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Case report

Risk reduction of atherosclerotic cardiovascular disease through triglycerides management: Case report

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Abstract Despite extensive studies of strategies to prevent and treat risk factors after myocardial infarction, current evidence documents disappointingly slow, and in many cases limited, implementation of these therapies in practice and daily life. Thus, secondary prevention programs were recognized by the guidelines and introduced in everyday clinical practice around Europe. Programs include a range of interventions with health education, lifestyle advice, risk factors control, stress management and physical exercise components – exercised based cardiac rehabilitation, in order to reduce risk of morbidity and mortality among cardiac patients

In 2019 new guidelines for the management of dyslipidaemias recommended drug treatment of hypertriglyceridemia in high risk individuals if triglyceride level is above 2.3 mmol/l. Through case report we aimed to present the steps in recommended risk reduction of atherosclerotic cardiovascular disease through triglycerides management.

Kew words risk factors, hypertriglyceridemia, drug treatment, secondary prevention programs, exercise based cardiac rehabilitation

Introduction

Current guidelines from the European Society of Cardiology recommend exercise-based cardiac rehabilitation (CR) for patients after myocardial infarction, as a part of secondary prevention programs. Specialized prevention programs are delivered as CR or other prevention programs for all patients with CVD or at high risk for CVD by cardiologist. The core components and goals of CR have been standardized, but the structure, length and type of program offered differs widely by country. CR is a comprehensive programmed involving exercise training, risk factor modification, education and psychological support (1-3)

In this case report we present a young patient who was referred to our cardiology department for out-patient exercise-based cardiac rehabilitation after myocardial infarction, with special emphases on triglycerides management and risk reduction of further atherosclerotic cardiovascular disease progression.

Case presentation

A 42-year-old male was referred to our Cardiology department for out-patient 12 weeks cardiac rehabilitation program after myocardial infarction. The patient was not able to attend the in-house program due to life circumflecses (unable to get paid 3 weeks leave of absence from his work, single parent)

Patient assessment on admission – mid june 2019
History of present illness and previous heart investigations

- In the end of April 2019 patient was admitted to Coronary Care Unit due to acute myocardial infarction – STEMI of inferoposterior wall, two hours after the beginning of chest pain
- PPCI was performed: two vessel diseases, RCA was infarct related artery, LAD was presented with medial stenosis of 30% and in distal segment was sub occluded, RCA was opened and drug eluted stent was implanted. POBA of LAD was scheduled and performed after 6 days of STEMI.
- Cardiac echo: Normal dimensions of chambers with wall motion abnormalities according infarction localization, EF 40%
- Lab analysis in acute settings: TC 5.27, LDL 2.13, TG 4.93mmol/l
- Risk factors for coronary artery disease: smoking, no familiar history, Wt 81kg, Ht 182cm, waist circumference 95cm

Past medical history: none

Physical activity level: sedentary lifestyle, walking up to 2 km, not on regular bases

Medications on discarge from acute hospital: ASA 100mg, Ticagrelor 90 mg 2x1, ramipril+ hidrohlotriazide 5mg+12,5mg 1x1, Bisoprolol 5 mg, , Rosuvastatin 20 mg 1x1, lansoprazol 15mg

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Discarged plan from acute hospital: TC, HDL, LDL, TRGL were order for first control scheduled in 6 weeks, plus CK, AST, ALT

Medications on admission to cardiac rehabilitation: ASA 100mg, Ticagrelor 90 mg 2x1, ramipril+ hidrohlotrtiazid 5mg+12,5mg 1x1, Bisoprolol 5 mg, Lansoprazol 15mg. Due to arise in ALT -Rosuvastatin 20 mg 1x1 were stopped two weeks before admission to Our Institution)

Vital signs on admission to secoundary prevention program:
BP 110/70mmHg • Pulse 72/min • Temp 36,6 °C • Resp 20 • Ht (1.82 m) • Wt 82 • BMI 24.8 kg/m2 • SpO2 99%, waist circumference 95cm
Labs: • WBC 5.8 • RBC 4.54; Hb 131; Ht 0,398, Na 139; K 4.0 TC 4.53, HDL 0.92, LDL 3,18, TG 3,3 • Glucose 5.14
Physical examination: no signs of heart failure, good blood pressure regulation, ECG: sin. rhythm, heart rate 72/min, q with negative T in D2, D3, aVF
Exercise capacity on entrance: estimated by exercised stress test: 10minutes and 6sec 25W, 50W, 75W and 100W for two minutes, max BP 165/105mmHg, heart rate 136/ min
Twelve weeks out-patients exercised- based cardiac rehabilitation program was created individually according to patient's age, past habits, risk factors, co-morbidities, preferences and goals, with aim to:

1. Improve exercise capacity – 30 min moderate intensity aerobic activity 3 days a week with progression to 45 minutes in follow up: continues endurance training with heart, ECG and blood pressure monitoring regarding the heart rate reserve + resistance training
2. Perform additional heart test – 24h ECG monitoring, BP monitoring, echocardiography (EF48%) and lab analysis – HBA1C
3. Optimize medical therapy:
   a. blood pressure control: doses optimized
   b. better lipid levels control: to archive not only LDL but also TG goals according the guidelines
   c. heart rate control
4. Educate the patient: diet intake, risk factors control, stop smoking, regular physical activity, limited alcohol intake

Medication during secoundary prevention program

1. ASA 100mg
2. Ticagrelor 2x90mg
3. Bisoprolol 5 mg OD
4. Ramipril 5 mg OD
5. Rosuvastatin 20 mg OD
6. Ezetimibe 10 mg OD
7. Fenofibrate 160 mg
8. Lansoprazol 15mg OD

Additional heart test were performed. The results were as follows:

1. During 24 hours of ECG recording the mean heart rate was 61/min, minimal heart was 46/min at 2.00am, maximal 111/min at 9.am. No episodes of atrial fibrillation were recorded; there were 11 SVES and 2 VES.
2. Echocardiography exam: left ventricle was normal in diameter with mid range ejection fraction, EF 48%
3. Lab analysis after 12 weeks: LDL 1,01 mmol/l, TG 0,73 mg/ml, HbA1C within the reference range

Exercise capacity at the end of the program: estimated by exercised stress test: 12minutes and 8sec 25W, 50W, 75W,100 W, 125 W for two minutes, max BP 190/115mmHg, heart rate 150/ min.

Secondary prevention: exercised based cardiac rehabilitation program:

1. It is recommended to initiate exercise training in a structured, supervised, centre-based program
2. It is mandatory that (sub) maximal exercise capacity is measured with a symptom-limited cardiopulmonary exercise test or exercise stress test. Based on the results:
   • training intensity and perform training adjustments were determined
   • risk and prognosis were determined
   • Re-test after exercise training program was done to objectify improvement in exercise capacity
3. A universal agreement on the best training modality in heart failure with mid range EF does not exist. An individualized approach is recommended. Training protocols vary in a number of ways: intensity (aerobic and anaerobic), type (endurance, resistance) and method (continuous and interval). Continuous endurance training is the best described form of exercise training and, because of its well-demonstrated efficacy and safety, is highly recommended in the guidelines. It is characterized by a moderate-to-high exercise intensity at steady-state condition of aerobic energetic yield, allowing the patient to perform prolonged training sessions (45-60 min duration). The exercise is usually performed on a bicycle or treadmill.
4. Resistance/strength training has been proposed to prevent the wasting syndrome and to incorporate upper body exercise, which is important to complete daily life tasks. It is important to prescribe dynamic resistive exercise training of small muscle groups and to avoid Valsalva maneuvers. The patient's preferences should be taken into account

Discussion

The previous ESC/EAS lipid Guidelines were published in August 2016.The emergence of a substantial body of evidence over the last few years has required new, up-to-date Guidelines. In 2019 ESC/EAS Guidelines were presented[3].
New evidence has confirmed that the key initiating event in atherogenesis is the retention of low-density lipoprotein (LDL) cholesterol (LDL-C) and other cholesterol-rich apolipoprotein (Apo) B-containing lipoproteins within the arterial wall[3].Several recent placebo-controlled clinical studies have shown that the addition of either ezetimibe or anti-proprotein convertase subtilisin/kexin type 9 monoclonal antibodies to statin therapy provides a further reduction in atherosclerotic cardiovascular disease (ASCVD) risk, which is directly and positively correlated with the incrementally achieved absolute LDL-C reduction.

What is new in 2019 Guidelines regarding triglicerydes?

Statin treatment is recommended as the first drug of choice for reducing CVD risk in a high –risk individuals with hypertrigliceridemia (TG >2.3 mmol/l – 200 mg/dl) as stated in new 2019 guidelines. In 2016 it was stated that statin treatment might be used as the first drug of choice in patients with hypetriglyceridemia without considering the cut off values. AHA guidelines from 2018 did not consider hypetrigliceridemia separately[4].

Since TG-rich VLDL particles and their remnants carry most of the circulating TGs, the plasma TG concentration reflects the concentration of circulating ApoB-containing TG-rich lipoproteins. According to 2019 guidelines[3] elevated plasma TG levels are associated with an increasing risk of ASCVD, but this association becomes null after adjusting for non-HDL-C, an estimate of the total concentration of all ApoB-containing lipoproteins. Lowering TG with fibrates reduces the risk of CV events by the same amount as LDL-C-lowering therapies when measured per unit change of non-HDL-C, suggesting that the effect of plasma TGs on ASCVD is mediated by changes in the concentration of TG-rich lipoproteins as estimated by non-HDL-C.

We presented the very high risk young patients (two vessel disease, STEMI recently, heart failure with mid range EF) 42 years of age that illustrate risk reduction of further atherosclerotic cardiovascular disease as part of secondary prevention programs through triglycerides management, potential misunderstandings and correct new guidelines interpretation. General management should address effective control of modifiable risk factors. All patients require lifelong follow up by cardiologist after MI

Cardiac rehabilitation is indicated and performed by cardiologist in Western and Central Europe but not strongly in US. Cardiac rehabilitation (CR) programs should be available for all patients with ASCVD. CR should be tailored according to individual risk profile, physical, psychological and social status assessed as part of medical history and examination[1].

Our patient had no possibilities to attend or 3 weeks inhouse cardiac rehabilitation program (patient-related gap). Thus, recently developed out- patients 12 weeks program in our Institution was indicated.

Patients with CVD understand poorly their disease and perceive themselves as having little control over its course, many lack interest in prevention and/or feel embarrassed about participating in preventive group sessions. Most of them do not receive robust information and/or encouragement from physicians and other health professionals regarding how to prevent recurrent events. Other factors, which hinder attendance, include lack of social support, poor psychological wellbeing, and inconvenient location with transport difficulties, competing work commitments and financial cost

Secondary prevention programs are created in order to promote physical activity, risk factors control, and adherence to therapy. Our patient was presented with normal BMI, no familiar history of CAD; with smoking, physical inactivity and inappropriate lipid profile low HDL, high LDL and high tryglicerides as risk factors. Thus our aim was to reduce risk by promote healthy lifestyle habits, appropriate physical activity and adherence to recommended drug therapy.

Lifestyle and triglyceride levels: Weight reduction improves insulin sensitivity and decreases TG levels. Regular physical exercise reduces plasma TG levels over and above the effect of weight reduction. Alcohol intake has a major impact on TG levels, particularly in individuals with HTG. Habitual consumption of significant amounts (>10% energy) of dietary fructose contributes to TG elevation, particularly in people with HTG or abdominal obesity. These effects are dose-dependent; with a habitual fructose consumption between 15–20% of total energy intake, plasma TG increases by as much as 30–40%. Sucrose, a disaccharide containing glucose and fructose, represents an important source of fructose in the diet[5-7].

Smoking cessation has clear benefits regarding overall CV risk, and specifically on HDL-C levels.[3]

Of great importance is regular exercise training. It was created according to clinical, baseline exercise capacity and prior habits. Endurance and resistance training were used. Moderate intensity aerobic endurance training composed of bicycling, walking and crossing over Nyllin steps, 3 times per week during 12 days. Exercise capacity of our patient was improved.

Lipid lowering drugs: Our goal was to achieve LDL levels beyond 1.4 mmol/l, and triglyceride levels below 2.3 mmol/l. Regarding LDL levels guidelines from both sides of the world (REF) are the same. During in patient CR program patient was educated in this term[3].

Statins reduce the synthesis of cholesterol in the liver by competitively inhibiting the enzyme HMG-CoA reductase, the rate-limiting step in cholesterol biosynthesis. The reduction in intracellular cholesterol promotes increased LDL receptor (LDLR) expression at the surface of the hepatocytes, which in turn results in increased uptake of LDL from the blood, and decreased plasma concentrations of LDL- and other ApoB-containing lipoproteins, including TG-rich particles[4]. Statins usually reduce TG levels by 10–20% from baseline values. (REF) More potent statins (atorvastatin, rosuvastatin, and pitavastatin) demonstrate robust lowering of TG levels, especially at high doses and in patients with elevated TGs (HTG), in whom the absolute risk, and therefore the absolute risk reduction, is larger.

Ezetimibe added to ongoing statin therapy reduces LDL-C levels by an additional 21–27% compared with placebo in patients with hypercholesterolaemia with or without established CHD. In statin-naïve patients, ezetimibe and statin combination therapy has resulted in around a 15% greater reduction in LDL-C when compared with the same statins and doses in monotherapy. Our patient was added ezetimibe to statin therapy to acchive target LDL[3].

Fibrates have good efficacy in lowering fasting TG levels, as well as post-prandial TGs and TG-rich lipoprotein (TRL) remnant particles as addition to statin therapy. In patients with high triglyceride levels [≥2.3 mmol/L (200 mg/dL)], lifestyle advice (with a focus on weight reduction

and alcohol abuse, if relevant) and improved glucose control are the main targets. Both the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) and ACCORD studies demonstrated that administration of fenofibrate on top of statins significantly reduced CV events, but only in patients who had both elevated triglyceride and reduced HDL-C levels If triglycerides are not controlled by statins or fibrates, high-dose omega-3 fatty acids (4 g/day) of icosapent ethyl may be used according to recently published REDUCE- IT investigators and guidelines (8-9).

Conclusion

2019 ESC/EAS guidelines for the management of dyslipidaemias differ to previous guidelines and 12018 AHA guidelines in term of risk reduction of atherosclerotic cardiovascular disease through triglycerides management. Statin treatment is recommended as the first drug of choice for reducing CVD risk in a high –risk individuals with hypertriglyceridemia (TG >2.3 mmol/l – 200 mg/dl)

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Sažetak

Redukcija rizika za aterosklerotsku bolest srca optimalnom terapijom triglicerida. Prikaz bolesnika

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Uprkos intenzivnim istraživanjima strategija za redukciju faktora rizika nakon infarkta miokarda u praksi, redukcija rizika je u mnogim slučajevima neadekvatna, a sprovođenje terapije ograničeno. Programi sekundarne prevencije prepoznati su u smernicama i uvedeni u svakodnevnu kliničku praksu širom Evrope. Obuhvataju niz mera koje se sastoje u edukaciji bolesnika, kontroli faktora rizika, optimalnoj terapiji, upravljaju strestom, fizičkoj aktivnosti kroz kardiološku rehabilitaciju baziranu na aerobnom treninigu. 2019 te godine smernice Evropskog druženja kardiologa preporučile su da u redukciji rizika za aterosklerotsku bolest terapija triglicerida zauzima značajno mesto. Kao prva terapijska linija preporučuju se statini ukloliko su vrednosti triglicerida više od 2.3 mmol/l.

Imali smo za cilj da kroz prikaz slučaja ukažemo na značaj sprovođenja svih mera sekundarne prevencije sa posebnim osvrtom na korekciju triglicerida u lipidnom statusu.

Ključne reči: *faktori rizika, hipetrigliceridemija, sekundarni preventivni programi, kardiološka rehabilitacija bazirana na fizičkom treningu*