CARDIAC DISFUNCTION ASSOCIATED WITH AMIODARONE-INDUCED THYROTOXICOSIS: A COMPARATIVE STUDY

T.Sh. Abdikadirova[1], A.V. Alieva[2], R.Kh. Trigulova[3], Kh.K. Nasirova[4]
Tashkent Pediatric Medical Institute[1,4]
Republican Specialized Scientific and Practical Medical Center of Endocrinology named after academician Ya.Kh. Turakulov[2]
Republican Specialized Scientific and Practical Medical Center of Cardiology[3]
https://doi.org/10.5281/zenodo.15766227

Abstract. *This cross-sectional study investigates cardiovascular changes in patients with amiodarone-induced thyrotoxicosis (AIT). Eight patients diagnosed with AIT and 48 euthyroid individuals were enrolled. Thyroid function tests, heart rate variability (HRV), and echocardiography parameters were assessed. Patients with AIT demonstrated significant alterations in thyroid hormone levels, increased heart rate, elevated SDNN values, and enlarged left atrial volume. These findings underscore the pronounced impact of AIT on myocardial function and support the need for rigorous thyroid monitoring during amiodarone therapy.*

Keywords: *amiodarone, thyrotoxicosis, heart rate variability, SDNN, echocardiography, hyperthyroidism.*

Introduction.

Amiodarone - is a highly effective class III antiarrhythmic drug that is widely used to treat and prevent various heart rhythm disorders. It is effective in ventricular and supraventricular arrhythmias [1,2,3].

Amiodarone has unique electrophysiological properties that affect the action potential of cardiomyocytes and prolong the refractory period of various parts of the heart, including the atria, ventricles and conduction system.

Amiodarone is used in adults to treat and prevent heart rhythm disorders: Ventricular and supraventricular tachycardia. WPW syndrome. Ventricular and supraventricular extrasystole. To prevent recurrent ventricular and atrial fibrillation. During the rehabilitation period after myocardial infarction, if the anamnesis indicates previously noted episodes of arrhythmia [4,5,6].

In regions with iodine deficiency, the thyroid gland is unable to adapt to the increased iodine load, which increases the risk of hyperthyroidism (Coronary Artery Spasm–Induced Cardiac Arrest Precipitated by Iodine Contrast Load in Unknown Pre-Existing Graves' Disease, n.d.) **[**6,7,8].

AIT incidence varies from 2% to 24%, depending on geographic and demographic factors (Ermolaeva & Fadeev, 2023). Pathogenesis includes hormone release from preformed stores and direct stimulation of the thyroid gland by iodine. Patients with nodular goiter, autoimmune thyroiditis, and elevated body mass index are particularly vulnerable.

The most vulnerable groups of patients:

- people with nodular goiter,
- patients with autoimmune thyroiditis,
- people with a high body mass index.

Clinical Presentation and Diagnosis: AIT diagnosis can be challenging due to overlapping symptoms with underlying cardiac disease. Common manifestations include weight loss, palpitations, tremors, and other signs of thyrotoxicosis. Diagnosis relies on hormonal assays and imaging to distinguish between:

- Type 1: increased hormone synthesis,
- Type 2: destructive thyroiditis.

In iodine-deficient settings, Type 2 AIT is more prevalent. Studies highlight BMI and pre-existing thyroid conditions as significant risk factors, and glucocorticoids demonstrate superior efficacy over thionamides in destructive AIT management (Ermolaeva & Fadeev, 2024).

Objective: To evaluate cardiovascular disturbances in patients with amiodarone-induced thyrotoxicosis.

Materials and Methods: Eight patients with confirmed AIT (mean age 50.1 ± 11.2 years) from the Aral Sea region were compared to 48 age- and sex-matched euthyroid controls. Assessments included TSH, T4, T3, anti-TSHR antibodies, Holter ECG (max/min/mean HR, PVCs, SDNN, RMSSD), and echocardiography (EF, LA volume, LVEDD, LVESD, IVS, LVPW).

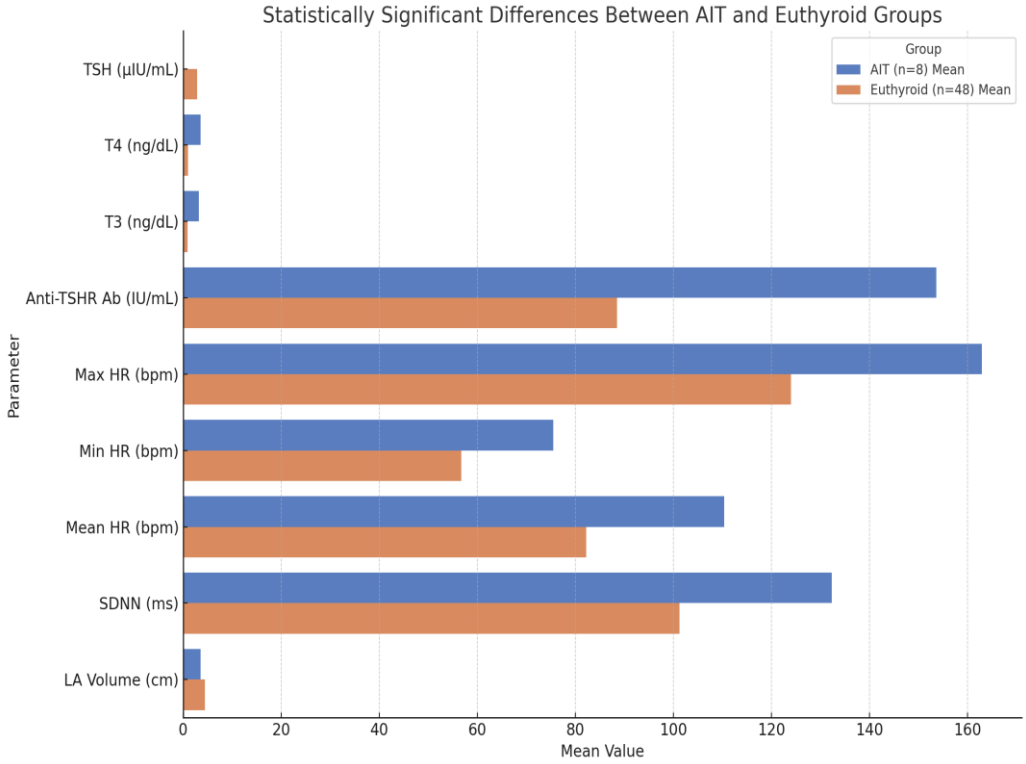
Results: AIT patients showed suppressed TSH (0.15±0.07 mIU/mL), both thyroid hormones – T3 and T4 were elevated: T4 (3.55±0.41 ng/dL), T3 (3.19±0.66 ng/dL). It should be emphasized that these patients had high level of anti-TSHR antibodies (153.63±22.59 IU/mL) indicating appearance of thyroid-stimulating antibodies after treatment with Amiodarone.

It is logical that having thyrotoxicosis patients with Amiodarone-induced thyrotoxicosis will have increased heart rate: mean HR was 110.38±23.85 bpm; maximum HR reached 162.88±40.85 bpm (p=0.011). But, interestingly, patients with AIT had increased SDNN (132.25±48.33 ms, p=0.048) indicating increased heart rate variability, and LA volume in these patients was significantly larger (3.58±0.4 cm, p<0.0001).

Parameter	**AIT (n=8) Mean**	**AIT SD**	**Euthyroid (n=48) Mean**	**Euthyroid SD**	**p-value**
Weight (kg)	84.38	21.02	88.19	13.83	0.622
TSH (BμIU/mL)	0.15	0.07	2.85	1.01	0.0
T4 (ng/dL)	3.55	0.41	0.99	0.47	0.0
T3 (ng/dL)	3.19	0.66	0.95	0.33	0.0
Anti-TSHR Ab (IU/mL)	153.63	22.59	88.52	5.58	0.0
Max HR (bpm)	162.88	40.85	123.92	23.35	0.011
Min HR (bpm)	75.5	16.14	56.73	10.77	0.002
Mean HR (bpm)	110.38	23.85	82.25	15.12	0.002
Single PVCs	32.88	73.63	148.52	509.24	0.144
Paired PVCs	1.25	2.44	7.56	36.06	0.237
Single NSVT	4.75	11.87	13.96	35.04	0.167
SDNN (ms)	132.25	136.69	101.25	18.61	0.048
RMSSD (ms)	91.5	154.31	87.96	28.01	0.524
EF (%)	44.59	9.54	49.29	13.38	0.232
LA Volume (cm)	3.58	0.4	4.41	0.95	0.0
LVEDD (cm)	5.46	0.52	5.29	0.99	0.866

LVESD (cm)	4.03	0.7	3.88	1.14	0.619
IVS (cm)	2.044	2.8142	1.09	0.1939	0.342
LVPW (cm)	1.013	0.1126	1.057	0.1692	0.911
RV (cm)	2.725	0.324	2.877	0.6752	0.289

Also, of notice, paradoxically, more PVCs and non-sustained arrhythmias were observed in controls, possibly due to baseline cardiac pathology and lower HRV.



The chart presents the parameters that showed statistically significant differences between patients with amiodarone-induced thyrotoxicosis (AIT) and the euthyroid control group.

Patients with AIT exhibited significantly reduced TSH levels and markedly elevated levels of T3, T4, and anti-TSHR antibodies, confirming the presence of active thyrotoxicosis. All differences were highly significant ($p < 0.0001$).

Heart Rate Parameters: Maximum, minimum, and average heart rates were significantly higher in the AIT group ($p = 0.011$, 0.002, and 0.002, respectively), indicating increased sympathetic activity.

The SDNN (standard deviation of NN intervals) value was also significantly higher in the AIT group ($p = 0.048$), reflecting increased heart rate variability typically associated with hyperthyroidism.

Left atrial volume was significantly increased in AIT patients ($p < 0.0001$), which may be a consequence of tachycardia and elevated diastolic pressure.

Discussion. The findings align with previous reports highlighting the sympathetic overdrive in thyrotoxicosis, reflected in HR elevation and increased SDNN (Biondi & Cooper, 2010; Kahaly, 2021). One should keep in mind that the observed left atrial dilation may result from diastolic dysfunction related to tachycardia and hormonal excess. Unlike hypothyroidism, which typically reduces ejection fraction, AIT promotes compensatory myocardial remodeling which in its turn may lead to exacerbation of cardiac dysfunction in patients already having arrythmia – the reason they were prescribed Amiodarone. So, appearance of AIT in patients with arrythmia treated

with Amiodarone may lead to further cardiac dysfunction and close the vicious cycle in progressing cardiovascular pathology.

Conclusion. Amiodarone-induced thyrotoxicosis significantly impacts cardiac function, as evidenced by increased HR, SDNN, and LA volume. Routine thyroid screening is imperative in patients on chronic amiodarone therapy, especially in iodine-deficient regions.

REFERENCES

1. Ermolaeva A.S., Fadeev V.V. (2023). Type 2 Amiodarone-Induced Thyrotoxicosis: Prevalence and Management. Probl Endocrinol.
2. Biondi B., Cooper D.S. (2010). The Clinical Significance of Subclinical Hyperthyroidism. Endocr Rev.
3. Kahaly G.J., Bartalena L. (2021). Thyroid Hormone Therapy in Hypofunction. Eur Thyroid J.
4. Coronary Artery Spasm–Induced Cardiac Arrest by Iodine Load in Graves' Disease. JACC Case Rep, 2020.
5. Taylor P.N., et al. (2018). Global Epidemiology of Hyperthyroidism and Hypothyroidism. Nat Rev Endocrinol.
6. Волошина И. Н. Тиотриазолин в лечении и профилактике заболеваний сердечно-сосудистой системы. – Strelbytskyy Multimedia Publishing, 2018.
7. Калдыркаева О. С. и др. Антиаритмические свойства и токсикологическая характеристика N-(2-(2-(диалкиламино) этокси) этил) карбоксамидов //Кардиологический вестник. – 2022.
8. Королева А. А. и др. Клинический случай амиодарон-индуцированного тиреотоксикоза //Рецепт. – 2024. – Т. 27. – №. 4.