5

Antithrombotic Therapy After Peripheral Angioplasty

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1. Introduction

Peripheral arterial disease affects approximately 12% of adults and 20% of adults over 70 years (Hiatt et al., 1995). This disease results from one or more lesions in the arterial system of the lower extremity that restrict blood flow. The restriction of blood flow during ambulation may cause intermittent claudication, i.e. muscular pain due to lack of blood supply. About one fifth of people with peripheral arterial disease have intermittent claudication. About half of people with peripheral arterial disease are asymptomatic. A small part of people with peripheral arterial disease (< 10%) have critical limb ischemia, i.e. rest muscular pain and/or ischemic ulceration or gangrene of toes. Based on the severity of symptoms, the stages of the disease are classified as Fontaine stages I-IV, where stage I is asymptomatic, stage IIa is the occurrence of intermittent claudication after a pain-free walking distance of more than 200 m, stage IIb is intermittent claudication after less than 200 m, stage III is rest pain, and stage IV is the presence of ischemic ulcers.
Patients with peripheral arterial disease, which is an expression of systemic atherosclerosis, have an increased risk of cardiovascular events (Hankey et al., 2006).
Medical therapy should include modification or elimination of atherosclerotic risk factors (cigarette smoking, diabetes mellitus, hypertension, hyperlipidemia), and antiplatelet therapies to decrease the risk of cardiovascular events and to improve survival. Moreover, the initial approach to the treatment of limb symptoms should focus to relieve discomfort, to improve exercise performance, and daily functional abilities by means of structured exercise and, in selected patients, pharmacotherapies to treat the exercise limitation of claudication (Norgren et al, 2007). Lower extremity revascularization is indicated for patients with a lifestyle-limiting disability due to intermittens claudication or with chronic critical limb ischemia (Hirsch et al., 2006; Norgren et al., 2007).
There are two types of revascularization procedure: endovascular or surgical. Percutaneous transluminal angioplasty with or without stenting is an endovascular technique for revascularizing obstructed arteries. It was first introduced by Dotter and Judkins (Dotter & Judkins, 1964), and subsequently improved by Grüntzig (Grüntzig & Hopff, 1974).
In peripheral transluminal angioplasty the recanalization of obstructed arteries is obtained by dilatation of a stenosis (i.e. a narrowing of the vessel diameter) or recanalization of a total occlusion, using a wire-guided inflatable balloon catheter. Usually the femoral artery in the

groin is cannulated and a deflated balloon catheter is inserted and pushed forward along the guide-wire to the sites of obstruction. Stenting is usually added to reduce the risk of reocclusion, especially if there is a major endothelial damage, arterial dissection or non-satisfactory dilatation with relevant residual stenosis. Self-expanding metallic stents are mainly applied at the aortic bifurcation or iliac segments, whereas the femoropopliteal level, until recently, was associated with a higher risk for reocclusion due to smaller vessel diameters in distal arteries (Do et al., 1992; Mahler et al., 1999; Palmaz et al., 1985; Strecker et al., 1988).

The implantation of drug-eluting stents, nitinol stents, paclitaxel-coated angioplasty balloons, or treatment by intravascular brachytherapy following peripheral angioplasty of the femoropopliteal arteries have been considered as interventions with the capacity of reducing the occurrence of restenosis/reocclusion (Schillinger et al., 2006; Gray et al., 2008).

In patients with peripheral arterial disease endovascular procedures are generally the treatment of choice for short-segment iliac or femoral-popliteal artery lesions (TASC-A, single stenosis less than 3 cm long). Longer segment iliac or femoral-popliteal artery lesions (TASC-B, single iliac stenosis 5-10 cm long, two iliac lesions 3-5 cm long, single occlusion of an iliac artery, tandem femoral-popliteal stenoses less than 3 cm long, single femoral-popliteal lesion 3-5 cm in length) are frequently treated by endovascular techniques (Norgren et al., 2007).

Restenosis (or reocclusion) is the main complication of peripheral transluminal angioplasty. Balloon angioplasty has been shown to induce endothelial injury and oxidative stress with subsequent endothelial dysfunction, platelet aggregation, macrophage activation, and smooth muscle cell proliferation (McBride et al., 1988; Taniyama & Griendling, 2003). Peripheral transluminal angioplasty induces a prothrombotic condition: atherosclerotic plaques are disrupted and platelets aggregate at the site of the damaged arterial wall (Fuster et al., 1995). Thus, as a result of platelet aggregation, activated blood clotting in the damaged atheromatous artery and low shear stress, restenosis (or reocclusion) is frequent (Schwartz, 1998; Wentzel et al., 2003).

In particular, the effects of balloon angioplasty on the platelet activation have been studied previously in vitro and in vivo. Peripheral transluminal angioplasty has been shown to result in significant imbalance between the production of prostacyclin, an effective vasodilatator and platelet antiaggregator produced in endothelial cells, and thromboxane A2, a potent smooth muscle constrictor and platelet aggregator formed in platelets, with shift more toward increased thromboxane A2 production. This finding is suggestive of significant platelet activation and may have implication for future failure of peripheral angioplasty (Parmar et al., 2010). An increased formation of thromboxane A2 was also seen in other two studies, one in patients undergoing peripheral angioplasty and one in patients after coronary angioplasty (Rossi et al., 1997; Peterson et al., 1986).

In addition, in the initial phase after balloon and stent procedures, coagulation system is activated, as demonstrated by increased serum levels of thrombin-antithrombin complexes, D-dimer and fibrinopeptide A. This condition favours early thrombotic occlusion, where 'early' is usually defined as a period covering the first 4 weeks after the intervention (Tsakiris et al., 1999; Tschöpl et al., 1997). Subsequently, intimal hyperplasia, a redundant healing of the arterial wall, which is responsible for restenosis and reocclusion in the mid- and long-term, may follow. Intimal hyperplasia occurs as a result of denudation (tearing off of the inner lining) of the endothelium caused by damage to the vessel wall with the catheter. Smooth muscle cells in the medial layer are stimulated to grow and migrate into the intimal layer (Haudenschild, 1995; Jørgensen et al., 1990).

Risk factors for restenosis/reocclusion include severity of atherosclerosis in run-off arteries, length of diseased segments, number of treated lesions, stage of disease, and presence of cardiovascular risk factors (Norgren et al., 2007). Female gender may be an independent predictor of decreased primary patency of external iliac artery stents (Timaran et al., 2001). Inflammation, revealed by an elevated C-reactive protein, was also considered as a risk factor for restenosis at six months after successful femoropopliteal angioplasty (Schillinger et al., 2002).

The rate of restenosis/reocclusion of suprainguinal (iliac) arteries after peripheral transluminal angioplasty ranges from 14% after one year to 29% after 5 years, while the rate of restenosis/reocclusion of infrainguinal (femoropopliteal) arteries after peripheral transluminal angioplasty with or without stenting ranges from 23-35% after one year to 45-58% after 5 years (Norgren et al., 2007). Patients with stenoses or occlusions of infrainguinal arteries of less than 3 cm had a favourable long-term patency rate of 74% (Gallino et al., 1984).

Patients subjected to local thrombolysis show higher incidences of restenosis/reocclusion (Decrinis et al., 1993).

It is important to define the lesion suitable for balloon angioplasty in both the suprainguinal and infrainguinal districts.

Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II) redefined the indications for endovascular or surgical revascularization on the basis of anatomical characteristics of the lesions. Endovascular interventions are recommended for: i) unilateral or bilateral stenosis of common iliac artery; unilateral or bilateral single short (≤ 3 cm) stenosis of external iliac artery; ii) single stenosis ≤ 10 cm in length of femoropopliteal arteries; single occlusion ≤ 5 cm in length of femoropopliteal arteries (TASC Type A lesions) (Norgren et al., 2007).

Endovascular interventions are the preferred treatments for: i) short (≤ 3 cm) stenosis of infrarenal aorta; unilateral common iliac artery occlusion; single or multiple stenosis totaling 3-10 cm involving the external iliac artery not extending into the common femoral artery; unilateral external iliac artery occlusion not involving the origin of internal iliac or common femoral artery; ii) multiple lesions (stenoses or occlusions), each ≤ 5 cm of femoropopliteal segment; single stenosis or occlusion ≤ 15 cm not involving the infra geniculate popliteal artery; single or multiple lesions in the absence of continuous tibial vessels to improve inflow for a distal bypass; heavily calcified occlusion ≤ 5 cm in length; single popliteal stenosis (TASC Type B lesions) (Norgren et al., 2007).

Provisional stent placement is indicated for iliac arteries as salvage therapy for a suboptimal or failed result from balloon dilatation (persistent translesional gradient, residual stenosis greater than 50%, flow-limiting dissection). Stenting is effective as primary therapy for common and external iliac artery stenoses and occlusions. Moreover, stents can be useful in the femoral, popliteal and tibial arteries as a salvage therapy for suboptimal or failed results from balloon dilatation (Hirsch et al., 2006).

As mentioned above, the implantation of drug-eluting stents, nitinol stents, paclitaxel-coated angioplasty balloons, or treatment by intravascular brachytherapy following peripheral angioplasty have been considered as interventions with the capacity of reducing the occurrence of restenosis/reocclusion. A study by Schillinger et al. showed better results at one year with self-expanding nitinol stent in femoropopliteal segments (Schillinger et al., 2006). Use of paclitaxel-coated angioplasty balloons during percutaneous treatment of

femoropopliteal disease has been shown to be associated with significant reductions in late lumen loss (Tepe et al., 2008). Endovascular brachytherapy has been proposed as a promising treatment modality to reduce restenosis after angioplasty (Minar et al., 2000). However, the phenomenon of late acute thrombotic occlusion in patients receiving endovascular brachytherapy after stenting of the femoropopliteal arteries may compromise the benefits of endovascular radiation. The fact that late acute thrombotic occlusions occurs concomitantly with stopping clopidogrel in patients treated with a double antiplatelet regimen (aspirin 100 mg / day and clopidogrel 75 mg / day) suggests an intensive and prolonged antithrombotic prevention in these patients (Bonvini et al., 2003).

There are much few data concerning antithrombotic therapy after peripheral arterial revascularization, and patients with peripheral arterial disease are often treated on the basis of experiences extrapolated from coronary arteries (Visonà et al., 2009).

Antithrombotic therapy has been shown to lower the incidence of associated cardiovascular events (Sobel & Verhaeghe, 2008). A meta-analysis of 42 trials has shown a statistically significant 23% reduction of vascular events (vascular death, nonfatal myocardial infarction or stroke) in 9,214 patients with peripheral arterial disease treated with antiplatelet therapy. Even patients having peripheral angioplasty benefited to a similar degree (Antithrombotic Trialists' Collaboration, 2002). Clopidogrel seems to be superior to aspirin in reducing cardiovascular events, particularly in patients with peripheral arterial disease (relative risk reduction of 23%) (CAPRIE Steering Committee, 1996), but this advantage is minimal. Life-long antiplatelet therapy is usually recommended for all patients with peripheral arterial disease to prevent death and disability from stroke and myocardial infarction.

Antithrombotic drugs to prevent restenosis would make an important contribution to the sustained success of endovascular treatment. The main questions concern the most effective and safe antithrombotic therapy and its duration.

2. Methods

We performed a Medline search of English language studies published between 1976 and 2010 with the keywords “antithrombotic therapy, peripheral angioplasty”. We also considered the reviews and meta-analyses. We selected two meta-analyses, two reviews, and fifteen original articles.

3. Results

Two meta-analyses and two reviews evaluated the efficacy and safety of antithrombotic agents for the prevention of restenosis after balloon angioplasty in patients with peripheral arterial disease (Girolami et al., 2000; Dörffler-Melly et al., 2005; Watson & Bergqvist, 2000; Visonà et al. 2009).

The first meta-analysis evaluated the efficacy of conservative adjuvant therapy after endovascular or surgical revascularization procedures. The meta-analysis, including thirty-two studies, showed that, compared to non-active control, aspirin (100-300 mg daily) with dipyridamole (225-450 mg daily) improves patency (odds ratio 0.69) and mortality (odds ratio 0.57). Similarly, ticlopidine has been shown to improve patency and amputation rates (odds ratio 0.53 and 1.01, respectively), and therefore may be used when aspirin is contraindicated. Data on the effectiveness of vitamin K inhibitors were not conclusive (Girolami et al., 2000).

The second meta-analysis is a Cochrane review of 14 randomized trials comparing different antithrombotic drugs (anticoagulants, antiplatelet agents and others) with no treatment or placebo to prevent restenosis/reocclusion following peripheral vascular treatment. The trials included patients with symptomatic peripheral arterial disease treated by endovascular revascularization of the iliac or femoropopliteal arteries. Various pharmacological interventions were analysed: anticoagulants, antiplatelet agents and other vasoactive drugs were compared with no treatment, placebo, or any other vasoactive drug. Clinical endpoints were reocclusion, amputation, death, myocardial infarction, stroke and major bleeding. The efficacy and safety of acetylsalcylic acid and low molecular weight heparins have been shown. Aspirin (50-300 mg daily) started prior to femoropopliteal peripheral transluminal angioplasty has been shown to be the most effective prophylactic treatment. Low molecular weight heparins seem to be more effective in preventing restenosis or reocclusion than unfractionated heparin (Dörffler-Melly et al., 2005).
Watson and Bergqvist identified eleven randomized trials with antithrombotic agents, but they didn't clarify their usefulness in reducing the likelihood of restenosis or reocclusion after balloon angioplasty of femoropopliteal lesions (Watson & Bergqvist, 2000).
Our group recently conducted a review on antithrombotic therapy after peripheral angioplasty (Visonà et al., 2009).
We analyse the studies identified in the following paragraphs (Table 1).

3.1 Aspirin with or without dipyridamole

Two studies compared aspirin combined with dipyridamole to placebo (Heiss et al., 1990; Study Group, 1994).
In a single-center trial 199 patients undergoing balloon angioplasty of femoropopliteal arteries were randomized to high dose aspirin (990 mg) combined with dipyridamole (225 mg), low dose aspirin (300 mg) plus dipyridamole (225 mg), or placebo. Clinical and angiographic improvement was observed in both treatment groups in comparison with placebo, but this was statistically significant only in the high-dose aspirin group (Heiss et al., 1990).
A multicenter study randomized 223 patients undergoing balloon angioplasty of iliac or femoropopliteal arteries to receive either placebo or aspirin (50 mg) plus dipyridamole (400 mg). No difference was observed between the two groups. A possible explanation of this result may be a higher percentage of patients with more favourable iliac lesions in the placebo group (65% versus 51%). Moreover, use of metallic stents was not performed (Study Group, 1994).
According the conclusions of the Cochrane review, a 60% reduction of restenosis/ reocclusion was found with aspirin 330 mg combined with dipyridamole as compared to placebo up to 12 months after angioplasty of femoropopliteal arteries. A similar positive effect on patency was found with aspirin 50 to 100 mg combined with dipyridamole as compared to placebo at 6 months, but this was not significant (Dörffler-Melly et al., 2005).
Aspirin/dipyridamole showed a superior effect on patency after femoropopliteal angioplasty compared to vitamin K antagonists at 3, 6, and 12 months, but even this effect was not significant (Do & Mahler, 1994; Pilger et al. 1991).
Aspirin 50 to 330 mg, with or without dipyridamole, started before femoropopliteal endovascular treatment, appeared to be the most effective and safest strategy, and reduced the incidence of restenosis/reocclusion at 6 and 12 months when compared with no therapy or vitamin K antagonists. Three trials compared the efficacy and safety of different doses of

aspirin after peripheral angioplasty. The doses tested ranged from 50 mg / day to 1000 mg / day. The three studies showed that higher doses of aspirin had no advantage on early reocclusion (within one month) and were more likely to cause gastrointestinal side effects including peptic ulcer (Weichert et al., 1994; Minar et al., 1995; Ranke et al., 1994).

3.2 Oral anticoagulants

Anticoagulation is frequently combined with antiplatelet therapy after femoropopliteal or tibial artery balloon angioplasty, although the results of three randomized controlled trials do not support this practice (Schneider et al., 1987, as cited in Sobel & Verhaeghe, 2008; Pilger et al., 1991; Do & Mahler, 1994). In fact, in all three studies no significant difference was observed in arterial patency rate between the anticoagulation groups and the antiplatelet therapy groups (only slightly lower patency rate and more bleeding complications in the anticoagulation groups).

3.3 Low molecular weight heparins

Intimal hyperplasia is responsible for restenosis and reocclusion after angioplasty in the mid- and long-term. Low molecular weight heparins have been shown in experimental studies to have antiproliferative effects in addition to their antithrombotic properties (Wilson et al., 1991). Their potential to reduce restenosis remains to be established. The hypothesis that low molecular weight heparins plus aspirin are more effective than aspirin alone in reducing incidence of restenosis after peripheral transluminal angioplasty was tested in two trials. Nadroparin, administered at a dose adjusted to weight for 7 days after femoropopliteal angioplasty, has been shown to be more effective to prevent reocclusion at 6 months than unfractionated heparin, without causing increased bleeding (Schweizer et al., 2001). Despite this interesting result, dalteparin 2500 UI, administered for 3 months after femoropopliteal angioplasty plus aspirin 100 mg/day versus aspirin alone, failed to reduce incidence of restenosis/reocclusion at 12 months. However, dalteparin appeared to be beneficial at the 12-month follow-up in the subgroup of patients with critical limb ischemia (Koppensteiner et al., 2006).

3.4 New antiplatelet drugs (abciximab, thienopyridines)

There are few studies available on potent new antiplatelet drugs such as abciximab and thienopyridines.

3.4.1 Abciximab

In one study in high-risk patients with long segmental femoropopliteal interventions adjunctive administration of abciximab had a favorable effect on patency and clinical outcome in patients undergoing complex femoropopliteal catheter interventions not hampered by serious bleeding. Treatment effect of abciximab observed at 30 days was maintained at 6 months (Dörffler-Melly et al., 2005).
In another study adjunctive abciximab after nitinol stenting of the superficial femoral artery did not appear to demonstrate any identifiable effect on functional outcomes at 9 months (Ansel et al., 2006).

3.4.2 Thienopyridines

The thienopyridines, ticlopidine and clopidogrel, interfere with the adenosine diphosphate (ADP) pathway. They might represent a useful alternative to aspirin, when it is not

tolerated, and might be combined with aspirin, when increased risk factors for restenosis/reocclusion are detected, although specific data are lacking.
In one study ticlopidine was compared to vitamin K inhibitors. No significant difference in efficacy was found between the two drugs (Schneider et al., 1987, as cited in Sobel & Verhaeghe, 2008).
The administration of clopidogrel and aspirin leads to a potent platelet inhibition, whose benefits have been demonstrated for patients with acute coronary syndrome, symptomatic vascular disease, and presence of multiple cardiovascular risk factors. A randomized double-blind trial showed that the administration of clopidogrel and aspirin significantly suppresses platelet function up to 30 days after lower limb angioplasty, compared to aspirin and placebo (Cassar et al., 2005a). On the other hand, addition of clopidogrel to the standard antithrombotic therapy with aspirin had no effect on the levels of markers of coagulation activation, such as D-dimer and thrombin-antithrombin III, in patients with intermittent claudication before or after endovascular intervention (Cassar et al., 2005b). Moreover, therapy with clopidogrel and aspirin had no significant effect on markers of vascular smooth muscle cell proliferation before and after peripheral angioplasty (Wilson et al., 2009).

3.4.3 Dual antiplatelet therapy

Dual antiplatelet therapy (clopidogrel plus aspirin), leading to a potent platelet inhibition, has been shown to be more effective than aspirin alone in reducing cardiovascular events in patients with acute non-ST coronary syndrome. This finding has not been confirmed in patients at high cardiovascular risk but not in the acute phase, where risk-benefit ratio is less favourable (Keller et al., 2007). A potential benefit of clopidogrel and aspirin versus aspirin alone in patients with symptomatic vascular disease has been suggested by the CHARISMA trial, which enrolled more than 15,000 patients with either evident clinical cardiovascular disease or multiple risk factors (Bhatt et al., 2006).
The benefit of more potent platelet inhibition with dual therapy, aspirin and clopidogrel, has been shown in a trial on acute coronary syndromes (CURE) (Fox et al., 2004). However, the efficacy and safety of this dual antiplatelet therapy after peripheral angioplasty have not been evaluated in a randomized controlled trial. The Clopidogrel and Aspirin in the Management of Peripheral Endovascular Revascularization study (CAMPER) was designed to evaluate this outcome after femoropopliteal angioplasty, but it was stopped, due to difficulties of randomization, perhaps because many patients were already treated off-label with clopidogrel and aspirin (Patrono et al., 2004).
The administration of ticlopidine and acetylsalicylic acid has been shown to improve neurological outcome after carotid stenting without an additional increase in bleeding complications in patients undergoing carotid stenting, compared to acetylsalicylic acid alone (Dalainas et al., 2006).
Aspirin and clopidogrel were used as standard therapy in two major randomized controlled trials of carotid stenting (preprocedure and at least for 30 days) (SPACE Collaborative Group, 2006; Mas et al., 2006).
Although it is questionable to extrapolate experience from one anatomic region to another, in the absence of data on peripheral interventions, dual antiplatelet therapy seems to be a reasonable approach to reduce thrombotic complications after lower extremity balloon angioplasty and stenting, especially in the femoropopliteal and tibial districts. In fact, many physicians in the world use dual antiplatelet therapy with aspirin (100 mg / day) and clopidogrel (75 mg / day) before and after peripheral transluminal angioplasty and stenting of peripheral arteries. Dual antiplatelet therapy is continued for 4 weeks after the intervention.

Then aspirin is continued indefinitely (Visonà et al., 2009). Treatment with a loading dose of clopidogrel 6-24 hours before angioplasty seems to improve the clinical outcome (Verheugt et al., 2007), and a 600 mg loading dose versus 300 mg at least 12 hours before the procedure provides greater benefit in coronary syndromes (Cuisset et al., 2006). In addition, an intra-arterial bolus of heparin (3000 to 5000 U) is often administered at the time of the procedure.

Drugs	Author, year	Treatments	Pts	Design
ASA ± dipyridamole	Heiss, 1990	ASA 300 mg / dipyridamole 225 mg ASA 990 mg / dipyridamole 225 mg Placebo	47 51 47	R, DB, 1C
	Study Group, 1994	ASA 50 mg / dipyridamole 400 mg Placebo	105 110	R, DB, 12C
	Hess, 1978	ASA 990 mg ASA 990 mg / dipirydamole 225 mg	50 51	R, DB, 1C
	Ranke, 1992	ASA 50 mg ASA 900 mg	184 175	R, DB, 2C
	Weichert, 1994	ASA 300 mg ASA 1000 mg	106 105	R, DB, 2C
	Minar, 1995	ASA 100 mg ASA 1000 mg	105 102	R, O, 1C
Oral anticoagulants	Do, 1994	ASA 50 mg / dipyridamole 400 mg Anticoagulant	51 61	R, O, 1C
	Pilger, 1991	ASA 500 mg / dipirydamole 225 mg Anticoagulant	66 63	R, O, 1C
LMWHs	Schweizer, 2001	Weight adjusted nadroparin + ASA 100 mg Unfractionated heparin + ASA 100 mg	86 86	R, O, 1C
	Koppensteiner, 2006	Dalteparin 2500 IU + ASA 100 mg ASA 100 mg	137 138	R, O, 1C
Ticlopidine	Schneider, 1987	Ticlopidine Anticoagulant	103 94	R, O, 3C
Abciximab	Dörffler-Melly, 2005	Abciximab + ASA 100 mg Placebo + ASA 100 mg	47 51	R, DB, 1C
	Ansel, 2006	Abciximab Placebo	27 24	R, O, 1C
Iloprost	Horrocks, 1997	Iloprost 72 h + ASA 300 mg after 72 h ASA 300 mg None 72 h + ASA 300 mg after 72 h	11 13 14	R, O, 2C
Cilostazol	Iida, 2008	Cilostazol 200 mg Ticlopidine 200 mg	63 64	R, O, 1C

Pts= patients; ASA=acetylsalicylic acid; LMWHs=low molecular weight heparins; R=randomized; DB=double blind; O=open; nC=number of centres

Table 1. Drugs, studies published, patients analysed and study designs

Currently, for patients undergoing lower extremity balloon angioplasty (with or without stenting), the American College of Chest Physicians (ACCP) recommends long-term aspirin (75-100 mg / day) (grade 1C), and recommends against anticoagulation with heparin or vitamin K inhibitors (grade 1A) (Sobel & Verhaeghe, 2008).
Randomized, prospective studies with dual therapy are needed for resolving some issues, such as real efficacy of dual therapy in peripheral district, the optimal loading dose in patients undergoing endovascular revascularization, and the optimal duration of dual therapy following peripheral angioplasty and stenting (Plosker & Lyseng-Williamson, 2007).

3.5 Vasoactive drugs

Some drugs have interesting vasoactive properties, that may improve outcome after peripheral angioplasty. Iloprost, the prostacyclin analogue, and cilostazol, a phosphodiesterase type 3 inhibitor, have multiple effects, such as inhibition of platelet activation, vasodilation, antiproliferation of vascular smooth muscle cells, and improvement of endothelial cell function. These effects may lead to the inhibition of neointimal hyperplasia after stenting.
Iloprost was investigated in a small study in conjunction with aspirin. A 3-day periinterventional intravenous infusion of iloprost plus long-term aspirin didn't reduce incidence of restenosis, compared to aspirin alone (Horrocks et al., 1997).
Cilostazol after endovascular therapy for femoropopliteal lesions was more effective in reducing restenosis than ticlopidine (Iida et al., 2008).
Further studies are needed.

4. Conclusion

Patients with peripheral arterial disease benefit from receiving life-long aspirin at a daily dose of 75 mg to 100 mg or clopidogrel at a daily dose of 75 mg. Patients undergoing peripheral transluminal angioplasty should receive aspirin at a daily dose of 75 mg to 100 mg, started before the intervention and continued life-long. Thienopyridines, e.g. clopidogrel, might represent a useful alternative to aspirin in cases of intolerance to aspirin. Although randomized clinical trials are lacking, it is reasonable to consider short-term dual antiplatelet therapy with aspirin and thienopyridines for infrainguinal stenting, given the relatively high rate of restenosis/reocclusion after interventions. It is reasonable to administer a 300-600 mg loading dose 6-24 hours before angioplasty, and to continue dual therapy for 4 weeks. If a drug-eluting peripheral stent was placed, dual therapy is maintained for 6-12 months. Use of low molecular weight heparins may be reserved for patients with critical limb iischemia. Abciximab may be useful after extended femoropopliteal interventions in patients at high risk of restenosis/reocclusion.

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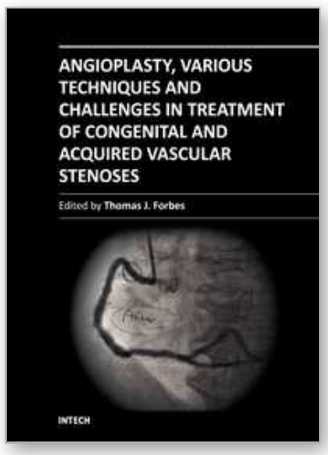

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The field of performing transcatheter interventions to treat vascular lesions has exploded over the past 20 years. Not only has the technology changed, especially in the arena of balloon/stent devices, but the techniques of approaching complex lesions has evolved over the past decade. Lesions that no one would have imagined treating back in the 1990's are now being done routinely in the catheterization suite. This book provides an update on the current techniques and devices used to treat a wide variety of lesions. Though, at first, the outward appearance of the topics appears to be varied, they are all related by the common thread of treating vascular lesions. We hope, by publishing this book, to accomplish two things: First, to offer insight from experts in their field to treat, both medically and procedurally, complex vascular lesions that we frequently encounter. Secondly, we hope to promote increased communication between areas of medicine that frequently don't communicate, between adult interventional cardiologists, pediatric interventional cardiologists, interventional radiologists, and neurosurgeons. Much can be learned from our respective colleagues in these areas which can further our own world of interventions.

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