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Title of Project:

“Intensive Management of Dyslipidemia in Patients with Peripheral Artery Disease Including Their Families in Primary Care”

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Inclusive Dates of Project: 2014-2016.

Acknowledgment of Agency: This project was supported by Pfizer, Inc. ((Independent Grants for Learning & Change (IGLC) Pfizer, Inc.)) and International Atherosclerosis Society.

Grant Award Number: ID: 11532049

Abstract:

Purpose: The main goal of this project was to improve effectiveness of the preventive care for patients with peripheral artery disease (PAD) through introducing intensive and individualized management of cardiovascular risk factors including family members. **Scope:** One one hand, this population is at extreme risk for cardiovascular events; on the other hand, it is in general less compliant for lifestyle measures. This population was invited for interview with nutritional specialist ,specific educational materials were developed and several parameters of effectivity of this intervention were evaluated. **Methods:** Algorithm was developed to establish cooperation between primary care physicians, angiologists, lipidologists and, most importantly, nutritional specialists. This approach was tested on 30 general practitioners, 6 specialists, 4 nutritional specialists and 300 patients and their relatives. **Results:** More than 300 patients were included together with their family members. The main factor was the change of LDL cholesterol. The final visit was accomplished in 73 patients. LDL cholesterol decreased by 0.6 mmol/l based on improved lifestyle changes but also based on increased compliance to hypolipemic therapy, mainly statins. Most robust changes were observed between the first and second visit/intervention. No substantial effect of inclusion of relatives was observed. Information about the study and its results was presented at meetings of professional societies, including conferences of general practitioners and through several websites of professional societies. Obtained results were published in the Czech journal for general practitioners. Main benefit of the project was implementation of specialized multidisciplinary care for patients with PAD.

Key words: peripheral artery disease – dyslipidemia – risk factors management - lifestyle intervention

OBJECTIVES OF THE STUDY:

The particular aims of the project were as follows:

1. To increase the awareness and effectiveness of treatment of dyslipidemia in patients with peripheral artery disease (PAD) while also including patients' relatives.
2. To establish a system of detection and care of these high-risk patients on a long term basis at the level of primary health care with the support of the team of specialists.

SCOPE:

One of the most endangered and, at the same time, almost neglected patient groups at high risk for cardiovascular are patients suffering from PAD. On one hand these patients are at extreme risk for cardiovascular events; on the other hand, these patients rank among those least compliant based on high prevalence of smoking, obesity and diabetes mellitus. In addition to these factors, these patients are also exposed mainly to mixed dyslipidemias, often resistant to simple drug/statin treatment. Combination of statins with fibrates could improve the situation only moderately and clinical outcomes from randomized studies focused on this combination are controversial. Other potentially effective approach is, therefore, intensive intervention of lifestyle including cessation of smoking, increased physical activity and appropriate change of dietary habits. If this approach is successful, it can substantially protect patients with PAD from cardiovascular events. In addition, the effectiveness in the care for patients with PAD could be substantially enhanced by an interdisciplinary approach between general practitioners, angiologists, lipidologists, but mainly by intensive cooperation with nutritional specialists and their tailored management of individual patients regarding favorable changes in lifestyle.

METHODS:

Regarding above discussed facts, we intended to expand the care for patients with PAD by a more intensive and individualized approach based on lifestyle measures and focused on lipid disorders.

In particular, this intervention was accomplished at the level of primary health providers/general practitioners in cooperation with three professional societies: Czech Atherosclerosis Society, Czech Society of Angiology and Forum for Healthy Nutrition. Czech Atherosclerosis Society was responsible for organization of the project and for education of management of dyslipidemias. Czech Society of Angiology was responsible for special care regarding patients with PAD and addressed primary care physicians from previous projects. To accomplish lifestyle intervention, the Forum of Healthy Nutrition and its specialists, namely nutritionists were involved and they developed

comprehensive educational materials. Comprehensive educational materials both for the education of health care professionals, but mainly for patients with PAD were developed. Interdisciplinary educational meetings were organized throughout the whole study. In summary, the team including lipidologists, angiologists and nutritionists collaborated with 30 selected primary care physicians in detecting and treating dyslipidemias in patients with PAD.

Primary care physicians/general practitioners

The first step was one-day meeting of the 30 selected primary care physicians. During the first meeting basics in angiology and lipidology were presented by specialists and participants filled the test, which was immediately evaluated. Subsequently, several other meeting were organized, focused on the education in the field of angiology and lipidology, another tests and their evaluation and at the end of the study mainly on discussions of complicated cases.

Patients

1. The first contact with patients with PAD was by general practitioner, who explained the purpose of the project. After patient approval, the first visit with nutritionist was scheduled including participation of family members. This was accomplished in 1-2 months in most participants.
2. During the first – inclusion – visit the patient and his/her family received educational materials, pedometer, and special tape for measurement of waist circumference with instructions how to use these instruments. At the time of this first visit, fasting plasma lipids, glycaemia, other appropriate biochemical factors (creatinine kinase, liver tests, plasma creatinine), and, if indicated, thyroid stimulating hormone (TSH) were measured. According to values of plasma lipids focused dietary instructions were given and treatment with hypolipemic drugs/statins was consulted. In the case, that serum LDL cholesterol was higher than 5 mmol/l and/or triglycerides more than 5 mmol/l or other problems (intolerance of statins, ...) were encountered, lipidologists (JP, MV) were involved and hypolipemic therapy managed immediately. In the case, that some angiological problem was encountered, angiologist was immediately informed (KR), with referral of the patient to appropriate department.
3. Following visits were scheduled according to the progress of patient status regarding risk factors under study, especially lipids and particularly LDL cholesterol. These visits were in 1-3 months intervals. During the whole follow up at least two visits with serum lipids measurements were scheduled.

Following parameters were monitored:

Data were obtained in a single sheet protocol for each patient and his/her family members. Data were collected in a simple database. The main goals of intervention were as follows:

1. To reach values of LDL cholesterol below 2,0 mmol/l in at least 75 % of patients
2. To reach values of triglycerides below 1,7 mmol/l in at least in 50 % of patients
3. To manage/achieve quitting smoking in at least 30 % patients/ active smokers
4. To decrease of waist circumference at least by 3 cm

Statistical processing of the data was done by program SigmaPlot 11.0,. Differences were evaluated by paired t-tests. Frequency analyzes were processed using MS Excel 2010. Differences between men and women, smokers and non-smokers and between patients with and without active family involvement were calculated using non-paired (Student) t-test in Excel and SigmaPlot 11.0.

RESULTS

Principal findings:

At the beginning of the study 60 physicians were addressed, 25 entered the study, 12-15 were able to visit workshops on a regular basis. More than 300 patients were addressed, 120 were able to be intervened at least at the first visit and continue in this activity and 73 were fully evaluated including repeated measurements of plasma lipids and other parameters. The relatives were able to come to the first visit in half of participants. Only 11 patients were able to participate through whole follow up with at least 2 family members involved.

Full data were analyzed in 73 patients (44 males), mean age 65.5 ± 31.5 , 32 (44 %) had a history of other cardiovascular diseases, 18 reported diabetes mellitus (25 %), 25 (34 %) reported active smoking and 45 (62 %) reported hypertension. By hypolipemics were treated 48 patients (65.8%), of whom 38 were taking statins (79.2 % of all hypolipemics), 1 patient was treated with the combination of statin with ezetimibe and 5 patients were treated by statin with fibrate (10.4 % of all hypolipemics).

Comparison of parameters under study with “background” Czech population and from previous study focused on statin treatment is shown in Table 1. The most striking difference was higher frequency of hypolipemic treatment in patients in our study ($p < 0.0001$) accompanied by lower LDL cholesterol ($p < 0.0001$) and lower triglycerides ($p = 0.03$).

TABLE 1:

Data from the study on patients with peripheral artery disease (MOET study).

	Patients with peripheral artery disease	Patients with peripheral artery disease	Czech population (Monica study)
Men/women (n)	77/49	2,455/1,466	1,229/1,392
Mean age \pm SD (years)	65.5 ± 31.5 *	65.8 ± 9.9	49 ± 11
Current smokers x nonsmokers	39.7 % x 60.2 %	34.7 x 43.8	33.8 x 66.1

(%)			
Diabetes mellitus (%)	27.4 %	36.5	13.8
Hypertension (%)	64.4 %	78.9	37.5
Stage PAD 1-3 (Fontain) (%)		90	-
Mean body mass index \pm SD (kg*m ⁻²)	28.98 \pm 5.41	28.6 \pm 4.5	28.4 \pm 4.5
Mean LDL cholesterol \pm SD (mmol/L)	3.15 \pm 1.14	3.63 \pm 1.05	3.70 \pm 1.1
Mean triglycerides \pm SD (mmol/L)	2.05 \pm 1.46	2.30 \pm 1.24	1.70 \pm 1.1
Mean HDL cholesterol \pm SD (mmol/L)	1.42 \pm 0.58	1.34 \pm 0.51	1.37 \pm 1.24
Treatment with statins * (%)	60.27 %	21 %	6 %

Legend:

* Youngest age - 34 years

**Statin + ezetimib 1,37 %; statin + fibráty 4,11 %; fybráty 5,48 %; bez hypolipidemik 28,77 %

Outcomes:

Changes of parameters under study in the whole group of patients:

In general, from qualitative point of view the main changes were observed in dietary habits. Patients reduced consumption of butter and lard, started to prefer vegetable oils and other fats containing more unsaturated fatty acids, they reduced consumption of sausages and other meat products, they increased consumption of vegetables and fruit, they reduced frequency of consumption of fried food, consumption of cakes and sweets and reduced consumption of sweetened drinks. In addition, they increased physical activity. On the contrary, reduction of smoking was minimal, persisted irregularity in taking meals and patients did not reduce consumption of high fat dairy products.

From quantitative point of view, statistically significant or marginally significant changes were observed in the following parameters: total cholesterol decreased from 5.23 mmol/l to 4.53 mmol/l (p=0.09), LDL cholesterol decreased from 3.15 mmol/l to 2.55 mmol/l (p=0.016). The most robust reduction in LDL cholesterol (p = 0.021) was observed in most of patients between the first and second visit/consultations, but then its level remained stable. Similar trends were observed in triglycerides and other parameters under study. HDL cholesterol moderately decreased. In addition, during the first follow up study the number of patients treated by hypolipaemics rose to 81.3 %, of which 88.5 % were treated with statins.

Regarding differences between men and women - at the beginning of the study: waist circumference was, as expected, lower in women ($p=0.026$), triglycerides were moderately lower in females ($p=0.072$), on the contrary, glycated hemoglobin was lower in men ($p = 0.054$).

Results of interventions between first and second visit were as follows (Table 2): statistically significant or marginally significant differences after intervention in men were found in the following parameters: LDL cholesterol moderately decreased ($p=0.096$), simultaneously decreased HDL cholesterol ($p=0.024$). No other marginal or statistically significant differences were encountered. In women, there was a statistically significant or marginally significant differences in these parameters, body mass index (BMI) decreased ($p=0.034$), LDL cholesterol decreased from 3.45 to 2.61 mmol/l ($p=0.088$). Changes of parameters under study did not differ between men and women. In addition, no significant effect of inclusion of relatives was detected and no difference in risk factor changes was observed between smokers and non-smokers.

As already mentioned, greatest effect of intervention was detected between 1st and 2nd visit (first follow-up) then this effect became moderate and in most parameters not significant and/or some kind of rebound phenomenon was observed with the exception of LDL cholesterol level. The latter finding was potentially caused also by the increase in statin treatment.

In general, in the whole population, LDL cholesterol goal below 2,0 mmol/l reached 30 patients (40 %) and 28 patients (38 %) reached triglyceride level below 1,7 mmol/l at the first visit. These percentages went little down at final visit.

TABLE 2

Changes in Risk Factors in Patients with Peripheral Artery Disease

(mean \pm SD if not stated differently, statistical significant differences described in the text),

Men (n=44), Women (n=29)

	1 st visit		2 nd visit		Final visit	
	Women	Men	Women	Men	Women	Men
Body mass index (kg*m ⁻²)	26.83 \pm 3.61	30.17 \pm 5.78	30.18 * \pm 5.01	28.44 \pm 3.48	30.18 * \pm 5.01	29.56 \pm 4.06
Waist circumference (cm)	98.35 \pm 11.07	106.67 \pm 14.75	102 * \pm 12.02	102.92 \pm 11.46	102 * \pm 12.02	108.25 \pm 8.1
LDL cholesterol (mmol/l)	3.13 \pm 1.74	3.13 \pm 1.15	2.61 \pm 0.8	2.51 \pm 0.91	2.89 \pm 1.3	2.35 \pm 0.61
Triglycerides	1.66	2.3	1.25	2.24	1.53	2.02

(mmol/l)	± 1.23	± 1.54	± 0.56	± 1.66	± 0.65	± 1.23
HDL cholesterol (mmol/l)	1.87 ± 0.63	1.15 ± 0.23	1.39 ± 0.37	1.23 ± 0.28	1.51 ± 0.55	1.22 ± 0.26
Glycemia (mmol/l)	5.56 ± 1.18	5.92 ± 1.23	5.43 ± 1.43	5.72 ± 0.93	5.82 ± 0.61	5.66 ± 0.98
Glyc. Hb mmol/mol	59 ± 8.72	52.9 ± 13.24	49.8 ± 15.69	44.5 ± 6.62	43	42.4 ± 4.51
Smoking (%)	37.93	40.9	33.33*	35.71	33.33*	35.71

Legend: * in women 2nd and final visit were merged

Discussion:

The overall ambition of this activity was to increase skills of primary care providers/general practitioners in detecting and treating dyslipidemias and to establish their cooperation with nutritional therapists, lipidologists and angiologists and thus improve overall cardiovascular risk profile in patients with PAD. Based on this cooperation and effort there was achieved the improvement of diet, physical activity and also increased compliance with hypolipemic drugs. These changes were reflected mainly in decreased body mass index, waist circumference, decreased LDL cholesterol and triglycerides. However, despite substantial decrease the level of LDL cholesterol was still above the safe values in more than half of patients in this population at extreme risk. Despite decrease of HDL cholesterol in men we believe, based on our previous data is not unfavorable change if associated with positive changes of other lipid parameters induced by diet and/or exercise.

Not achieved was smoking cessation and two thirds of patients were not able/willing to finish the whole follow-up including repeated lipid measurements. Also only third of primary care physicians were able to stay in the project during the whole period. Nevertheless, several remaining physicians are enthusiastic to continue this project beyond scope of this study and without further financial support.

It is of interest to compare this study with our past experience in the study entitled “Monitoring of Effective Therapy in PAD” (MOET study) focused on statin treatment in patients with PAD. This study led to an important decrease in total cholesterol, LDL-cholesterol, triacylglycerol levels after 12 months, however, almost exclusively caused by more intensive statin treatment. In addition, no further data after one year of this study are available. In MOET study, lifestyle intervention was done only in very general terms by non-trained physicians. Therefore, the main effect was increased treatment with statins – at the beginning only 21 % of patients with PAD were on statins (Table 1), at the end more than 90 % - close to our numbers at the end of the project. In contrast to MOET, our project was more

focused on lifestyle intervention and on more complex management, as to our opinion more favorable and durable approach.

Conclusion:

Algorithm in the care for patients with PAD was established regarding cooperation between primary care providers/general practitioners, angiologists, lipidologists and, most importantly, nutritional specialists. This algorithm was tested in everyday practice. Despite that only third of primary care providers and patients were able to complete the whole follow-up including detailed measurements of lipid parameters it had substantial impact on complex risk profile, mainly plasma lipids. Nevertheless, the main change was observed between first and second visit. Therefore, the effect of lifestyle intervention is attenuated after certain period of time in most of patients. This implicates need for sustained lifestyle intervention not limited by predefined time periods.

Significance:

Main benefit of the project in addition to already mentioned template how to decrease cardiovascular risk in patients with PAD is that this information is now available for high number (thousands) of primary care providers and hundreds of specialists. This was accomplished by presentation on web pages, conferences and publications in medical journals. Another benefit was, that educational materials were developed, which could be used not only for patients with PAD but also for other populations at high/extreme cardiovascular risk.

Implications:

Information regarding this project is now well known in Czech Republic and will be spread further in this year (2017). In addition, we recently applied for grant support from Ministry of Health, Czech Republic for prolongation of this project; in this application we used data and experiences obtained at this project. Another step is to negotiate with healthcare authorities, providers and payers (professional societies, Ministry of Health, insurance companies) to include this approach into regular (and thus funded) medical care including more intensive involvement of professional and certificated nutritionists in the care of high risk patients including patients with PAD. Because of high prevalence of PAD and other cardiovascular diseases of atherosclerotic origin in Czech Republic this approach could have robust impact on cardiovascular risk and subsequent cardiovascular events.

LIST OF PUBLICATIONS , PRESENTATIONS, VIDEO

Publications:

Pitha J, Boháčová V, Doubková K, et al. Projekt intenzivního ovlivnění dyslipidemií u pacientů s ischemickou chorobou dolních končetin Practicus (XII), 2016, p. 9-11 (<http://web.practicus.eu/sites/cz/Documents/Practicus-2016-10/09-ICHDK.pdf>).

Video:

https://drive.google.com/open?id=0B_DK0P2BKVVvRnVtTVBPR3U5YTA

Web pages/educational materials:

<http://www.prevence-ichdk.cz/index.php/konzultace-lekari>

Congresses:

40th Czech Angiology days 2015, Prague, February 2015

XXIIIrd Annual Congress of Czech Society of Cardiology, Brno, May 2015

XXXIVth Annual conference of Czech Society of General Practice, Zlín, November 2015

Šobra Day - XXIXth Conference on Hyperlipoproteinemias, Prague, June 2015

19th Congress on Atherosclerosis, Špindlerův Mlýn, December 2015

41st Czech Angiology days 2016, Prague, February 2016

Spring Interactive Conference of Czech Society of General Practice, Prague, April 2016

Cardiovascular Prevention Course, Prague, September 2016

Cardiovascular Prevention Course, Brno, September 2016

Specialized Nutrition konference Exercise and Nutrition, Prague, October 2016

XXXVth Annual conference of Czech Society of General Practice, Karlovy Vary, November 2016

20th Congress on Atherosclerosis, Špindlerův Mlýn, December 2016

XXXth Seminar Prevention of coronary heart disease from childhood, Poděbrady, January 2017

42nd Czech Angiology days 2017, Prague, February 2017