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Conservative management of chronic lower limb ischaemia among elderly according to current recommendations

Leczenie zachowawcze przewlekłego niedokrwienia kończyn dolnych u osób w wieku podeszłym w świetle najnowszych wytycznych

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S u m m a r y

Manifestations of chronic atherosclerosis, such as an ischaemic heart disease, central nervous system ischaemia and chronic lower limb ischaemia (PAD) constitute almost half of the causes of death in Europe every year. Chronic lower limb ischaemia does not have to be strictly related to clinical symptoms and it is often asymptomatic. PAD (peripheral artery disease) is not only a limb ischaemia, the development of atherosclerosis is a general disease and also applies to the brain, heart and other internal organs. In relation to the above fact, patients with PAD are exposed to serious complications of vascular-ischaemic nature, including e.g. myocardial infarction or central nervous system ischaemia. The number of patients with PAD is drastically growing and has so far reached the level of 16% of the society aged over 55 – as a result, this group of patients requires a holistic approach to the problem. The diagnostic and treatment process should cover both atherosclerosis development risk factors modification as well as an antiplatelet drug therapy in order to reduce the occurrence of thromboembolism. State-of-the-art recommendations also cover the application of statins with a view of treating hypercholesterolemia, ACE inhibitors to reduce arterial hypertension and acetylsalicylic acid or clopidogrel as antiplatelet drugs. In the treatment of intermittent claudication it is also recommended to initially introduce a supervised training – marching and/or incorporate cilostazol therapy as a drug of best proven effectiveness. In patients qualified for vascular surgery, it is recommended to apply an antiplatelet therapy as an antithrombus prevention. It is also recommended to apply beta-blockers to reduce perioperative complications.

S t r e s z c z e n i e

Manifestacje przewlekłego procesu miażdżycowego, takie jak choroba niedokrwienna serca, niedokrwienie OUN oraz przewlekłe niedokrwienie kończyn dolnych (PAD), stanowią prawie połowę przyczyn śmierci w Europie każdego roku. Przewlekłe niedokrwienie kończyn dolnych nie musi mieć ścisłego związku z objawami klinicznymi i bardzo często przebiega bezobjawowo. PAD nie jest tylko chorobą niedokrwienną kończyn, rozwój procesu miażdżycowego jest chorobą uogólnioną i dotyczy również mózgu, serca oraz innych organów wewnętrznych. W związku z tym pacjenci z PAD narażeni są na poważne komplikacje o charakterze naczyniowo-niedokrwiennym, w tym np. na zawał mięśnia sercowego lub niedokrwienie OUN. Liczba osób z PAD drastycznie wzrasta i w chwili obecnej osiąga 16% społeczeństwa w wieku ponad 55 lat, w związku z tym ta grupa pacjentów wymaga całościowego podejścia do tego problemu. Proces diagnostyczno-leczniczy powinien obejmować zarówno modyfikację czynników ryzyka rozwoju miażdżycy, jak również terapię lekami przeciwpłytkowymi mającymi na celu redukcję wystąpienie powikłań zakrzepowo-zatorowych. Najnowsze zalecenia obejmują również stosowanie statyn celem leczenia hipercholesterolemii, inhibitorów ACE celem redukcji nadciśnienia tętniczego oraz kwasu acetylosalicylowego lub klopidogrelu jako leków p/płytkowych. W leczeniu chromania przestankowego zaleca się początkowo wprowadzenie nadzorowanego treningu marszowego i/lub włączenie terapii cilostazolem, jako leku o najlepiej udowodnionej skuteczności. U pacjentów kwalifikowanych do operacji naczyniowych zaleca się stosowanie terapii antypłytkowej jako prewencji zakrzepowej. Rekomenduje się również stosowanie B-blokerów celem redukcji powikłań okołooperacyjnych.

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INTRODUCTION

Chronic lower limbs ischaemia (PAD) is one of the most common and the most significant manifestations of general atherosclerosis. The disease develops with age regardless of sex (1, 2). Being over 40, the risk of PAD development increases 2-3 times every decade. PAD is strictly related to the co-presence of atherosclerosis risk factors: smoking cigarettes, diabetes, hyperlipidemia and arterial hypertension (2-4).

Along with the development of PAD, the risk of vascular and ischaemic complications increases on the side of the myocardium, central nervous system as well as the risk of death increases due to other vascular reasons (5). It is being estimated that among patients with PAD, the risk of death due to any vascular reasons is three times higher and the risk of death due to heart problems as much as 6 times higher than among the remaining population of patients (6). Sex is of no importance at this point, and the risk still remains high despite no ischaemic heart disease in the past (7, 8). It has been proven that along with the increase in the severity of lower limb ischaemia measured with determining the ankle-brachial index, proportionally the risk of myocardial infarction increases as well as of ischaemic stroke and death due to other vascular reasons (9, 10). The main goal of pharmacological treatment is aggressive modification of risk factors, which is of utmost importance in inhibiting the development of lower limb ischaemia as well as in lowering the risk of other vascular complications. Inclusion of an antiplatelet therapy along with ACE inhibitors brings some measurable benefits in reducing the occurrence of unfavourable vascular episodes.

The most common manifestation of ischaemic lower limb disease is intermittent claudication. Conservative management means first of all giving up smoking, supervised marching and pharmacological therapy aimed at inhibiting the disease's development as well as lowering the risk of the presence of vascular incidents. Patients with critical ischaemia of lower limbs require having a procedure performed supplying blood to the limb to ensure optimum treatment conditions as regards ischaemic lesions. In such cases pharmacological treatment means treatment supporting the primary procedure.

What is of significant importance in the group of patients treated with an operation is prevention against ischaemia of the myocardium in a perioperative course and long-term protection against vascular graft coagulation. Reaching these goals makes it possible to apply Beta-blockers and acetylsalicylic acid in the perioperative course.

This article constitutes a review of current recommendations concerning conservative management of chronic lower limb ischaemia the goal of which is to modify heart and vascular risk factors and lengthen intermittent claudication. Conservative management should take into account also prevention against disease development, concomitant diseases treatment, improvement in limb blood supply, prevention against necrotic lesions, treatment of skin lesions.

As it has already been stated, patients with PAD constitute a group of patients with significantly increased risk of a cardiovascular event. One should take into account the fact that the majority of them report no lower limb ischaemic disease symptoms, and half of them have had no cardiovascular events yet. History and preliminary clinical studies may be the cause of underestimation of the real number of patients with PAD. Circulation 2001' featured an article concerning the positive correlation between the coexistence of PAD and the ankle-brachial index ABI ≤ 0.9 (11). On the basis of the study of A. Hirsch published in JAMA 2003' (12) there were recommendations concerning the ABI measurement in all the patients with such symptoms, in all the patients aged 60-69 with a coexisting risk factor of a cardiovascular disease and in all the patients over 70.

The article cites the recommendations of Trans-Atlantic Inter-Society Consensus – its second edition (TASC II) (13) concerning the diagnostics and treatment of peripheral artery diseases. It is the effect of cooperation among fourteen scientific associations from Europe and North America involved in the issues of vascular diseases.

PHARMACOLOGICAL MODIFICATION OF CARDIOVASCULAR RISK FACTORS

Patients with PAD are often encumbered with multiple risk factors concerning cardiovascular complications occurrence. Many wide scope studies proved the basic role of their modification.

Giving up smoking

Smoking cigarettes is related to a significant increase in the risk of vascular complications and the development of chronic lower limb ischaemia due to atherosclerosis (14). The number of cigarettes smoked a year is significantly related to the increase in the risk of amputation, occlusion of the vascular graft and death (15). Moreover, while exercising on a track, patients-smokers with PAD reported significantly less severe pain of the shank than non-smokers (16). Therefore, giving up smoking is a significant factor in reducing the number of cardiovascular complications, yet only if it is combined with a formal programme covering the use of nicotine replacement therapy (17) and antidepressants – bupropion (18). Only the introduction of such a plan entails reaching 22% coefficient of giving up smoking within five years and compared to a 5% coefficient reached among patients treated with a standard procedure, the importance of introducing the above recommendations is visible. However, patients must be informed about the goal of giving up smoking, which is not making the claudication distance longer, but a significant reduction in the occurrence of vascular-ischaemic risk factors. None of the wide scope studies proved unambiguously that giv-

ing up smoking is related to significant increase in the length of claudication distance (19, 20). It is something the patients must be aware of, so that lack of visible lengthening in the claudication distance does not destroy the effort put into therapy (tab. 1).

Tab. 1. Recommendation 1 – TASC. Giving up smoking in peripheral artery disease

All the smoker-patients should be absolutely advised to give up smoking [B]. All the smoker-patients should be provided with a programme of doctor's advice, therapeutic groups advice and advice programme as well as a programme of nicotine substitutions [A]. The coefficients of giving up smoking may be improved with the use of an antidepressant therapy (bupropion) along with nicotine substitution [A].

Hyperlipidemia

An independent risk factor of lower limb atherosclerosis is increased concentration of total cholesterol, low-density lipoproteins (LDL) and triglycerides (TG) (21). On the other hand, increase in the level of high-density lipoproteins (HDL) is a protective factor in the development of PAD (22). Contemporary recommendations concerning treating lipid disorders in patients with PAD recommend keeping the LDL concentration in the serum < 100 mg/dl, yet in patients with PAD and another vascular disease (e.g. coronary disease) the value of LDL concentration in the serum should amount to < 70 mg/dl. The main method of lowering LDL and decreasing the risk of a cardiovascular episode is the application of statins. Fibrates are recommended in the reduction of triglyceride concentration. Data originating from a wide scope, randomised trial covering the population of over 20 thousand patients – Heart Protection Study (HPS) emphasise the role of decreasing LDL in order to reduce the adverse cardiovascular episodes. The application of simvastatin (40 mg/day) for the period of five years entailed a 12% decrease in the general number of deaths, a 17% decrease in the number of vascular-related deaths, 24% decrease in the number of adverse vascular episodes and 27% reduction in the number of all strokes (23). Moreover, HPS showed that a long-term statin therapy involved reduction in the occurrence of myocardial infarction, stroke and vascular-related death in patients with PAD (tab. 2).

Arterial hypertension

Arterial hypertension is another independent factor increasing two or three times the risk of lower limb ischaemia due to atherosclerosis (24). It is recommended to keep the arterial pressure value in patients with atherosclerosis at the level of 130/85 mmHg (25). Beta-blockers are not contraindicated in the therapy of lower limb ischaemia, as presented in the previous studies. Nowadays, it is believed that patients qualified for lower limb ischaemia procedure should take Beta-blockers due to their cardioprotective operation in this group of patients (26). HOPE (Heart Outcomes Prevention Evaluation) carried out among over four thousand participants proved the positive impact of the application of ACE inhibitors on reducing arterial hypertension in the group of patients with PAD (27). As a result, it is recommended to apply ACE inhibitors in the group of high risk patients as regards cardiovascular complications with PAD and arterial hypertension (tab. 3).

Tab. 2. Recommendation 2 – TASC. Lipid control in peripheral artery disease (PAD) patients

Lower the LDL fraction cholesterol concentration in all the patients with PAD symptoms to < 2.59 mmol/l (< 100 mg/dl) [A]. Among patients with PAD and a vascular disease in history (e.g. coronary disease), it is appropriate to lower the LDL fraction cholesterol to < 1.81 mmol/l (< 70 mg/dl) [B]. Lower the LDL fraction cholesterol concentration in all the patients with PAD symptoms without a cardiovascular disease symptoms to the value of < 2.59 mmol/l (< 100 mg/dl) [C]. Among patients with increased triglycerides concentration in whom it is impossible to accurately calculate the LDL fraction cholesterol concentration, measure the LDL fraction concentration directly and apply treatment designed to obtain the values specified above. Alternatively, it is possible to calculate the non-HDL cholesterol concentration (high-density lipoproteins) to reach the concentration of < 3.36 mmol/l (< 130 mg/dl) and among high-risk patients the concentration should reach the value of < 2.59 mmol/l (< 100 mg/dl). To control and treat lipid disorders, it is imperative to modify the diet first [B]. Among patients with the symptoms of PAD, the main method to decrease the LDL-fraction cholesterol concentration and reduce the risk of a cardiovascular episode should be the application of statins [A]. Fibrates and/or niacin should be applied to increase the HDL-fraction cholesterol concentration and decrease triglycerides concentration in patients with PAD with present incorrectness as regards these fractions [B].

Tab. 3. Recommendation 3 – TASC. Arterial hypertension control in patients with peripheral artery disease (PAD)

All the patients with hypertension are advised to reach the target values of arterial pressure amounting to < 140/90 mmHg or < 130/80 mmHg if it is accompanied by diabetes or renal failure [A]. Arterial hypertension treatment among patients with PAD should be in conformity with the recommendations of JNC VII and the guidelines binding in Europe [A]. Hypotension treatment among PAD-patients should be started with thiazides and ACE inhibitors to reduce the risk of a cardiovascular episode [B]. Beta blockers are not contraindicated in PAD [A].

Diabetes

Diabetes is a factor increasing the risk of PAD approx. 3 times as well as the risk of intermittent claudication approx. 5 times (28). The risk of other complications, such as peripheral neuropathies or skin infections leading to non-healing ulcerations is also a few times higher in the case of diabetes. A lot of research over diabetes of the first and mixed type has proven that appropriate glycaemia control may prevent against complications in terms of microcirculation, especially in diabetic retinopathy. However, clear positive impact of glycaemia control on the reduction in cardiovascular episodes and the development of PAD has not been proven yet (29). American Diabetes Association recommends maintaining the glycated haemoglobin concentration at the level of 7%, but so far it remains unclear whether it has any impact on the reduction of PAD development (tab. 4).

Tab. 4. Recommendation 4 – TASC. Diabetes control in peripheral artery disease (PAD)

As regards patients with diabetes and PAD, apply strict glycaemia control and maintain haemoglobin concentration A1c < 7.0% or as close to 6% as possible [C].

Homocysteinemia

Increased homocysteine concentration in blood serum is an independent PAD development factor (30). However, positive impact of the application of vitamin B supplements on the reduction in the number of cardiovascular events has not been proven (tab. 5).

Tab. 5. Recommendation 5 – TASC. Folic acid supplementation in peripheral artery disease (PAD) patients

Patients with PAD and patients with other cardiovascular diseases symptoms should not take folic acid in order to minimise the risk of cardiovascular episodes [B].

Hypercoagulability

Hypercoagulability is the most common reason for venous thrombosis, which was proven in multiple studies (31). Pathologies as regards coagulation in patients with PAD are the subject matter of many studies proving the coexistence of increased concentration of blood platelet activation markers and PAD (32).

Antiplatelet therapy

Acetylsalicylic acid (ASA) is a well-known medication which brings proven benefits for patients with heart diseases of vascular origin. The study of Antithrombotic Trialists Collaboration proved the effectiveness of that medication in patients with ischaemic heart disease (33). The study also proved that low dose of ASA (75-160 mg a day) is safe for the alimentary canal. Owing to the above, the present recommendations advise to use small doses of ASA in patients with cardiovascular diseases. Antiplatelet drugs are certainly recommended in general PAD treatment, despite ASA effectiveness and the benefits flowing from its use are visible only in the case when PAD coexists with cardiovascular diseases (34).

Thienopyridines constitute the next class of antiplatelet drugs studied in terms of chronic lower limb ischaemia treatment. Despite the benefits flowing from taking such drugs in patients with chronic lower limb ischaemia resulting from the reduction in the occurrence of myocardial infarction, stroke and vascular death it is not recommended to use it due to the risk of adverse effects (neutropenia, thrombocytopenia) (35). Opposite to ticlopidine, clopidogrel proved a highly effective drug in preventing the risk of vascular and ischaemic episodes in patients with PAD, with the acceptable frequency of adverse effects. It was confirmed by the study Clopidogrel versus Aspirin in the Prevention of Recurrent Ischemic Events (36, 37). Recent publications concerning patients with acute coronary syndromes suggest that a combined therapy of ASA and clopidogrel is more effective than ASA monotherapy, yet it entails a higher risk of haemorrhage (38). The last study performed concerning this issue proved no general advantage of a dual therapy (ASA and clopidogrel) over the ASA monotherapy in preventing heart attacks, strokes or vascular-related deaths (39). Combined therapy is therefore not recommended for patients with PAD. In the case clopidogrel is taken into account, it should be applied in monotherapy (tab. 6).

Tab. 6. Recommendation 6 – TASC. Antiplatelet therapy in peripheral artery disease (PAD) treatment

All the patients with a positive history as regards cardiovascular diseases, regardless of having the symptoms or not, should take long-term antiplatelet drugs in order to minimise the risk of incidence of cardiovascular diseases and reduce the mortality [A]. The administration of ASA is beneficial in patients with PAD with another form of a cardiovascular disease diagnosed (coronary arteries or carotid arteries) [A]. The application of ASA may be taken into account in patients with PAD with no other form of a cardiovascular disease diagnosed [C]. Clopidogrel effectively reduces the frequency of cardiovascular episodes in the subgroup of patients with symptomatic PAD regardless of whether there are other clinical symptoms of a cardiovascular system disease, or not [B].

INTERMITTENT CLAUDICATION TREATMENT

General procedure

At first, treatment should cover the introduction of physical exercises, pharmacotherapy among some patients. Modifying the risk factors and antiplatelet therapy are intended to reduce the risk of cardiovascular episodes occurrence. In the case the patient does not react to the applied conservative management, surgical treatment should be considered.

Physical exercises

Running a supervised march is the most effective conservative therapy in intermittent claudication (40). It is advised to perform physical exercises 3 times a week. Initially, training should last for 30 minutes, later it should be longer – up to one hour. While exercising on a track, set its inclination and speed so as to trigger pain within 3-5 minutes. Pain should be moderate. In the case the patient stops at the moment of pain occurrence, response to the training will be lower. Training should be repeated three times a week for at least three months (tab. 7).

Tab. 7. Recommendation 14 – TASC. Motor therapy in the case of intermittent claudication

All the patients with PAD should be provided with access to a supervised training programme being part of the initial treatment [A]. In the most effective programmes, effort on the track is intense enough to trigger claudication. Later, the patient rests and the whole session lasts 30-60 minutes. Training sessions are conducted 3 times a week for 3 months [A].

Intermittent claudication pharmacotherapy

All the patients with intermittent claudication should be provided with appropriate treatment and guidelines in order to modify vascular diseases risk factors. However, one should not expect a radical improvement dur-

ing conservative management. Despite promoting so many medications, only a small percentage has proven clinical operation. The therapeutic impact of march is still undervalued, it will never be substituted by and pharmacological products.

Once widely used products in a group of vasodilators have no documented therapeutic effect (41). In 1984, pentoxyphylline was approved for treating intermittent claudication. However, latest clinical trials showed that the medication failed to prove more effective in treating intermittent claudication than placebo (42).

The only medication with a proven clinical effect in intermittent claudication is cilostazol, however the drug not being registered in Poland makes it impossible to be used. Its vasodilating, metabolic and antiplatelet operation is based on inhibiting phosphodiesterase-3 (43). Four clinical trials with the participation of over 1500 patients taking 100 mg of cilostazol 2 times a day proved clear benefits flowing from taking the drug as compared to placebo (significant lengthening in the claudication distance) (44). Studies comparing cilostazol and pentoxifylline proved that cilostazol is more effective (45). A contraindication to use cilostazol in patients with a chronic lower limb ischaemia is cardiac failure (46). However, despite the recent information denying the negative effect of cilostazol in this group of patients, it is recommended to avoid therapy using this drug among patients with cardiac failure.

Acetylsalicylic acid and other antiplatelet drugs are important constituents of a long-term therapy among patients with PAD aimed at reducing the risk of cardiovascular episodes. No study showed a beneficial effect of an antiplatelet therapy or antithrombotic therapy on treating intermittent claudication (47).

Prostaglandins have been the subject matter of many studies, however it has not been proven clearly that the application of such medications has a favourable effect in the intermittent claudication therapy (48). Also, the remaining drugs used until recently in vascular diseases: buflomedil, vitamin E, chelation, omega-3 fatty acid, ginkgo biloba turned out to have no proven clinical operation (tab. 8) (49).

Tab. 8. Recommendation 15 – TASC. Pharmacotherapy as regards intermittent claudication symptoms

First-line pharmacotherapy should be a 3-6-month long course of administering cilostazol in order to reduce the symptoms of claudication, since the results show improvement in physical fitness on track and improvement in the quality of life [A]. Naftidrofuryl may also be taken into account in treating the symptoms of intermittent claudication [A].

The future of intermittent claudication treatment

Since the 1990s there have been reports concerning the possibility of applying a gene therapy in patients with lower limb ischaemia (50). Studies focus on the application of a multigene therapy inducing the activity of both angiogenic cytokines and other factors of basic importance in the angiogenesis process, such as nitrogen oxide synthesis or angiopoietin. In recent years, interest of scientists has also been raised by other angiogenic growth factors: vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF). Following bFGF protein administration intraarterially among patients with intermittent claudication, there was an improvement in the form of lengthening the claudication distance. The latest method of angiogenic agents administration is gene therapy with the use of a viral vector introduced intramuscularly. At first, huge hopes were put into the method, but multi-scope clinical trials conducted among a large number of patients showed no expected effectiveness of treatment with the use of VEGF (51). Therefore, there is a need to carry out a larger number of studies with the use of angiogenic growth factors in the lower limb ischaemia therapy.

Perioperative treatment

There are many proofs that chronic application of antiplatelet drugs – especially acetylsalicylic acid – contributes to the reduction in vascular unfavourable incidents and makes the patency of vascular grafts longer. Metaanalysis of Antithrombotic Trialists' Collaboration among 3000 patients following peripheral graft procedures taking acetylsalicylic acid noted that there were 16% cases reported of graft occlusion as compared to 25% as regards the group taking placebo. Small doses of acetylsalicylic acid (50-100 mg) showed a similar effectiveness as large doses (900-1000 mg) (52).

Justified nature of the applications of anticoagulation treatment in the form of low molecular weight heparin following vascular procedures in order to increase the patency of the graft was studies in multiple clinical trials. It has been proven that longer application of low molecular weight heparin may positively affect the long-term patency of the graft, yet it is related to the increase in postoperative haemorrhage (53).

Oral anticoagulants therapy is more controversial. In some studies concerning warfarin therapy among patients following vascular grafts below the inguinal ligament (venous graft, vascular prosthesis and endarterectomy procedures) it was impossible to prove the advantage of this type of treatment over antiplatelet treatment in the form of making the period of graft patency or vessel longer. Warfarin application entailed increase in the postoperative haemorrhage risk (54).

Some clinical trials compared the effects of anticoagulation treatment and antiplatelet treatment. One of them included patients following vascular grafts from a prosthesis below the inguinal ligament. Postoperative patients were randomised for the treatment in the form of taking low molecular weight heparin and dual therapy in the form of acetylsalicylic acid (300 mg a day) and thienopyridine. The application of heparin entailed making the patency of the graft longer. There was no difference between groups as regards the occurrence of postoperative haemorrhage, yet there were slightly more deaths in the group taking low molecular weight heparin (55).

In one of the largest clinical trials comparing the oral anticoagulants therapy and the acetylsalicylic acid therapy (Dutch Bypass Oral Anticoagulants or Aspirin Study) in patients following a graft below inguinal ligament, the authors suggest oral anticoagulants therapy in patients following vascular grafts with the use of own vein, while in patients following a graft with the use of a vascular prosthesis, better long-term effects were obtained among patients taking acetylsalicylic acid (56).

Combined therapy of oral anticoagulants and antiplatelet drugs in patients with a high vascular risk is the subject matter of many studies. However, no one has proven the definite advantage of the dual therapy over only acetylsalicylic acid therapy, while the applications of both antiplatelet drugs and oral anticoagulants is related to a higher risk of perioperative haemorrhage (57).

In conclusion, antiplatelet therapy is a significant therapy for postoperative vascular patients. It reduces the risk of vascular or vascular graft occlusion as well as has a positive impact on lowering the frequency of occurrence of adverse situation in the form of myocardial infarction or stroke. The previous clinical trials provided no clear answer to the question – which group of drugs or what combination of drugs is the best, the longest supportive treatment for patients following vascular operations. The safest and best researched medication seems to be acetylsalicylic acid. The recently published articles expressed a concern that patients subject to an intervention due to chronic lower limb ischaemia fail to be given appropriate atherosclerosis-related treatment. As it has already been stated, all the patients should be subjected to treatment related to atherosclerosis regardless of the need to start actions to save the limb (tab. 9).

Tab. 9. Recommendation 41 – TASC. Antiplatelet drugs as a supportive pharmacotherapy following revascularisation

Antiplatelet treatment should be implemented prior to the operation and continued as a supportive pharmacotherapy following an intravascular or surgical procedure [A]. In the case of no contraindications, it should be continued until the end of life [A].

Perioperative protection of the myocardium

Patients operated on due to vascular diseases are exposed to a high risk of cardiovascular complications (58). There are many publications suggesting stratification of the preoperative risk in these patients through a thorough physical examination and interview as well as the assessment of the competence of the myocardium using non-invasive methods (59). Basic and most typical risk factors in the case of cardiovascular complications in surgical patients include: aged > 70, ischaemic heart disease, myocardium ischaemia in the past, cardiac failure, cardiac infarction (60). Patients with any symptoms of coronary instability should be referred to a cardiologist in order to implement appropriate treatment. As regards patients with a stable coronary disease, treatment should be dependent on the severity of symptoms. In the majority of patients with coronary symptoms, it will prove necessary to carry out coronary angiography in order to determine appropriate method of revascularisation. All the patients should have appropriate therapy introduced. Usually, it is not advised to perform preventive coronary revascularisation prior to vascular surgery in patients without high cardiovascular risk, yet in the majority of patients perioperative use of beta-blockers entails lower cardiovascular risk (tab. 10, 11) (61).

Tab. 10. Recommendation 7. Coronary artery disease (CAD) treatment in peripheral artery disease (PAD) patients

Patients with clinical signs of CAS (angina pectoris, congestive ischaemic heart disease) should be diagnosed and treated in accordance with the current guidelines [C]. Patients with PAD qualified for vascular surgery may undergo further risk assessment, and those who are qualified to the high risk group should be treated in accordance with the current guidelines for coronary revascularisation [C]. It is not recommended to apply routine coronary revascularisation in preparing for vascular surgeries [A].

Tab. 11. Recommendation 8. The application of beta-blockers prior to vascular surgery

In the case of no contraindications, patients with peripheral artery disease qualified for vascular surgery should be perioperatively administered with b-andrenergic drugs to minimise the risk of cardiac complications [A].

Summary

Patients with chronic ischaemia visiting doctors are largely incorrectly diagnosed and treated. It sometimes happens that they are referred to a vascular surgeon in the condition of developed limb ischaemia, then surgery options are limited. Therefore, such situations are common when patients with serious vascular problems fail to be given adequate surgical aid within optimum time. That is why, in order to limit disease development, one should earlier introduce a therapy modifying risk factors of atherosclerosis development. The main elements of such a procedure include giving up smoking, maintaining the LDL cholesterol level below the limit of 100 mg/dl, maintaining arterial pressure < 130/85 mmHg and maintaining the glycated haemoglobin concentration in diabetics < 7.0%. The recommended pharmacological treatment covers the application of statins to reduce the high concentration of LDL cholesterol, ACE inhibitors to treat arterial hypertension and the use of beta-blockers with no contraindications. All the patients should be provided with antiplatelet treatment all the time. Apart from the reduction in atherosclerosis risk factors, in symptomatic patients with intermittent claudication further treatment covers introducing a programme of supervised physical exercise. The only drug approved to treat intermittent claudication is cilostazol, it is recommended to undergo a course on pharmacotherapy lasting minimum three months in patients with no contraindications, mentioned above. Patients subjected to procedure treatment due to intermittent claudication or critical limb ischaemia (procedure or angioplasty) must take antiplatelet drugs to make the revascularisation effect longer. It is recommended to take acetylsalicylic

acid all the time. Multidrug therapy and its combinations in this population of patients is not approved.

CONCLUSIONS

Peripheral artery disease (PAD) is a common manifestation of systemic atherosclerosis that is associated with a high risk of cardiovascular mortality and significant limitation in function because of limb ischaemia. Patients with PAD should be considered to have significant coronary and cerebral arterial disease that requires aggressive risk factor management, including the prescription of antiplatelet drugs, to lower the subsequent risk of myocardial infarction, stroke, and death. In the population with PAD evidence supports the use of statin for lipid management, angiotensin-converting enzyme-1 inhibitors for blood pressure control, and aspirin or clopidogrel as antiplatelet agents. Once this is accomplished, the severity of limb symptoms should be assessed, and a structured exercise programme or the selected use of drugs such as cilostazol to treat claudication should be prescribed. In patients primarily considered for surgical treatment, antiplatelet and anticoagulant drug therapy can be used as a means of promoting graft patency, and beta-adrenergic blockers can be used as a means of reducing the perioperative risks associated with vascular surgery.

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