests.

A general physical examination was done to rule out any co-morbid medical condition. DSM-5 diagnostic criteria have been used for diagnosing the patients having depression. 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, when appropriate, by dimensional measures that cross diagnostic boundaries, and a brief digest of information about the diagnosis, risk factors, associated features, research advances, and various expressions of the disorder. Diagnosis was confirmed by the consultant in the department. 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 [9,10].

Baseline thyroid function test was performed in these patients and these patients were given approved/adequate dose of escitalopram. Informed consent of the patients was obtained. Patients were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). TFT were performed on all 191 inpatients.

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 analysed by ultrasensitive sandwich chemiluminescence immunoassay. Normal ranges were defined as 0.50-6.50 IU/mL for serum TSH, 0.70-2.50 ng/mL for T3, and 4-13 µg/dL for T4. Then, after 6 and 12 weeks thyroid function test and HAM-D scale was repeated.

Statistical analyses

Statistical Software SPSS (Version 20.0) and Microsoft Excel were used to carry out the statistical analysis of data. Continuous variables were summarized as means and standard deviations and categorical variables were expressed as percentages. Paired t-test was employed for intra group analysis of parametric data. Chi-square test or Fisher's exact test, whichever appropriate, was used for comparison of categorical variables. Graphically the data was presented by bar and line diagrams. A P-value of less than 0.05 was considered statistically significant.

Inclusion and exclusion criteria

The patients above 18 years of age and patients with depression (MDD) without psychotic features were included in the study.

The following patients were excluded from the study:

- Patients who don't give written informed consent.
- Depression with psychotic features.
- Depression in pregnancy or lactation.
- Any patient with suicidal attempts.
- Bipolar and related disorders.
- Family history of Bipolar and related disorders.

- Patients less than 18 years of age.
- Current or recent treatment with an antidepressant.
- History of thyroid disease or current treatment with thyroid hormones.
- History of treatment with lithium in past.
- Any co-morbid general medical conditions.
- History of substance abuse or dependence.

OBSERVATIONS AND RESULTS

A total of 191 patients were included in this prospective study. Table 1 shows demographic distribution of studied patients, with mean age of 35.3 years (Mean \pm SD=35.3 \pm 13.56). Table 2 shows family history of psychiatric illness and thyroid disorder in studied patients. Tables 3, 4, 5 and 6 indicate HAMD, mean TSH, mean T3, mean T4 in patients before and after treatment respectively. Table 7 exhibits thyroid changes in patients at 1st and second follow up. Tables 8 and 9 show association of thyroid changes with gender and age in studied patients respectively. Association of thyroid changes with family history of psychiatric illness and thyroid disorder in studied patients is shown in Tables 10 and 11.

Table 1 Demographic distribution data of 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 \pm SD=35.3 \pm 13.56		
Gender		
Male	106	55.5%
Female	85	44.5%
Area		
Rural	101	52.9%
Urban	90	47.1%
Educational status		
Uneducated	98	51.3%
Primary (5th)	8	4.2%
Middle (8th)	16	8.4%
Matric	29	15.2%
Graduate	32	16.8%
Postgraduate	8	4.2%
Occupation		
Student	15	7.9%
Unemployed	97	50.8%
Employed	79	41.4%
Marital Status		
Married	104	54.5%
Unmarried	73	38.2%
Widow	7	3.7%
Divorcee	7	3.7%
Socio economic status		
Upper Class	15	7.9%
Middle Class	119	62.3%
Lower Class	57	29.8%

Table 2 Family history of psychiatric illness and thyroid disorder in studied patients

History		No. of Patients	Percentage
Family History of Psychiatric Illness	Yes	38	19.9
	No	153	80.1
Family History of Thyroid Disorder	Yes	22	11.5
	No	169	88.5

Table 3 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	3.08	I vs II	2.1	<0.001*
1st Follow Up (II)	11.24	2.742	I vs III	3.38	<0.001*
Second Follow Up (III)	9.96	2.335	II vs III	1.28	<0.001*

*Statistically Significant Difference (p<0.05); \$p-value by Paired t-test

Table 4 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*
1st Follow Up (II)	4.55	1.697	I vs III	-1.08	<0.001*
Second Follow Up (III)	4.53	1.596	II vs III	0.02	0.791

*Statistically Significant Difference (p<0.05); \$p-value by Paired t-test

Table 5 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*
1st Follow Up (II)	1.07	0.419	I vs III	-0.02	0.038*
Second Follow Up (III)	1.07	0.404	II vs III	0.00	0.791

*Statistically Significant Difference (p<0.05); \$p-value by Paired t-test

Table 6 Shows 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
1st Follow Up (II)	5.8	1.466	I vs III	0.05	0.293
Second Follow Up (III)	5.74	1.509	II vs III	0.06	0.3

Table 7 Thyroid changes in patients at 1st and second follow up

Thyroid Changes	1st Follow Up		Second Follow Up	
	No. of Patients	Percentage	No. of Patients	Percentage
Negligible or No change	104	54.5%	103	53.9%
Change within Euthyroid range	58	30.4%	86	45.0%
Change Within Sub-clinical range	29	15.2%	2	1.0%

Table 8 Association of thyroid changes with gender in studied patients

Thyroid changes		Male		Female		P-value
		No.	percentage	No.	percentage	
1st Follow Up	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%	
Second Follow Up	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	0.00%	

Table 9 Association of thyroid changes with age in studied patients

Thyroid changes		Age (years)					P-value
		18-29	30-39	40-49	50-59	≥ 60	
1st Follow Up	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%)	
Second Follow Up	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%)	

Table 10 Association of thyroid changes with family history of psychiatric illness in studied patients

Thyroid changes		Psychiatric Illness Present		Psychiatric Illness Absent		P-value
		No.	percentage	No.	percentage	
1st Follow Up	Negligible or No change	24	63.2%	80	52.3%	0.08
	Change within Euthyroid range	6	15.8%	52	34.0%	
	Change Within Sub-clinical range	8	21.1%	21	13.7%	
Second Follow Up	Negligible or No change	24	63.2%	79	51.6%	0.377
	Change within Euthyroid range	14	36.8%	72	47.1%	
	Change Within Sub-clinical range	0	0.00%	2	1.3%	

Table 11 Association of thyroid changes with family history of thyroid disorder in studied patients

Thyroid changes		Thyroid Disorder Present		Thyroid Disorder Absent		P-value
		No.	percentage	No.	percentage	
1st Follow Up	Negligible or No change	10	45.5%	94	55.6%	0.068
	Change within Euthyroid range	5	22.7%	53	31.4%	
	Change Within Sub-clinical range	7	31.8%	22	13.0%	
Second Follow Up	Negligible or No change	10	45.5%	93	55.0%	0.185
	Change within Euthyroid range	11	50.0%	75	44.4%	
	Change Within Sub-clinical range	1	4.5%	1	0.6%	

DISCUSSION

Depression can deteriorate the quality of life of a person and can lead to socio-occupational impairment may increase the risk of other medical illnesses [11,12]. Depression has multiple causes and many patients with physical illnesses e.g. endocrine disorders present with depression [13,14]. Among endocrine disorders thyroid disorders are major cause of psychiatric disorders, the prevalence of mood and anxiety disorders is higher [15]. Subclinical hypothyroidism is a condition when patients with normal peripheral thyroid hormones with or without physical features of hypothyroidism

but may have psychological and emotional impairment [16,17]. In subclinical hypothyroidism patients may become vulnerable to depression and patients respond to treatment and the outcome for the treatment is very poor [18].

In our study, mean age was 35.3 ± 13.56 years and Majority of our patients 81 (42.4%) were aged between 18-29 years and 42 (22.0%) were 30-39 years of age and 6 (2.1%) patients were >60 years. Age distribution was close relation to the study conducted by Rajiv Radhakrishnan, et al., where the mean age of the study subjects was 37.46 ± 13.56 yr. The mean age in another study is in close relation with our study conducted by Gitlin, et al. with a mean age of 37.6 (SD=9, range 27-58) years. In our study, out of a total of 191 patients, males constituted 106 (55.5%) while as females 85 (44.5%). The results were close to the study conducted by Rajiv Radhakrishnan, et al. Males were 173 (50.4%) and female=169 (49.3%) [19]. The results were contradicted to the study conducted by Noor, et al. in their study, out of 100 patients included in the study, 43 were males and 57 were females [20]. In a study conducted by Shoib, et al., males constituted 21.4% i.e., 115 of the total patient size and females Constituted 78.6% i.e., 422 of the total patient size [21].

In our study, majority of patients i.e., 101 (52.9%) patients who belongs to rural areas and 90 (47.1%) were from urban areas. Shoib, et al. in their study patients who belong to urban 189 (35.19%) and rural 348 (64.80%) which was close to our study. Another study conducted by Maqbool, et al., where majority of patients belong to rural areas was 57.14% and patients who belong to urban areas were urban 42.8%. [22].

In our study, out of a total of 191 patients, 98 (51.3%) were uneducated, 32 (16.8%) were graduates and 29 (15.2%) were matriculates, 16 (8.4%) were middle pass, 8 (4.2%) patients were primary pass and 8 (4.2%) postgraduates. The results were similar to the study conducted by Maqbool, et al., in their study Illiterate 205 (37.7%) primary 79 (14.7%) secondary 106 (19.7%) matric 73 (13.6%) graduate 66 (13.3%) postgraduate 8 (1.5%). Gitlin, et al., in their study, four subjects had a high school education or less, 10 were college graduates and 5 had graduate school experience. In our study, as far as occupation is concerned, 15 (7.9%) were students, 97 (50.8%) were unemployed and 79 (41.4%) were employed similar results found by study conducted by Shoib, et al., in their study household 323 (60.1%) unskilled 112 (20.9%) semiskilled 51 (9.5%) skilled 46 (8.6%) professional 5 (0.9%). In our study, the marital status of the majority of patients were i.e., 104 (54.5%) married (men and women) and 73 (38.2%) were unmarried, 7 (3.7%) were widow and 7 (3.7%) were divorcee. The study conducted by Shoib, et al., 66.7% i.e., 358 patients was married, 26.3% i.e., 141 patients were unmarried, 4.1% i.e., 22 were widowed and 3% i.e., 16 were separated.

In our study as per socio-economic status is concerned, majority of patients i.e., 119 (62.3%) patients were belonging to middle socio-economic class, 57 (29.8%) patients belong to lower socio-economic class and 15 (7.9%) patients were from upper socio-economic class. The study conducted by Shoib, et al., in their study there were lower socio-economic status in 92 (17.13%) upper lower 258 (48.04%) middle 143 (26.62%) upper middle 35 (6.51%) and upper 9 (1.67%). In our study there were only 38 (19.9%) who had family history of psychiatric illness while as 153 (80.1%) were not having any significant family history of psychiatric illnesses and also in our study and 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 significant family history of thyroid disorder. In a study by Thapa, et al., 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. Among the detected cases i.e., 16.7% have mental disorders which includes anxiety disorder unspecified and bipolar affective disorder were found both in 5% (3) of the cases while depression and migraine headache were found both in 3.3% (2) of the cases [23]. In our study the HAMD score pre-treatment was 13.34 ± 3.08 ($p < 0.001$) and after treatment of Escitalopram in first follow up (6 weeks) was 11.24 ± 2.74 ($p < 0.001$) and in second follow up (12 weeks) was 9.96 ± 2.33 ($p < 0.001$), which was statistically significant, so there was significant difference in HAM-D score before and after treatment. Michael Gitlin, et al., in their study 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). Zhenhe Zhou, Suxia Cao, et al., in their study the results revealed that the 8-week escitalopram treatment decreased the HAMD scores [24]. In our study the mean TSH pre-treatment (I) of escitalopram was 3.45 ± 1.526 ($p < 0.001$) and after treatment of escitalopram in first follow up (6 weeks) was 4.55 ± 1.697 ($p < 0.001$) which was statistically significant and in second follow up (12 weeks) was 4.53 ± 1.596 ($p < 0.791$) and was statistically insignificant, so in our study there was increase in TSH after treatment after 1st follow up. Gitlin, et al., in their study, TSH (mU/L) before treatment was 1.23 ± 0.17 and after treatment was 1.51 ± 0.29 , $p < 0.14$, so there was a slight increase in TSH.

In our study, mean T3 in patient pre-treatment with escitalopram was 1.05 ± 0.399 ($p < 0.005$) and after treatment of escitalopram in first follow up (6 weeks) was 1.07 ± 0.419 ($p < 0.038$), which was statistically significant and after second follow up (12 weeks) was 1.07 ± 0.404 ($p < 0.791$), which was statistically insignificant. There is slight increase in T3 after treatment. In our study mean T4 in patient pre-treatment was 5.79 ± 1.438 ($p < 0.861$) and after treatment of escitalopram in first follow up (6 weeks) was 5.8 ± 1.466 ($p < 0.293$) which was statistically significant and after second follow up (12 weeks) was 5.74 ± 1.509 ($p < 0.300$), which was statistically insignificant, so there is slight increase in T4 after treatment. Our study was contradicted to the study conducted by Gitlin, et al., in their study, there was a slight decrease in T4, T3 and free T4 after treatment. These differences were statistically significant for T4 and T3, but not for free T4 or TSH. In their study T3 (nmol/L) before and after treatment was 1.58 ± 0.10 and 1.41 ± 0.07 ($p < 0.05$). T4 (nmol/L) before and after treatment was 95.88 ± 7.34 and 78.50 ± 5.28 ($p < 0.02$) and Free T4 (pmol/L) before and after treatment was 19.18 ± 0.90 and 16.99 ± 0.77 ($p < 0.09$). In our study, there was negligible or no change in thyroid status of 104 (54.5%) patients, on second visit 103 (53.9%) patients observed no or negligible change in their thyroid status. 58 (30.4%) patients had thyroid changes within euthyroid range on their first follow up, while as 86 (45.0%) patients observed thyroid changes within euthyroid range on their second follow up. 29 (15.2%) patients had thyroid changes within sub-clinical range on their first follow up, while as 2 (1.0%) patients observed thyroid changes within sub-clinical range on their second follow up.

In our study, on first follow up there was no or negligible change in thyroid in 51 (48.1%) male patients and 53 (62.4%) female patients, 36 (34.0%) male patients and 22 (25.9%) female patients observed thyroid changes within euthyroid range and 19 (17.9%) males and 10 (11.8%) females had thyroid changes within sub-clinical range. So, there was insignificant thyroid changes in gender ($p = 0.065$) after first follow up. On second follow up there was no or negligible change in thyroid in 50 (47.2%) male patients and 53 (62.4%) female patients, 54 (50.9%) male patients and 32 (37.6%) female patients observed change within euthyroid range and 2 (1.9%) males and 0 (0.0%) females had changes within sub-clinical range. So there was insignificant thyroid change both male and female patients after 12 weeks $p = 0.139$. Osama, et al., in their study, found that the mean baseline TSH was $1.5 (\pm 0.7)$ mIU/L, FT4 was $1.1 (\pm 1.2)$ ng/dL, FT3 was $3.0 (\pm 1.5)$ ng/mL, and TT3 was $120.2 (\pm 20.9)$ ng/dL. And mean TSH in males was $1.27 (\pm 0.51)$ mIU/L, FT4 was $2.78 (\pm 1.23)$ ng/dL, FT3 was $2.86 (\pm 1.05)$ ng/mL, and TT3 was $120.22 (\pm 10.29)$ ng/dL. And mean TSH in females was $1.5 (\pm 0.7)$ mIU/L, FT4 was $3.65 (\pm 1.03)$ ng/dL, FT3 was $3.02 (\pm 1.79)$ ng/mL, and TT3 was $120.21 (\pm 26.0)$ ng/dL, and P value for TSH was $p = 0.12$ and FT4 $p = 0.08$, FT3 was 0.81, and TT3, $p = 0.99$ respectively. No significant gender differences were observed in any of the baseline thyroid indices [25,26].

In our study, on first follow up there was no or negligible change in thyroid 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%) 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 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. $p = 0.761$ which is statistically insignificant. So, there is slight change in thyroid function in different age groups which is statistically insignificant.

On second follow up there was no or negligible change in thyroid 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%) 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. Only 1 (1.2%) patient 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. $p = 0.852$ which is statistically insignificant, so thyroid changes are insignificant after treatment with escitalopram in different age groups for depression. In our study, on first follow up there was no or negligible change in thyroid status in 24 (63.2%) patients with significant family history of psychiatric illness, 80 (52.3%) patients with no family history of psychiatric illness. There were 6 (15.8%) patients with family history of psychiatric illnesses and 52 (34.0%) patients with no family history of psychiatric illness with thyroid changes within euthyroid range. Only 8 (21.1%) patients in our study had psychiatric illnesses and 21 (13.7%) did not have any family history of psychiatric illnesses with thyroid changes within sub-clinical range. $p = 0.08$, these changes were slight and were statistically insignificant.

There were no significant thyroid changes even in patients with family history of psychiatric illness after receiving treatment for six weeks.

On second follow up there was no or negligible change in thyroid status in 24 (63.2%) patients with significant family history of psychiatric illness, 79 (51.6%) patients with no significant 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 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 of psychiatric illnesses with thyroid changes within sub-clinical range. $p=0.377$, which is statistically insignificant, thus insignificant increase in thyroid changes in patients in patients with family history of depression than those who have no family history.

In our study, the thyroid changes in patients with family history of thyroid disorders was no or negligible in 10 (45.5%) and change within euthyroid range was in 5 (22.7%) patients and change within sub-clinical range was in 7 (31.8%) patients and thyroid changes in patients without family history of thyroid disorders was in no or negligible in 94 (55.6) and change within euthyroid range was in 53 (31.4) patients and change within sub-clinical range was in 22 (13.0) patients in the first follow up after treatment with escitalopram, $p=0.068$. Thus, there was slight increase thyroid changes in patients without family history of thyroid disorders than those with family history of thyroid disorders, but the difference was statistically insignificant.

On second follow i.e., after 12 weeks up the thyroid changes in patients with family history of thyroid disorders was no or negligible in 10 (45.5%) and change within Euthyroid range was in 11 (50) patients and change within sub-clinical range was in 1 (4.5) patients and thyroid changes in patients without family history of thyroid disorders was in no or negligible in 93 (55) and change within Euthyroid range was in 75 (44) patients and change within sub-clinical range was in 1 (0.6) patients in the 2nd follow up after treatment with escitalopram, $p=0.185$. Thus, there was slight increase thyroid changes in patients without family history of thyroid disorders than those with family history of thyroid disorders, but the difference was statistically insignificant.

CONCLUSION

It is concluded that escitalopram was not associated with clinically significant changes in thyroid function in normal thyroid function patients with depression. However, results suggest that patients with normal thyroid function, who was treated with escitalopram, are more susceptible to minor changes. To the best of our knowledge, this is the first study to demonstrate the safety of administering escitalopram in euthyroid patients with depression.

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