Efficiency of the Intravenous Laser Therapy in Metabolic Disorders Correction

Skuteczność laseroterapii dożylnej w leczeniu chorób metabolicznych

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SUMMARY

Despite the wide range of medicines which are used for the treatment of any disease, today increasing attention is paid to physiotherapy methods, namely the method of the intravenous laser therapy (ILT) which has been successfully used for the last 30 years in almost all areas of medicine. To estimate the effectiveness of ILT in the treatment of patients with hypothyroidism combined with nonalcoholic fatty liver disease (NAFLD) 180 people with dyslipidemia were examined. The 1st group included 60 patients who didn't have any complaints but had dyslipidemia. The 2nd group included 60 patients with NAFLD, the 3rd group included 60 patients with hypothyroidism combined with NAFLD. Based on the genetic research of polymorphic variants of the *CYP7A1* gene, patients were divided into the following subgroups: 1 AA – 52 patients, 1 CC – 8 patients; 2 AA – 50 patients, 2 CC – 10 patients; 3 AA – 48 patients, 3 CC – 12 patients. Treatment was provided with Omega-3 Acid Ethyl Esters and ILT with laser wavelength λ=635 nm and laser power equals to 1,5 mW. The most pronounced effect was achieved in 2 CC and 3 CC groups due to reducing of TC, LDL, TG and the Atherogenic Index. Patients of 2 AA and 3 AA groups had statistically significant dynamics of HDL increasing. The dynamics of normalization of cytolysis syndrome indices didn't have genetically determined differences and prevailed in the 2nd group compared to the 3rd group in which the presence of hormonal imbalance delayed the activation of reparative mechanisms of damaged liver cells.

Key words: intravenous laser therapy, hypothyroidism, nonalcoholic fatty liver disease, dyslipidemia

STRESZCZENIE

Pomimo dostępności dużej liczby leków stosowanych w różnych schorzeniach obecnie rośnie zainteresowanie metodami fizjoterapeutycznymi, a konkretnie laseroterapią dożylną (ILT), która jest z powodzeniem stosowana od 30 lat niemal we wszystkich dziedzinach medycyny. W celu oceny skuteczności ILT w leczeniu osób z niedoczynnością tarczycy połączoną z niealkoholową stłuszczeniową chorobą wątroby (NAFLD) przebadano 180 pacjentów z dyslipidemią. Do pierwszej grupy (60 osób) należeli pacjenci, u których występowała dyslipidemia, ale którzy nie odczuwali żadnych objawów chorobowych. Do drugiej grupy (60 osób) włączono pacjentów z NAFLD, zaś w trzeciej grupie (60 osób) znaleźli się pacjenci z niedoczynnością tarczycy połączoną z NAFLD. Pacjentów podzielono na następujące podgrupy na podstawie genetycznych badań wariantów polimorficznych genu CYP7A1: 1 AA – 52 pacjentów, 1 CC – 8 pacjentów; 2 AA – 50 pacjentów, 2 CC – 10 pacjentów; 3 AA – 48 pacjentów, 3 CC – 12 pacjentów. Pacjentów leczono podając estry etylowe kwasów omega-3 oraz stosując ILT z długością fali λ=635 nm i mocą równą 1,5 mW. Najwyraźniejsze efekty zaobserwowano w grupach 2 CC i 3 CC w związku ze zmniejszeniem TC, LDL, TG oraz wskaźnika aterogenności. Pacjenci z grupy 2 AA i 3 AA wykazali statystycznie istotną dynamikę wzrostu HDL. Dynamika normalizacji wskaźników zespołu cytolizy nie cechowała się genetycznie uwarunkowanymi różnicami i przeważała w grupie drugiej w przeciwieństwie do grupy trzeciej, w której obecność zaburzeń hormonalnych opóźniała aktywację mechanizmów naprawczych uszkodzonych komórek wątroby.

Słowa kluczowe: laseroterapia dożylna, niedoczynność tarczycy, niealkoholowa stłuszczeniowa choroba wątroby, dyslipidemia

Acta Balneol, TOM LIX, Nr 1(147);2017;16-21

INTRODUCTION

Over the last decade one can mark active introduction of laser technology in various areas of medicine. Laser technology has been actively used due to its universality, limited list of contraindication, a minimum level of side effects and affordability of this method [1, 2]. In this case, the current task of the modern medicine is to study the optimization of the treatment using laser therapy.

In the early 60s of the XX century the first laser was appeared. This invention made it possible to identify the high biological activity of laser irradiation with low intensity which doesn't cause thermal heating and tissue damage [3]. First, biostimulation effect was invented; it allowed the laser to treat venous ulcers, wounds that don't heal for a long time, etc. [4]. Then antiinflammatory, analgesic, immunomodulatory, stimulating microcirculation and other physiological effects of low intensity laser irradiation were invented. These effects proved a great advantage of the therapeutic laser and became the basis for the development of different medical procedures with the use of laser therapy in clinical medicine [5].

The most common non-infectious diseases of the XXI century are diseases of the thyroid gland which occupy one of the leading place in the structure of endocrine pathology (47.3%) [6], including hypothyroidism which is important too [7, 8]. Pathogenic mechanisms lead to hypothyroidism course of severe metabolic disorders that includes nonalcoholic fatty liver disease (NAFLD) [9].

Today we have a few experimental and clinical works that focus on impact of the intravenous laser therapy (ILT) on liver diseases. During experimental researches the models of acute toxic hepatitis have shown that using of ILT reduced the intensity of protein and fatty liver dystrophy, the amount of necrotic areas and intensity of inflammatory infiltration in the liver parenchyma as well [10]. Exchange application of ILT in treatment of patients with chronic diffuse liver disease has antioxidant, antiperoxide and membrane stabilizing effects and leads to decrease of ceruloplasmin, cytolysis syndrome and lipid peroxidation which provides activation of the body's own antiradical protection (catalase activity increased on 11,1%, glutathione peroxidase – on 11,4%). The therapeutic effect lasts for one month [11]. One of the most important applications of the ILT therapeutic effects is improving of the rheological properties of blood and normalization of lipid metabolism which allows using of ILT in the treatment of dyslipidemia in pathologies [11].

AIM

Was to evaluate the efficiency of the intravenous laser therapy in the treatment of patients with hypothyroidism combined with nonalcoholic fatty liver disease.

MATERIAL AND METHODS

The research was performed on clinical bases of the Department of Family and Social Medicine in Medical Institute of Sumy State University: MI «Sumy City Clinical Hospital № 1» and MI «The Center of Primary Care № 3». The course of the intravenous laser therapy was held at Sumy Laser Clinic. Genetic study was conducted in the laboratory of LL "Elasko-Arnika", Odessa, Ukraine.

All patients and healthy individuals gave membership agreement to participate in the study according to the Helsinki Declaration of the World Medical Association "Ethical Principles for Medical Research Involving Human as the Object of Study".

The study included 180 people. The 1st group included 60 patients who passed the annual medical examination and didn't have any disorders of the thyroid gland and hepatobiliary system, but turned out to have dyslipidemia which was found during the analysis of biochemical parameters of blood. The 2nd group included 60 patients with NAFLD, the 3rd group included 60 patients with hypothyroidism combined with NAFLD. Based on the genetic research of polymorphic variants of *CYP7A1* gene patients were divided into the following subgroups: 1 AA – 52 people, 1 CC – 8 people; 2 AA – 50 people, 2 CC – 10 people; 3 AA – 48 people, 3 CC – 12 people. Clinical examination included the collection of anamnesis morbi and life and an objective review. From the anamnesis morbi it was found that all patients accepted statins for one month, but the result wasn't achieved. The study provided lipid profile with the determination of total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), high density lipoproteins (HDL) and the Atherogenic Index (AI), which was calculated according the following formula: AI = (TC-HDL)/HDL. To evaluate the functional status of the liver, biochemical parameters of liver functional activity were investigated: alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), *alkaline phosphatase level test (ALP), which was performed by using semi-automatic biochemical analyzer «HumanaLyzer 3000», the manufacturer «Human», Germany. Hypothyroidism was diagnosed on the basis of hormonal blood tests – thyroid-stimulating hormone (TSH)* ≥ 10 mIU/ml, *free thyroxine (T4 free)* ≤ 10 *pmol/L. These tests were conducted with the help of ELISA and by using the analyzer miniVIDAS, the manufacturer bioMerieux, France.*

Real time thyroid and hepatic ultrasound was performed using SonoScape ultrasound system with linear and convex multifrequency transducers (frequency bandwidth 3-14MHz) by a single radiologist.

Considering qualitative and quantitative sonographic criteria (hepatorenal echo contrast, liver echogenicity brightness, liver sizes, acoustic deep attenuation and vascular margins blurring) the following stages of the hepatic steatosis were found: stage I – minimal diffuse increase in the liver echogenicity, liver appears bright compared to the cortex of the kidney, normal visualization of diaphragm and intrahepatic vessel margins; stage II – increasing the size of the liver, the lower body of the left hepatic lobe - angle of more than 45 degrees, poorly visualization of the intrahepatic vessels and diaphragm; stage III – enlargement of the liver, diffuse liver hyperechogenicity, blurred image of portal vein branches, diaphragm, and posterior portion of the right lobe, deep beam attenuation [12, 13].

To assess the degree of progression of fibrosis in the liver, the test "FibroMax" with the help of computer software of the

company Materialise Ukraine was conducted. According to the system METAVIR following degree of the liver fibrosis were established: F0 – (0,00-0,21), F0-F1 – (0,22-0,27), F1 – (0,28-0,31), F1-F2 – (0,32-0,48), F2 – (0,49-0,58), F3 – (0,59-0,72), F3-F4 – (0,7300,74), F4 – (0,75-1,00). In order to establish genetic predisposition to the occurrence of dyslipidemia polymorphic variants -204A> C (rs 3808607) *CYP7A1* gene were studied: AA, AC or CC using polymerase chain reaction (PCR).

To correct lipid metabolism, patients have been taken Omega-3 Acid Ethyl Esters during 3 months in a dose of 1000 mg 2 times a day. Hypothyroid patients of the 3rd group received hormone replacement therapy with L-thyroxine in a daily dose from 50 to 100 mcg for compensation. To normalize the biochemical parameters of liver functional activity, 10-day course of the intravenous laser therapy for 15 minutes every day with a wavelength λ = 635 nm and a power equals to 1.5 mW was prescribed. ILT was performed on the apparatus «Lazmik» (Figure 1).

Monitoring of biochemical parameters of liver functional activity was performed after the 2-week course of ILT. Control of blood lipid profile was performed in 1 month after the started treatment. Statistical analysis of the survey results was performed with the help of software Statistica 10.

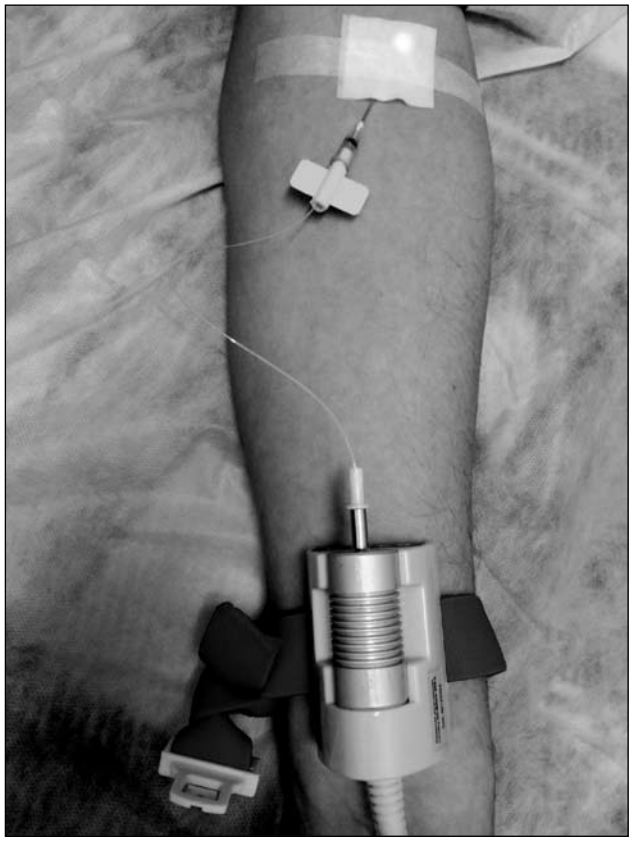

Figure 1. The procedure of the intravenous laser therapy in a patient of the 2nd group. A wavelength λ = 635 nm and a power equals to 1.5 mW

Rycina 1. *Zabieg laseroterapii dożylnej u pacjenta z grupy drugiej. Długość fali λ = 635 nm, moc równa 1,5 mW*

RESULTS

According to steatosis stage the patients were divided into the following groups: in the 2nd group the I stage steatosis was found in 30 patients (50% of the total number patients in the group), II stage steatosis – in 12 patients (20%), III stage steatosis – in 8 patients (13,3%); in the 3rd group I stage steatosis was found in 26 patients (43,3% of the total number patients in the group), II stage steatosis – in 10 patients (16,6%), III stage steatosis – in 5 patients (8,3%) (Figures 2, 3).

Analysis of the «FibroMax» test showed that in the 2nd group F0-F1 degree of the liver fibrosis was detected in 15 patients (25% of the total number patients in the group), F1 – in 16 patients (26,6%), F1-F2 – in 10 patients (16,6%), F2 – in 7 patients (11,6%), F3 – in 7 patients (11,6%); in the 3rd group F0-F1 degree of the liver fibrosis was detected in 13 patients (21,6% of the total number patients in the

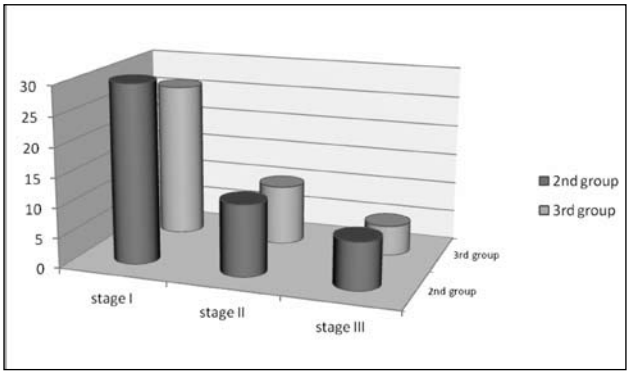

Figure 2. The amount of patients in the 2nd and in the 3rd groups according to steatosis stage.

Rycina 2. *Liczba pacjentów w grupie drugiej i trzeciej według stadium stłuszczenia*

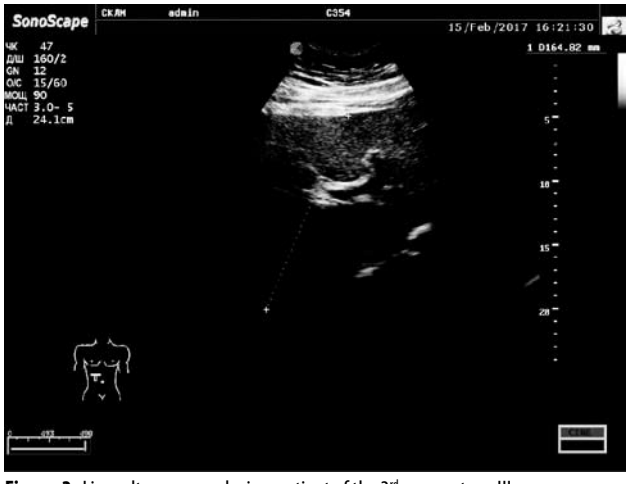

Figure 3. Liver ultrasonography in a patient of the 3rd grope, stage III

Rycina 3. *Badanie USG wątroby u pacjenta z grupy trzeciej, stadium III*

group), F1 – in 10 patients (16,6%), F1-F2 – in 9 patients (15%), F2 – in 7 patients (11,6%), F3 – in 2 patients (3,3%) (Figure 4).

Based on the genetic testing, heterogeneity of the groups were identified by mutation of the *CYP7A1* gene: in the 1st group patients with the AA genotype (52 patients) lipidohrama indicators were within normal limits, whereas patients with the genotype CC (8 patients) indicators were also in the normal range, but were of statistical significance p < 0.001 above in relation to the levels of TC, LDL and with reliability p < 0.01 to the levels of TG than in those with the genotype AA, the levels of the HDL were significantly lower than in the AA genotype (p < 0.001); in the 2nd group the examined patients with the genotype CC (10 patients) turned out to have increased levels of TC and TG (higher than in those with the genotype AA (50 patients)), the levels of the LDL was within normal limits and didn't differ from that of patients with the genotype AA (p > 0.05) and the levels of the HDL were significantly reduced; in the 3rd group the examined patients with the CC genotype (12 patients) turned out to have increased levels of TC, LDL and TG (significantly higher than in those with the genotype AA (48 patients) – p < 0.001) and the levels of the HDL were significantly lower than with genotype AA - p < 0.00 (Table I).

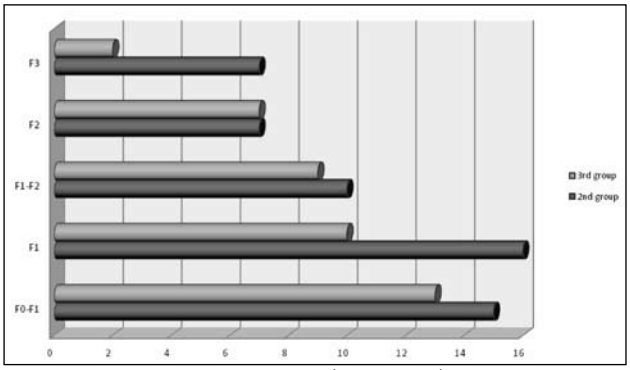

Figure 4. The amount of patients in the 2nd and in the 3rd groups according to the «FibroMax» test.

Rycina 4. *Liczba pacjentów w grupie drugiej i trzeciej według testu FibroMax*

Analysis of plasma lipid profile indicators after one month of combined treatment showed positive dynamics of decreasing their levels in all study groups, but the rate of decrease were different in subgroups: in the 1 CC subgroup the level of TC decreased on 6,3%, the level of TG – on 68,6%, the level of LDL – on 2,7%, the level of HDL increased on 4,3% and the level of AI decreased on 2,4%; in the 2 AA subgroup the level of TC decreased on 4,1%, the level of TG – on 14,6%, the level of LDL – on 2,8%, the level of HDL increased on 8,7% and the level of AI decreased by 14,3%;

Table 1. The influence of the intravenous laser therapy in complex therapy in disorders of lipid metabolism

Tabela 1. *Wpływ laseroterapii dożylnej w kompleksowym leczeniu zaburzeń metabolizmu tłuszczów*

Groups	Genotypes	Indexes				
		TC, mmol/L	TG, mmol/L	LDL, mmol/L	HDL, mmol/L	AI
After genetic testing and before treatment						
the 1st group	CC (n=8)	4,80 ± 0,20	1,4 ± 0,5	3,7 ± 0,6	1,38 ± 0,1	2,48± 0,11
the 2nd group	AA (n=50)	6,05 ± 0,45	1,37 ± 0,28	5,03 ±0,4	1,15 ± 0,22	4,38± 0,64
	CC (n=10)	6,70 ± 0,25	3,4 ± 0,15	4,8 ± 0,37	0,9 ± 0, 28	7,14± 2,26
the 3rd group	AA (n=48)	6,00 ± 0,40	2,1 ± 0,54	4,5 ± 0,14	1,02 ±0,18	4,95± 0,65
	CC (n=12)	6,60 ± 0,54	3,4 ± 0,45	3,85 ± 0,25	0,8 ± 0,12	6,5 ± 0,6
After one month of combined treatment						
the 1st group	CC (n=5)	4,5 ± 0,18	0,44 ± 0,13	3,6 ± 0,6	1,32 ± 0,12	2,42± 0,18
p*		< 0.01	< 0.01	< 0.01	< 0.001	< 0.01
the 2nd group	AA (n=50)	5,8 ± 0,33	1,17 ± 0,26	4,89 ± 0,41	1,25 ± 0,23	3,75± 0,61
p**		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	CC (n=10)	6,54 ± 0,23	2,06 ± 0,55	4,62 ± 0,12	1,2 ± 0,27	4,65± 1,05
p***		< 0.01	< 0.001	< 0.01	< 0.001	< 0.001
the 3rd group	AA (n=48)	5,05 ± 0,42	1,79 ± 0,51	3,87 ± 0,16	1,12 ± 0,2	3,45± 0,32
p****		< 0.001	< 0.001	< 0.001	< 0.01	< 0.001
	CC (n=12)	5,9 ± 0,27	2,18 ± 0,4	3,68 ± 0,31	1,04 ±0,18	4,8 ± 0,7
p*****		< 0.001	< 0.001	< 0.01	< 0.001	< 0.001

p* - significance between indexes in the 1st group patients with CC genotype before and after treatment; p** - significance between indexes in the 2nd group patients with the AA genotype before and after treatment; p*** - significance between indexes in the 2nd group patients with the CC genotype before and after treatment; p**** - significance between indexes in the 3rd group patients with the AA genotype before and after treatment; p***** - significance between indexes in the 3rd group patients with the CC genotype before and after treatment.

Table 2. The evolution of cytolysis syndrome before and after using ILT in the 2nd group and in the 3rd group

Tabela 2. *Ewolucja zespołu cytolizy przed i po zastosowaniu ILT w grupie 2 i w grupie 3*

Indexes	the 2nd group (n=60)	the 3rd group (n=60)
Before using ILT		
ALT, U/L	46 ± 17	36 ± 6
AST, U/L	42 ± 2	40 ± 4
GGT, U/L	100 ± 48	96 ± 14
ALP, U/L	98 ± 18	134 ±12
After 2 weeks		
ALT, U/L	34 ± 6	32 ± 4
p*	< 0.001	< 0.001
AST, U/L	25 ± 4	34 ± 6
p**	< 0.001	< 0.001
GGT, U/L	75 ± 33	83 ± 5
p***	< 0.001	< 0.001
ALP, U/L	84 ± 14	122 ± 8
p****	< 0.001	< 0.001

p*- significance between ALT level before and after using ILT; p** - significance between AST level before and after using ILT; p*** - significance between GGT level before and after using ILT; p**** - significance between ALP level before and after using ILT.

in the 2 CC subgroup the level of TC decreased on 2,4%, the level of TG – on 40%, the level of LDL – on 3,7%, the level of HDL increased on 33%, and the level of AI decreased on 35%; in the 3 AA subgroup the level of TC decreased on 15,8%, the level of TG – on 14,7%, the level of LDL – on 14%, the level of HDL increased on 9,8% and the level of AI decreased on 30,3%; in the 3 CC subgroup the level of TC decreased on 10,6%, the level of TG – on 36%, the level of LDL – on 4,4%, the level of HDL increased on 30% and the level of AI decreased on 26,1% (Table 1).

There wasn't a significant difference between the variants of genotypes and biochemical indicators of liver functional activity in subgroups, that's why the dynamics of the assessment of the functional state of the liver was carried out between patients in the 2nd and 3rd groups in general. The results showed that after 2 weeks of using of ILT, the following data concerning patients of the 2nd group were found: the level of ALT decreased on 26%, the level of AST – on 40,4%, the level of GGT – on 25%, the ALP test – on 14,3%. At the same time, the dynamics of biochemical parameters in patients of the 3rd group were significantly slower – the lever of ALT decreased on 11,1%, the level of AST – on 15%, the level of GGT – on 13,5%, the ALP test – on 9% (Table 2).

In this manner, the received results showed that there is a statistically significant positive dynamics of indicators of lipid profile in the groups. This dynamics changed for the better after using of ILT in both the control group and in the groups with NAFLD within month. The most pronounced effect was achieved in 2 CC and 3 CC groups because of reducing levers of TC, LDL, TG and the Atherogenic Index. Patients of 2 AA and 3 AA groups had statistically significant dynamics of HDL increasing.

Given the fact that the most atherogenic lipid profile at the time of enrolment in the study was observed in genotype CC in the 2nd and 3rd groups, the resulting dynamics demonstrated the significant impact of laser irradiation on the functional activity of hepatocytes. The dynamics of normalization of cytolysis syndrome wasn't caused by genetic differences and prevailed in the 2nd group compared to the 3rd group in which the presence of hormonal imbalance delayed activation of reparative mechanisms of damaged liver cells.

CONCLUSION

The use of ELT in the complex treatment of lipid disorders and cytolysis syndrome contributes the regeneration of disturbed functions of hepatocytes, reduces the activity of mesenchymal and inflammatory reactions that allows slowing down the progression of fibrosis even in patients with a genetic predisposing to dyslipidemia and with metabolic disorders caused by hypothyroidism.

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Authors' contribution:
According to the order of the Authorship

Conflict of interest:
The Authors declare no conflict of interest

Received: 20.12.2016
Accepted: 06.02.2017

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