

Effects of Aescusan on Fibrinolytic Plasma Activity in Patients with Hypothyroidism

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Abstract: The administration of Aescusan into the complex treatment program of patients with hypothyroidism was found to increase total plasma fibrinolysis almost to the control level, normalize the intensity of non-enzymatic fibrinolysis, considerably elevate the enzymatic lysis of fibrine and more effectively, as compared with standard treatment program, restore normal structure of plasma fibrinolysis.

Keywords: *Aescusan*, hypothyroidism, fibrinolytic activity, plasma fibrinolysis.

INTRODUCTION

The literary evidences suggest, that thyroid gland diseases are followed by phase disturbances of anticoagulant process, including fibrinolytic activity [1-4], moreover not only the character of coagulation and local fibrinolysis in the thyroid tissue itself is changed, but a functional condition of the external system of coagulation and fibrinolysis are found to be modified as well [5-7].

At the same time, contradictions of modern literary reports concerning the character and clinical importance of hemocoagulation disorders, their dependence on the level of thyroid hormones impede the formulation of straight diagnostic and rational treatment criteria for patients with thyroid pathology.

An evident fact of a direct correlation between the severity of thyroid disease and fibrinolytic blood potential in patients with hypothyroidism substantiates the search of therapeutic methods, regulating fibrinolysis, hemodynamic and rheologic disturbances. Horse chestnut (*Aesculus hippocastanum* L.) preparations known to provide, besides significant vasoprotective and vasotonic, anti-inflammatory and anti-edematous, antioxidant properties, anticoagulant and fibrinolytic effects as well, were found to be perspective in this concern [8, 9].

Horse chestnut is one of 12 species of the genus *Aesculus* L., officially recognized as a source of herbal products in traditional medicine [10]. The bark, leaves, horse chestnut seed extract (HCSE) from *A. hippocastanum* have been used in modern medicine. HCSE is gaining wider acceptance possessing diverse pharmacological activities due to the primary active constituent – aescin. Aescin is a mixture of triterpene saponins present in two forms, α and β , of

which β -aescin is the major active component in HCSE saponin mixture [10, 11]. The anti-inflammatory, anti-edematous, venotonic and antiangiogenic (vascular protective), anti-tumor, antioxidant, antigenotoxic, anticoagulant and fibrinolytic activities of HCSE are related to aescin [10-12]. Other constituents include bioflavonoids (quercetin and kaempferol), proanthocyanidin A2 (an antioxidant), and the coumarins fraxin and aesculin [11]. The latest ones inhibit the activity of the enzymes elastase and hyaluronidase, involved in enzymatic proteoglycan degradation. These properties make HCSE ideal for the prevention of vascular leakage.

The objective of this study was to assess therapeutic potential, mostly anticoagulant and fibrinolytic properties of HCSE preparations in case of changed thyroid status. Research strategy has been developed to investigate the effects of thyroid hormone deficiency on blood plasma fibrinolytic potential and to study the possibility of administration of HCSE preparation Aescusan (AESCUSAN DROPS, Pharma Wernigerode GmbH, Germany) in complex treatment of patients with hypothyroidism. Indicated for management of post-trombophlebitic syndrome, chronic venous insufficiency of various etiologies and its complications, thrombophlebitis, varicose veins, hemorrhoids and etc., being safe, well tolerated and acceptable to patients, AESCUSAN DROPS consist of 41.67 mg of HCSE/g, standardised to aescin, and was administered to support conventional therapy of hypothyroidism and to improve its efficacy.

MATERIALS AND METHODOLOGY

53 patients with subcompensated primary hypothyroidism, aged between 14 and 74 years, participated in this study. The verification of the diagnosis was based on thorough clinical-anamnestic and laboratory-instrumental investigations according to the criteria, proposed by the who experts committee. The duration of hypothyroidism in the examined pa-

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Table 1. Clinical Effects of Aescusan on Fibrinolytic Plasma Activity in Patients with Hypothyroidism

Indices	Group (number of examined patients)				
	Healthy Individuals (n=18)	Control Group (n=26)		Basic Group (n=27)	
		Before Treatment	After Treatment	Before Treatment	After Treatment
Total fibrinolytic activity, mkg of azofibrin/ml at 1 hour	3.24±0.15	1.78±0.05 P<0.001	2.53±0.10 P<0.001	1.68±0.06 P<0.001 P ₁ >0.2	2.65±0.10 P<0.01 P ₂ >0.4
Non-enzymatic fibrinolytic activity, mkg of azofibrin/ml at 1 hour	0.55±0.03	0.77±0.03 P<0.001	0.81±0.04 P<0.001	0.73±0.03 P<0.001 P ₁ >0.3	0.49±0.03 P>0.1 P ₂ <0.001
Enzymatic fibrinolytic activity, mkg of azofibrin/ml at 1 hour	2.69±0.15	1.01±0.03 P<0.001	1.72±0.07 P<0.001	0.95±0.04 P<0.001 P ₁ >0.2	2.16±0.07 P<0.001 P ₂ <0.001

Note: values are expressed as means ± standard errors; P – significant difference in comparison with healthy individuals (P≤0.05); P₁ – significant difference between patients of control and basic groups before treatment (P≤0.05); P₂ – significant difference between patients of control and basic groups after treatment (P≤0.05); n – number of patients in a group.

tients before their enrollment to the study was nearly 12 years. The severity of the disease was assessed by the degree of clinical symptoms manifestation. Since the examination of patients was carried out during their hospital treatment, individuals with mild hypothyroidism were absent among those involved into the study, and in overwhelming majority of the patients moderate (30%) and severe (70%) forms of the disease were diagnosed. It should be noted, that moderate severity of hypothyroidism was identified in cases of its duration to five years (13%), whereas severe form of the disease was observed in cases of hypothyroidism duration over 10 years (40%).

The patients for this study were divided in two groups: control group consists of 26 patients with hypothyroidism under standard treatment program for this disease and the basic group consists of 27 patients under complex treatment with administration of Aescusan 20 drops orally three times a day for 15 days. In addition, 18 healthy individuals served as a control group. The total, enzymatic, and non-enzymatic plasma fibrinolytic activities in examined subjects (TFA, EFA and NEFA respectively) were determined according to lysis of azofibrin (Simko Ltd., Ukraine) [13, 14].

Statistical variance analysis of the obtained data was performed by means of Biostat software, using paired Student's t-criterion.

RESULTS AND DISCUSSION

The study showed there is no significant difference concerning the intensity of enzymatic fibrinolysis in patients of control and basic groups before treatment (Table 1). Thus, TFA of blood plasma in patients with hypothyroidism of control group before treatment appeared to be lower of the corresponding index in healthy individuals by 45.1%. Moreover, NEFA increased by 40.0%, whereas the intensity of enzymatic fibrinolysis 2.7 times reduced.

After standard treatment program total intensity of plasma fibrinolysis was elevated by 42.1%, remaining lower

than in healthy individuals by 21.9%. NEFA didn't demonstrate any significant changes, exceeding normal indices by 47.3%. The intensity of enzymatic lysis of fibrin was enhanced by 70.3%, however, not getting normalized, and still remaining lower than in healthy subjects by 36.1%. The structure of plasma fibrinolysis in patients with hypothyroidism was mostly contributed by NEFA before as well as after treatment (Fig. 1).

TFA of blood plasma in patients with hypothyroidism of basic group was found to be lower than that in healthy individuals by 48.1%, NEFA exceeded normal index by 32.7%, whereas EFA was 2.8 times decreased.

After complex treatment with administration of Aescusan the total intensity of plasma fibrinolysis increased by 57.7%, being only 18.2% lower as compared with that in healthy subjects. NEFA reduced by 32.9% and didn't differ from the normal rate.

The enzymatic lysis of fibrin was found to be 2.3 times higher, demonstrating lower intensity concerning the normal index only by 19.7%. If before treatment the contribution of non-enzymatic fibrinolysis into TFA was elevated, after treatment the structure of plasma fibrinolysis in patients with hypothyroidism was tending to that in healthy individuals (Fig. 2).

Thus, despite opposite directions of enzymatic and non-enzymatic fibrinolysis disturbances under condition of thyroid hormone deficiency, Aescusan, used in our current study, appeared to have the ability to normalize them.

CONCLUSIONS

Total plasma fibrinolysis is markedly inhibited in patients with hypothyroidism as the result of enzymatic fibrinolysis reduction, whereas low-effective non-enzymatic lysis of fibrin, on the contrary, increases, changing the structure of plasma fibrinolysis. The above mentioned changes are observed even after standard course of hospital treatment. Administration of Aescusan into the complex treatment of pa-

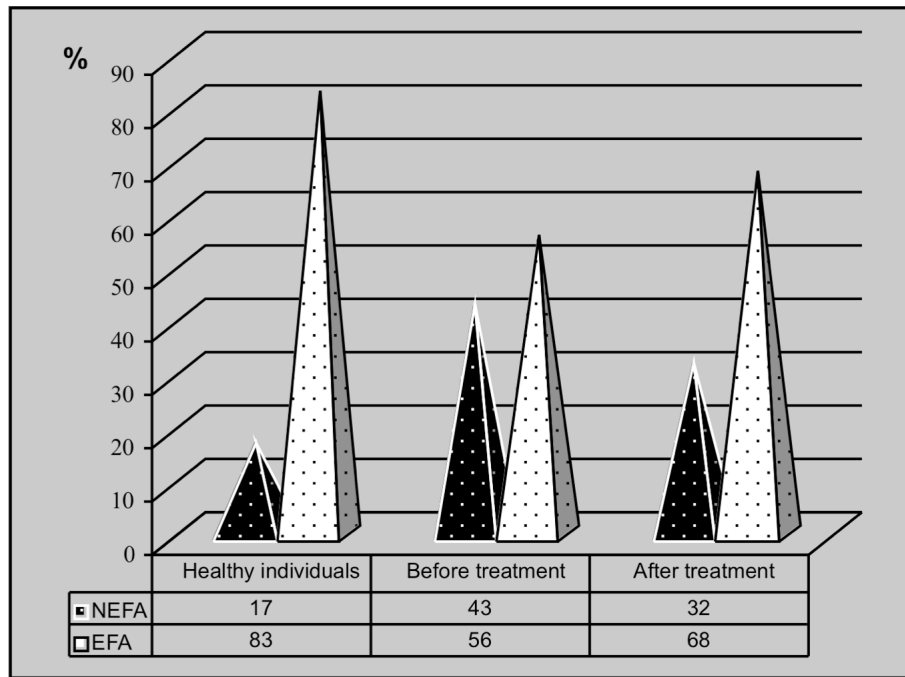


Fig. (1). Structure of plasma fibrinolysis in patients with hypothyroidism of control group (% of TFA).

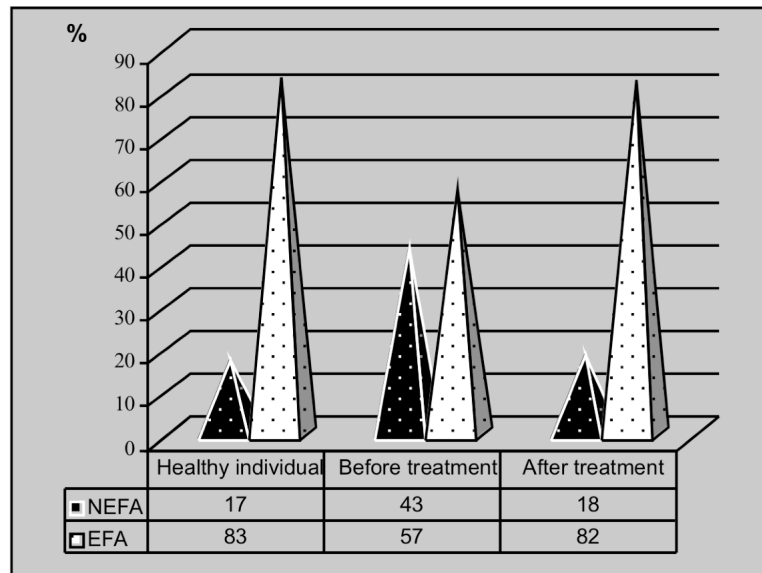


Fig. (2). Structure of plasma fibrinolysis in patients with hypothyroidism of basic group (% of TFA).

tients with hypothyroidism promotes the increase of total plasma fibrinolysis almost up to the control level, normalizes the intensity of non-enzymatic fibrinolysis, significantly elevates enzymatic fibrinolytic activity and resumes normal structure of plasma fibrinolysis more effectively as compared with standard treatment program.

ABBREVIATIONS

- EFA = Enzymatic fibrinolytic activity
- HCSE = Horse chestnut seed extract

- NEFA = Non-enzymatic fibrinolytic activity
- TFA = Total fibrinolytic activity

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