Original paper

The lipid disorders therapy in overweight patients

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Abstract

Introduction: The study was aimed to assess effects of hypercholesterolemia and the dyslipidemia therapy within one year of recommended lifestyle and diet modifications.
Material and methods: The study included 157 consecutive patients referred to the Outpatient Department of Metabolic Disorders with hypercholesterolemia diagnosis. Patients were assigned based on body weight and BMI into three groups: 1) patients with normal body weight (BMI 18.5<25); 2) overweight patients (BMI >25-30) and 3) obese patients (BMI >30). The therapeutical effects were studied 6 and 12 months after the initiated therapy. The degree of body weight reduction, incidence and time frame of normal lipid panel, incidence and time of drop-outs in relation to the remaining IND and CVI risk factors were studied.
Results: Total cholesterol was significantly increased before the study in overweight patients. After 6 months, the percentage of patients who reached the therapeutical targets was 30.56% in obese patients, 35.29% in overweight patients, and 29.41% in patients with normal body weight. After 12 months, the highest percentage of patients reaching therapeutical targets was 47.06% in the group with normal body weight.
Conclusions:
1. Time frame and incidence of successful therapy and eventual, normal lipids panel is remarkably related with initial body weight.
2. Subjects with normal body weight benefited from the 12 months therapy to the largest extent.
3. Overweight and obese patients are less motivated to diet and lifestyle changes resulting in the highest number of patients with increased body weight during the dyslipidemia therapy.

Key words: obesity, hypercholesterolemia, arterial hypertension, ischemic heart disease.

Introduction

The common risk factors for ischemic heart disease (IHD) and cardiovascular incidents (CVI) include arterial hypertension, diabetes, cigarette

smoking, lipid disorders and obesity. The relation between obesity, hypercholesterolemia and cardiovascular diseases is well established. Obesity is the state of fat accumulation to the extent that jeopardizes one's health. Obesity accelerates arterial hypertension, diabetes mellitus, hypercholesterolemia, dyslipidemia and atherogenesis in the arteries and is a strong predictor of IHD and CVI. The disease prevalence and mortality related with overweight and obesity is an increasing serious health problem in Poland. The increased body weight is associated not only with metabolic disorders and cardiovascular diseases but also with respiratory, muscle and skeletal diseases and markedly decreases the quality of life. Further, obesity increases the overall risk of death [1].

The national health plan for 2004-2014 identifies the prevalence of subjects with BMI reaching 30 as 30% in this country. Overweight is more frequent among males, whereas obesity is more common among women. In Poland, there are still insufficient epidemiological data concerning obesity and there are no data on regional incidence. The program of cardiovascular disease prevention (POL-MONICA) determined that in the population of the capital city there are 45% overweight men and 35% women, and 22% obese men and 29% obese women. Other studies indicate that there are 36% obese women and 10% obese men in the non-urban population. Obesity is particularly widespread in the central and eastern Europe and the USA (approximately 30%) [2, 3].

There has been an epidemic increase of adults obesity in the US in recent years. The percentage of obese subjects has doubled within last 20 years and it increased from 15% to 31% [4], whereas the incidence of obesity in children and teenagers has tripled from 5% to 15% [5]. The fat tissue is not only the lipid storage of energy but it is also a metabolically active endocrine tissue. The expression of proinflammatory cytokines and interleukin-6 (IL-6) and tumor necrosis factors α (TNF-α) was found in the fat tissue [6]. The serum concentration of IL-6 in healthy males and females increases in parallel with obesity [7]. The synthesis of IL-6 in liver is regulated mainly by IL-6 [8]. The increased serum CRP concentration is always related with the increase of acute CVI implying inflammatory mechanisms in the cardiovascular diseases. The chronic inflammatory reaction is associated with oxidant stress and atherogenesis. The increased degree of obesity is significantly correlated with increased levels of CRP [9, 10]. The notion that obesity is accompanied by chronic inflammatory reaction and oxidative stress is a founding for therapeutical strategies aimed to reduce body weight effectively and prevent it from increasing with diet and lifestyle modifications. It was demonstrated that some statins, including simvastatin, lead to a relevant decrease of chronic inflammation markers excreted in urine [11]. Therefore, the therapy of hypercholesterolemia and dyslipidemia is crucial for the prevention of an acute cardiovascular incident in patients with obesity.

Material and methods

The study included 157 consecutive patients referred to the Outpatient Department of Metabolic Disorders and Arterial Hypertension with hypercholesterolemia diagnosis. Patients were assigned based on body weight and BMI (body mass index) into three groups:
1) patients with normal body weight (BMI 18.5<25),
2) overweight patients (BMI >25-30),
3) obese patients (BMI >30).

The therapeutical effects were studied 6 and 12 months after the initiated therapy. The degree of body weight reduction, incidence and time frame of normal lipid panel, incidence and time of drop-outs in relation to the remaining IND and CVI risk factors were studied.

The exclusion criteria were: neoclassic disorders, chronic liver disease, renal failure, illicit drug, psychoactive drugs and alcohol abuse. The study groups were comparable with respect to age and sex. The majority of study subjects were women. At the initial visit, anthropometric data were collected in addition to medical history with emphasis on coexisting diseases and current medication. At the time of enrollment into the study, the patients did not receive any hypolipemic medications within three preceding months.

The study subjects individual cardiovascular risk was considered to determine target total, LDL cholesterol and triglyceride levels based on the III NCEP report. Hypolipemic drug dosages were determined empirically. The patients in each group received similar doses of lovastatin, simvastatin and atorvastatin in a similar daily schedule. The average dose of a statin was 20 mg. The medical history of stroke, TIA (transient ischemic attack) and arteriosclerosis obliterans was within similar frequency among the study groups. In patients with obesity, the incidence of diabetes mellitus was increased up to 25%. Also, among overweight patients, the incidence of diabetes mellitus was 17.65%. Arterial hypertension was diagnosed in 80.39% overweight patients. The percentage of patients with arterial hypertension was comparable in obese and normal body weight subjects; it was 69.4% and 64.71%, respectively. The highest percentage of patients with IHD (58.82%) was found in the patients with normal body weight. The concomitant medication included: hypotensive drugs (ACE inhibitor in 40.76% study subjects), diuretics (39.5%), calcium channel blockers (23.57% patients), (metformin (12.1% patients), sulphonylurea

Table I. The BMI index and lipid concentrations at control visits

Study subjects	n	Age (years)	% studied	Initial BMI	% patients with reduced BMI after 12 months	% patients without BMI change after 12 months	% patients with increased BMI after 12 months	Mean BMI after 12 months	Mean lipid concentration in control intervalsmmol/l			
									study parameter	before therapy	6 months	12 months
All	157 (105 K, 52 M)	59.22±10	100	29,6±5.2	30.6	32.5	29.3	29.5±5.61	Chol C	7.0±1	5.5±1.12	5.21±1.1
									Chol HDL	1.58±0.47	1.57±0.42	1.52±0.36
									Chol LDL	4.45±1	3.36±0.86	3.07±0.99
									TRIG	1.98±1.17	1.61±0.99	1.44±0.75
BMI >30	72 (46 K, 26 M)	57.03±8.67	45.9	34.2±3.6	30.6	20.8	40.28	34.53±3.86	Chol C	6.3±0.87	5.42±1	5.16±1.18
									Chol HDL	1.5±0.4*	1.5±0.31	1.43±0.29*
									Chol LDL	4.17±1.01	3.23±0.89	3.05±1.04
									TRIG	2.17±1*	1.69±0.9*	1.64±0.8*
BMI 25<30	51 (40 K, 11 M)	61.92±10.37	32.5	27.5±1.7	29.4	35.3	25.5	27.44±2.15	Chol C	7.28±1.19*	5.49±1.3	5.4±1.03
									Chol HDL	1.6±0.53	1.62±0.52	1.59±0.43
									Chol LDL	4.81±1.1	3.45±0.96	3.2±1.03
									TRIG	1.92±1.39	1.68±1.01	1.38±0.68*
BMI 18.5<25	34 (19 K, 15 M)	59.79±11.23	21.7	23.2±1.4	32.4	52.9	11.76	22.99±1.72	Chol C	6.94±0.85	5.7±1.04	5.03±1.04
									Chol HDL	1.68±0.51	1.62±0.41	1.57±0.35
									Chol LDL	4.46±0.63	3.47±0.62	2.92±0.84
									TRIG	1.71±1.1	1.38±1.11	1.15±0.44

derivatives (13.36% patients), beta-blockers (33.76% patients) and 75 mg aspirin (36.94% patients). The study subjects were educated with respect to an appropriate diet and healthy lifestyle. Patients visits were scheduled every three months during the study and three months after its termination. The anthropometric evaluation and lipid panel was performed 6 and 12 months after the study enrollment. The degree of body weight reduction, incidence and the time of normalized lipid panel in relation to the remaining risk factors of IHD and CVI (according to the NCEP III report) [12] was assessed in the study groups as well as the time and the reasons of study dropouts. Subjects who gave up the hypolipemic therapy were included among those who did not obtain the therapeutical targets. The effective body weight reduction was defined as its decrease by at least 2 kg on the consecutive measurements. The body weight increase was defined as its increase by at least 2 kg on the consecutive check-up. Also, the body weight changes less than 2 kg were defined as the lack of body mass changes.

Statistical analysis

The data are expressed as mean ±standard deviation. Comparison were computed with two tailed t-test and F test with two samples for variations. The level of p less or equal to 0.05 was considered significant.

Results

The highest serum total cholesterol level was found in the overweight patients at the beginning of the study. After six months, the percentage of patients achieving therapeutical targets was 30.56% in the obese group and 29.41% in the normal weight patients. The percentage of patients who achieved therapeutical targets after six months was higher in the overweight patients (35.29%). After twelve months, the highest percentage of patients achieving therapeutical targets was 47.06% in patients with normal weight. The percentage of successful therapeutical outcomes did not change among the obese patients. However, there was the highest percentage of those who failed to reach the therapeutical targets among the obese patients (69.44%). Among the overweight patients, the percentage of failures was 60.78%, whereas in the patients with normal body weight it was 52.94%. The lowest fraction of dropouts from the hypolipemic therapy was noted in the obese and the overweight groups: 12.5% and 13.73%, respectively. The highest percentage of incompliant patients or failing to continue the therapy for a whole study period was found among subjects with normal body weight. After 12 months, the similar number of patients lost weight: 30.6%, 29.4% and 32.4% in the obese, overweight and normal subjects, respectively. The highest number of obese patients further gained weight: 40.28% among

Table II. Patients and the time frame to reach target TCHOL and LDL levels (III NCEP) and concomitant disease

Study subjects	n	Target levels reached after 6 mths therapy		Target levels reached after 12 mths therapy		All patients with target levels reached and maintained after 12 mths therapy		No target levels reached after 12 mths therapy		Drop-outs due to lack of motivation %		Drop-out due to side effects		Hyperlipidemia associate diseases									
		N	%	N	%	N	%	N	%	N	%	N	%	HA		IHD		TIA/stroke		diabetes		AO	
														N	%	N	%	N	%	N	%	N	%
Total	157 (105 K, 52 M)	50	31.85	27	17.2	58	36.94	99	63.06	23	14.65	3	1.91	113	71.97	87	55.41	6	3.82	28	17.83	6	3.82
BMI >30	72 (46 K, 26 M)	22	30.56	9	12.5	22	30.56	50	69.44	**9**	12.5	2	2.78	50	69.4	23	31.94	3	4.17	18	25	2	2.78
BMI 25<30	51 (40 K, 11 M)	18	35.29	8	15.69	20	39.21	31	60.78	7	13.73	1	1.96	41	80.39	**24**	**47.06**	1	1.96	9	17.65	3	5.88
BMI 18.5<25	34 (19 K, 15 M)	10	29.41	10	29.41	16	47.06	18	52.94	7	20.59	0	0	22	64.71	20	58.82	2	5.28	1	2.94	1	2.94

this group. The lowest percentage of patients who gained weight was noted among overweight patients – 25.5%, whereas the lowest number of patients who gained weight was noted among the normal weight subjects. The most benefits related with the hypolipemic therapy were found in patients with normal body weight. After 12 months of therapy their total cholesterol was the lowest (this level was not significantly different from the levels in the remaining groups), whereas HDL cholesterol was significantly increased and triglycerides significantly decreased compared with the obese group. The serum level of triglycerides was significantly increased at all studied time points in the obese patients. After a 12 month therapy, obese patients had the lowest and significantly decreased total cholesterol. The side effects of hypolipemic medications were rarely found in the obese and the overweight groups. One patient complained of chronic muscle pain, another suffered from intense headache and hair loss and one patient reported gastrointestinal disorders. The hypolipemic therapy was discontinued in these patients due to the side effects. The detailed results are depicted in Tables I and II.

Discussion

The most benefits from hypolipemic therapy were demonstrated in patients with normal body weight. These benefits could have been even greater if the patients had not been more prone to be non-compliant and quit the therapy more readily than others. The obese patients were the least likely to quit the therapy, however they were most often non-compliant with diet recommendations and gained on weight. The moderate benefits form the therapy were demonstrated in the overweight patients. There was a remarkably high percentage of patients who failed to achieve the therapeutical targets regardless of the study group. It was apparently related with low target levels of cholesterol in patients with numerous risk factors of IHD and CVI. According to the recommendations from the III NCEP report, these patients should reach LDL cholesterol level below 100 mg/dl. The non-compliance with diet recommendations and the schedule of hypolipemic pharmacotherapy were the main reasons of failure in reaching the therapy targets. It also is likely that obese and overweight patients should be considered for the initial therapy with a statin at the increased dose with a strong inhibitory effect on liver cholesterol synthesis (i.e. simvastatin, atorvastatin).

Conclusions

1. The time period and likelihood of achieving normal serum lipid panel is markedly related with initial body weight. The same doses of hypolipemic medications were less likely to bring successful results in the overweight patients if compared with the patients with normal weight.
2. The most benefits from the 12 months hypolipemic therapy were demonstrated in the patients with normal body weight.
3. The obese and overweight patients were less motivated to diet and lifestyle changes, which is related with the increased incidence of those who gained on weight during the therapy.
4. The patients with normal body weight were the least motivated to be compliant with regular doses of hypolipemic medications and were the most likely to quit the therapy.

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