Babaeva A.R. et al /J. Pharm. Sci. & Res. Vol. 10(10), 2018, 2424-2427

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Thyroid Hormones Imbalance in Patients with Functional Dyspepsia

Babaeva A.R.[1], Osadchuk M.A.[2], Vidiker R.V.[1], Reutova E.Yu.[1], Solodenkova K.S.[1] , Korzhenkov N.P.[2], Osadchuk M.M.[2] and Trushin M.V.[3]

[1.] Volgograd State Medical University of the Ministry of Public Health of the Russian Federation, Volgograd, Russia
[2.]The Federal State Autonomous Education Institution of Higher Training the First Sechenov Moscow State Medical University under Ministry of Health of the Russian Federation (Sechenovskiy University), Moscow, Russia
[3.] Kazan Federal University, Kazan, Russia

Abstract

The article presents the results of our research into the analysis of the thyroid dysfunction role in the pathogenesis and clinical manifestations of functional dyspepsia (FD). It was revealed that 31% of patients with FD had a T3 and/or FT4 level drop at normal or moderately reduced levels of TSH in the blood, which corresponds to the notion of euthyroid pathology syndrome. These changes in the thyroid hormones level were more often found in the postprandial FD case than in the one with epigastric pain syndrome. Besides this, FD patients had a rise in the average level of antithyroid antibodies compared to the healthy controls. A direct relationship was discovered between the degree of FD clinical signs and thyroid system functional disorders. The results obtained allow us to make a conclusion concerning the significance of thyroid hormones imbalance in FD pathogenesis and clinical picture

Key words: functional dyspepsia, sick euthyroid syndrome, thyroid gland hormones

1.INTRODUCTION

Functional gastrointestinal disorders (FGIDs) are among the main causes of digestive system pathology. In some countries including Russia functional dyspepsia (FD) is detected in 30-40% of the population (4,5,10). The high medical and social significance of FGIDs is determined by the young age of patients having severe dyspeptic and/or abdominal pain syndrome, which leads to lower quality of life, disability, professional decline and unfavourable psychological and social consequences. Difficulties in verifying the diagnosis and abundance of therapeutic regimens for FD and other FGIDs are largely due to an insufficiently clear picture of their pathogenesis (6). Modern FGIDs consensus considers FD as a complex set of interrelated mental, motor, hormonal and neurohumoral disorders in genetically predisposed individuals (1, 8, 12). The role of the functional state of individual hormonal systems (e.g. the diffuse endocrine system) in the formation of FGIDs has been repeatedly demonstrated in experimental and clinical studies (4,7). Nevertheless, there are neurohormonal systems whose participation in the development of FGIDs requires further study. This fully applies to the thyroid system, which is important for the regulation of the secretory, motor and evacuation activity of the gastrointestinal tract (GIT), as well as in the processes of cell proliferation, differentiation and apoptosis(10). Hyper- and hypofunction of the thyroid gland are known to be characterized by gastrointestinal pathology in more than 30% of cases (11). Alongside with this there are various somatic diseases including organic pathology of GIT that can lead to dysfunction of the thyroid gland (TG) without a proven pathology of the pituitary-thyroid system (6,13). In this regard the problem of thyroid dysfunction in a number of somatic diseases has been of particular interest in recent decades. A number of terms have been proposed for this condition: “nonthyroidal illness syndrome” ,”euthyroidal pathological syndrome”, “sick euthyroid syndrome”,”thyroidal pseudo-dysfunction syndrome”, ”euthyroid pathology syndrome” (1,8,11). Of particular interest is the study of thyroid imbalance in the FGIDs pathogenesis due to the fact that impaired motility and secretion of the digestive organs are often accompanied by different types of thyroid dysfunction caused by the presence of gastrointestinal effects in thyroid hormones (2,3). All the above emphasizes the relevance of the problem of the relationship between the thyroid system pathology and FGIDs taking into account the assessment of thyroid imbalance impact on the GIT neurohumoral regulation. Solving these issues would expand the current understanding of the TG functional activity role in the somatic syndromes formation, evaluate the thyroid pathology contribution to the FGIDs pathogenesis and clinical signs as well as outline approaches to the rational correction of thyroid dysfunction in FD patients.

The study aimed at assessing thyroid imbalance in FD pathogenesis as well as analyzing the relationship between identified disorders and the main clinical FD manifestations .

2. MATERIALS AND METHODS

117 patients with FD (68 females and 49 males) aged from 18 to 45 meeting Roman criteria for the FD diagnosis were included in the study. The comparison group comprised 20 patients (12 females and 8 males) aged from 21 to 47 with verified peptic ulcer (PU).The control group was represented by 45 age-comparable apparently healthy subjects (30 females and 15 males). All the FD patients were divided into subgroups according to the predominant clinical syndrome: either that of epigastric pain, or postprandial distress. 54(46.15%) subjects were diagnosed with functional dyspepsia epigastric pain syndrome (FD-EPS) and 63(53.85%) subjects with functional dyspepsia postprandial distress syndrome (FD-PDS).All the patients were examined under a compulsory programme of instrumental studies (FGDS, US of abdominal and pelvic organs , rectal endoscopy and irrigography). They also went through the diagnostic laboratory test minimum : general uranalysis and blood count including total protein, protein fractions of blood, blood glucose, electrolytes, biochemical blood assay (bilirubin, transaminase, urea, creatinine). The thyroid status study included TG palpation with an increase degree estimate according to the WHO classification, TG US (volume and structure), TG function evaluation of T3, FT4, TSH, antithyroid antibodies level (anti-TG i.e. ATG - to the thyroglobulin and anti-TPO i.e. ATP - to the thyroid perioxidase). The concentration of T3, FT4, TSH, anti-TG(ATG) and anti-TPO(ATP) in the blood serum was determined by the solid –phase method ELISA using standard test kits of CJSC Alkor Bio. The statistical processing of the research results was carried out using the methods of variation statistics and correlation analysis. The use of parametric methods of statistical analysis is due to the normal distribution of indicators in the samples under study according to the Shapiro-Wilk criterion and the Gauss curve.

3. RESULTS AND DISCUSSION

We found by means of the sonographic research method that the average TG volume in the patients with FD as well as in the patients with PU did not exceed that of the healthy individuals according to the US data. No substantial

differences in the TG size were observed in the patients with FD and PU. We analyzed the frequency and form of organic thyreopathy based on the US data in the FD patients compared to the patients with organic GIT pathology. The analysis showed that TG structural shifts in the FD patients were represented by diffuse changes (9%),calcinations (12%), nodular (12.6%) and cystic (26%) formations. There were no statistically significant differences between the groups of FD and PU patients, although the above mentioned sonographic signs were definitely more frequent in the FD patients than in the healthy individuals. At the same time, the detection frequency of TG diffuse changes in the FD-PDS group was higher than in the FD-EBS one. For this reason in al l the FD patients the TSH values corresponded to the physiological limits for this indicator. A study of the pituitary –thyroid hormones system in the FD , PU patients and the control subjects revealed that in the FD group the average values of the hormones under study did not go beyond the reference values. There was no statistically significant difference between the same indicators in the group of healthy individuals and patients with PU (Table 1).

Content analysis of T3, FT4 and TSH in the FD patients` serum depending on the disease clinical variant showed that the T3, FT4 and TSH levels in the FD-PDS and FD-EBS groups had no notable differences with both the control group and PU patients. At the same time a comparison of the FD-PDS and FD-EBS groups revealed statistical differences of T3 and FT4 levels : more pronounced shifts (T3 drop and FT4 rise) occurred in the case of FD-PDS (Table 2).

Analysis of the detection frequency of thyroid imbalance in FD patients showed that the most common form of thyroid dysfunction was a moderate decrease in T3 found in 1/5 of the patients and only in 6.7% of the control group. An elevated serum concentration of FT4 was more often observed in the FD group than in the PU patients and healthy controls.

We analyzed the detection frequency of the changed levels of T3 and T4 in groups with different clinical FD types. Both of them were characterized by a more frequent reduction of T3 level , while in the group of patients with postprandial discomfort their number was higher (21.95%) than in the FD-EPS group (13.04%). At the same time , an increase in the serum FT4 was spotted more often with FD-PDS than with FD-EBS (14.63% and 8.7% respectively). It is not impossible that the concentration change of thyroid hormones in the serum of the patients with FD-PDS affects the motor and contractile activity of the stomach. It can manifest itself as tachy- and bradigastria , gastric accommodation disorders and even gastroparesis.

Table 1.Mean serum concentration analysis of T3, FT4 and TSH in patients with FD, PU and healthy controls, M±m

Group of patients		Concentration of T3, M±m, nmol/l	Concentration of FT4, M±m, pmol/l	Concentration of TSH, M±m, mcIU/ml
FD patients		1,41±0,15	14,17±3,46	1,52±0,8
	t1	0,43	0,24	0,31
	p1	>0,05	>0,05	>0,05
	t2	0,22	0,04	0,08
	p2	>0,05	>0,05	>0,05
PU patients		1,5±0,37	13,99±2,86	1,43±0,82
	t1	0,25	0,32	0,4
	p1	>0,05	>0,05	>0,05
Healthy controls		1,68±0,62	15,13±2,04	1,83±0,6

Note: p1 – significance of differences between the experimental groups and the healthy controls; p2 – significance of PU indicators` differences.

Table 2 Mean serum concentration analysis of T3 , FT4 and TSH in patients with FD-PDS, FD- EPS, PU and healthy controls , M±m

Group of patients		Concentration of T3, M±m, nmol/l	Concentration of FT4, M±m, pmol/l	Concentraion of TSH, M±m, mcIU/ml
FD-PDS patients		0,69±0,27	18,5±2,81	1,38±046
	t1	1,48	0,97	0,59
	p2	>0,05	>0,05	>0,05
	t2	1,76	1,12	0,05
	p2	>0,05	>0,05	>0,05
FD-EBS patients		2,13±0,52	9,84±2,35	1,66±0,37
	t1	0,56	1,7	0,24
	p2	>0,05	>0,05	>0,05
	t2	0,98	1,12	0,26
	p2	>0,05	>0,05	>0,05
	t3	2,48	2,37	0,47
	p3	<0,05	<0,05	>0,05
PU patients		1,5±0,37	13,99±2,86	1,43±0,82
	t1	0,25	0,32	0,4
	p1	>0,05	>0,05	>0,05
Healthy controls		1,68±0,62	15,13±2,04	1,83±0,6

Note: p1 – significance of differences between the experimental group and the healthy controls; p2 – significance of PU indicators` differences ; p3 – significance of FD-PDS indicators`differences.

Table 3Frequency of changes in the serum concentrations of T3, FT4, TSH in FD, PU patients and healthy controls , %

Changes in concentration		FD patients	PU patients	Healthy controls
T3	Decreased level	22,64%	20,00%	6,67%
T3	Increased level	5,98%	5,00%	4,44%
FT4	Decreased level	3,77%	2,67%	5,6%
FT4	Increased level	12,5%	5,60%	2,28%
TSH	Decreased level	-	25,00%	10%

We identified two groups of the FD patients based on the obtained laboratory data : the patients with a normal thyroid hormones level i.e. the so called group of euthyroid FD patients without the “sick euthyroid syndrome”(SES) and the patients with changes in at least one thyroid hormone i.e. with the presence of SES (“FD without SES” and “FD with SES 27” respectively). These patients with subclinical thyroid dysfunction had at least one hormonal change: T3 and/or FT4. Analysis of the pituitary-thyroid hormones levels in the FD-with-SES and FD-without-SES patients showed that although the FT4 and TSH concentration in the FD-with-SES patients was not statistically different from the similar indicators in the FD-without-SES , PU patients and the healthy controls , the average T3 level in the FD patients with thyroid pseudodysfunction was significantly lower than the one in the FD-without-SES patients (Table 4).

The multidirectional shifts in the content of thyroid hormones in FD patients confirmed the feasibility of studying the specific autoantibodies level that play an extremely important role in the productivity of thyroid hormones and the realization of their biological effects. In the FD group the mean ATP and ATG levels were substantially higher than those of the healthy controls. However, notable differences with the PU comparison group were only found in the ATG level (Table5).

Table 4 Mean serum concentration analysis of T3, FT4 and TSH in FD-without- SES, FD-with-SES patients, PU patients and healthy controls, M±m

Group of patients		Concentration of T3, M±m, nmol/l	Concentration of FT4, M±m, pmol/l	Concentration of TSH, M±m, mcIU/ml
FD-without-SES patients		2,35±0,32	13,24±1,57	1,31±0,26
	t1	0,97	0,74	0,79
	p1	>0,05	>0,05	>0,05
	t2	1,73	0,23	0,14
	p2	>0,05	>0,05	>0,05
FD-with-SES patients		1,07±0,18	11,6±2,68	1,28±0,24
	t1	0,95	1,05	0,85
	p1	>0,05	>0,05	>0,05
	t2	1,05	0,61	0,18
	p2	>0,05	>0,05	>0,05
	t3	3,56	0,53	0,08
	p3	<0,05	>0,05	>0,05
PU patients		1,5±0,37	13,99±2,86	1,43±0,82
	t1	0,25	0,32	0,4
	p1	>0,05	>0,05	>0,05
Healthy controls		1,68±0,62	15,13±2,04	1,83±0,6

Note: p1 – significance of differences with the healthy controls; p2 – significance of PU indicators` differences; p3 –significance of FD-without-SES indicators` differences.

Table 5 Mean serum concentration analysis of antithyroid antibodies in FD, PU patients and healthy controls, M±m, U/ml

Group of patients		Concentration of ATP,M±m, U/ml	Concentration of ATG, M±m, U/ml
FD patients		56,65±4,72	45,5±2,48
	t1	4,87	2,18
	p1	<0,05	<0,05
	t2	0,69	2,14
	p2	>0,05	<0,05
PU patients		52,07±4,64	54,02±3,12
	t1	4,32	3,76
	p1	<0,05	<0,05
Healthy controls		17,7±6,45	35,8±3,7

Note: p1 – significance of differences with the healthy controls; p2 – significance of PU indicators` differences.

Table 6. Mean serum concentration analysis of ATP and ATG in patients with FD-PDS, FD-EBS, PU and healthy controls , M±m, U/ml

Group of patients		Concentration of ATP, M±m, U/ml	Concentration of ATG, M±m, U/ml
FD-PDS patients		48,52±3,19	52,84±4,26
	t1	4,28	3,02
	p1	<0,05	<0,05
	t2	0,63	0,22
	p2	>0,05	>0,05
FD-EBS patients		64,78±4,36	38,16±3,1
	t1	6,04	0,49
	p1	<0,05	>0,05
	t2	2,0	3,6
	p2	<0,05	<0,05
	t3	3,01	2,79
	p3	<0,05	<0,05
PU patients		52,07±4,64	54,02±3,12
	t1	4,32	3,76
	p1	<0,05	<0,05
Healthy controls		17,7±6,45	35,8±3,7

Note: p1 –significance of differences with the healthy controls ; p2 –significance of PU indicators`differences; p3 –significance of FD-PDS indicators` differences .

Based on reference values we analyzed the frequency of positive samples in all clinical groups. In the FD patients an increased concentration of ATP and ATG was detected more often than in the healthy individuals (23.44% and 9.38% respectively), but it was slightly lower compared to the patients with organic GIT pathology (35.0% and 25.0% respectively). Analysis of the dependence of antithyroid antibodies level on clinical FD variants showed that the average ATP level in the FD-EBS patients was higher and the ATG level was slightly lower than in the FD-PDS group (Table 6).

Detection frequency analysis of increased ATP and ATG levels showed that in the FD-PDS group these antibodies were spotted with a frequency of no more than 10% for each indicator. As for the FD-EBS group, an elevated ATP level was detected several times more often than that of ATG (in 47.83% and 8.7% of cases, respectively). We conducted correlation analysis for a more complete assessment of the relationship between the level of thyroid hormones in the blood serum and the intensity of organ manifestations in FD and PU cases. An inverse correlation of moderate strength was found between the FD clinical manifestation and the blood serum T3 level (-0,3<r<-0,7). A direct correlation was identified between a moderate increase in the level of FT4 and the intensity of epigastralgia. In the study of the interdependence of the clinical variants` leading symptoms a moderately strong inverse correlation was discovered between the T3 level and the FD-PDS typical manifestations.

4. CONCLUSION

Structural changes in the absence of notable increase or decrease in the thyroid volume according to sonography were identified in 75.56% of the FD patients, which significantly exceeded the frequency of registration of organic thyreopathy in the control group. In addition, in the FD group thyroid dysfunction defined as “sick euthyroid syndrome”(SES) was found more often than in the healthy individuals. SES characterized by a decrease in T3 was discovered in 19% of the FD patients whereas a moderate increase in FT4 as a manifestation of SES occurred in 12.5% of the FD patients. It should be emphasized that the decrease in the T3 level and the increase in the FT4 fraction was more pronounced and more often observed with FD-PDS than with FD-EBS. At the same time both FD types were characterized by a more frequent drop in the serum T3 level than by its rise. The average concentration of ATP and ATG in the FD group was notably higher than in the healthy controls. A higher frequency of the elevated ATP content was typical for the FD-EPS variant. A moderate correlation was found between the FD organ manifestations` severity on the one hand and the T3 and FT4 level on the other. There was observed a very close relationship between the intensity of FD-PDS in the FD group and the level of T3 reduction. Analysis of the relationship between the level of thyroid hormones and the severity of the main clinical signs in the FD patients depending on the presence of SES showed that the features of thyroid dysfunction were combined with a more severe course of the disease.

Thus, the results obtained indicate the involvement of thyroid hormones in the pathogenesis of functional disorders .They also make it possible to discuss the thyroid disfunction role in the development and clinical manifestation of FD.

REFERENCES

1. Abramova NO, Pashkovskaya NV (2017) Modern ideas about the syndrome of euthyroid pathology in clinical practice. J Vrachebnoe Delo (Medicine) (1-2) : 31-38
2. Babaeva AR, Rodionova ON, Vidiker RV, Reutova EYu (2009)

Features of neurohumoral dysregulation ,cytokine and thyroid profiles in patients with functional gastrointestinal disorders. The Bulletin of St.Petersburg University 1(11) : 51-57

3. Babaeva AR, Rodionova ON, Reutova EYu , Galchenko OE (2010) Euthyroid pathology syndrome in patients with functional diseases of gastrointestinal tract. The Bulletin of Volgograd State Medical University 4(36) : 65-67
4. Butorova LI, Osadchuk MA (2015) Optimization of therapeutic pathology in functional dyspepsia syndrome. Doctor Ru. Gastroenterology 12(113) : 80-86
5. Ivashkin VT, Maev I V, Sheptulin AA and others (2017) Clinical recommendations of the Russian Gastroenterological Association for the diagnosis and treatment of functional dyspepsia . Ros Zhurn gastroenterol koloproktol 27(1) : 50-61
6. Osadchuk MA, Osadchuk MM (2015) Chiasm syndrome of functional dyspepsia ,gastroesophageal reflux disease and irritable bowel syndrome : therapy optimization. RMJ “Medical Review” (28) : 1690-1692
7. De Vries E M, Fliers E, Boelen A (2015) The molecular basis of the non-thyroidal illness syndrome. J Endocrinol. 225 (3) : 67–81
8. Drossman DA, Hasler WL, Rome IV (2016) Functional GI disorders: disorders of gut-brain interaction. Gastroenterology 150(6): 1257-1261
9. Farwell A P (2013) Nonthyroidal illness syndrome. Curr Opin Endocrinol Diabetes Obes. 20(5) : 478–484
10. Keightley PC, Koloski NA, Talley NJ (2015) Pathways in gut-brain communication: evidence for distinct gut-to-brain and brain-to-gut syndromes. Aust N Z J Psychiatry 49(3):207-214
11. Krysiak R[1], Kędzia A[1], Kowalcze K[1], Okopień B[1](2017) Euthyroid sick syndrome: an important clinical problem. Polish, 70(2 pt 2) : 376-385
12. Lado-Abeal J (2015) Thyroid hormones are needed to sustain ”inappropriately” normal TSH during non-thyroidal illness syndrome: a clinical observation in severely ill patients with primary hypothyroidism. Neuroendocrin. Lett. 36(1) : 41–47
13. Mebis L, Van den Berghe G (2011) Thyroid axis function and dysfunction in critical illness. Clin. Endocrinol. & Metabolism. 25(5) : 745–757