Effects of prostaglandin E₁ infusion on blood flow in a patient with Buerger’s disease: a case report

Takashi Umemura, MD, PhD¹, Kenji Nishioka, MD, PhD², Kazuaki Chayama, MD, PhD¹ and Yukihito Higashi, MD, PhD, FAHA²³

Abstract:
A 45-year-old male patient with Buerger’s disease presented with intermittent claudication, sharp rest pain in his right foot, and several episodes of lower extremity superficial thrombophlebitis. He had no cardiovascular risk factors and his glucose levels were within normal ranges. However, he had a smoking history of more than 26 years; he had stopped smoking 3 years prior. Early treatment with antithrombotic and vasodilating agents as well as intravenous infusion of prostaglandin E₁ did not improve his condition. Intra-arterial infusion of prostaglandin E₁ once a day for 2 weeks slightly increased blood flow in the areas with previous low blood flow and improved his condition from Fontaine stage III to II.

Key words:
Buerger’s disease, Prostaglandin E₁, Laser doppler perfusion image

Introduction
Thromboangiitis obliterans (Buerger’s disease) is recognized as a segmental inflammatory obliterator arteriopathy of small- and medium-sized distal arteries, veins, and nerves. It is distinct from atherosclerosis²,³, and is a rare disease that affects approximately less than 10,000 people in Japan. Although inflammatory processes caused by altered autoimmune response are thought to contribute to the pathology of Buerger’s disease, the precise pathogenesis of Buerger’s disease remains unclear. The frequency of Buerger’s disease is greater in men than in women. However, the frequency of Buerger’s disease increases in young women with increased tobacco use, while it is decreasing in men. Treatment strategies for Buerger’s disease include smoking cessation, administration of anti-platelet agents, use of vasodilators, revascularization, sympathectomy, and cell therapy. However, some cases of Buerger’s disease progress to critical limb ischemia, requiring major amputation. Therefore, it is clinically important to improve or control the progression of Buerger’s disease.

Case Report
We report the case of a 45-year-old man with a 13-year history of Buerger’s disease presenting with intermittent claudication, sharp rest pain in his right foot, and several episodes of lower extremity superficial thrombophlebitis. He had no cardiovascular risk factors, such as elevated blood pressure, cholesterol, and glucose, but had a smoking history of more than 26 years (3.2 pack-years); he had stopped smoking 3 years prior. Tests for rheumatoid factor and lupus anticoagulants, and serologic investigations had returned negative results. Early treatment with antithrombotic and vasodilating agents did not improve his condition. Although right lumbar sympathectomy improved his symptoms transiently, his symptoms deteriorated within 4 weeks after sympathectomy. Intravenous infusion of lipo prostaglandin E₁,
alprostadil alfadex (20 μg) for 30 minutes twice a day for 2 weeks also did not improve his condition.

Laser Doppler perfusion imaging (LDPI) showed very low blood flow areas at the great, second, and third toes and multiple low blood flow areas in the dorsum pedis (Figure 1A, 1B, 1C). Alfadex was intra-arterially infused through a 24-gauge catheter into the right femoral artery. Blood flow of the right dorsum pedis immediately increased and reached a peak level at 10 minutes after intra-arterial infusion of alprostadil (0.5 ng/kg/min) for 5 minutes (Figure 1A, arrow) and returned to the baseline level at 30 minutes after alprostadil infusion. However, blood flow of the right dorsum pedis did not change during and after intravenous infusion of alprostadil (10 ng/kg/min) for 60 minutes (Figure 1B). Intra-arterial infusion of alprostadil (10 ng/kg/min) for 10 minutes once a day for 2 weeks slightly increased blood flow in the previous low blood flow areas (Figure 1C, arrow) and improved his condition from Fontaine stage III to II.

**Discussion**

LDPI enables non-invasive and repeated determination of not only blood flow but also distribution of blood flow in extremities. We confirmed that ischemic extremities in patients with peripheral diseases (n=38, 34 males and 4 females) can be divided into 3 types according to observation by LDPI during and after the intravenous infusion of alprostadil (10 ng/kg/min) for 60 minutes. First, in most cases (n=32, 29 males and 3 females), intravenous infusion of alprostadil immediately increased blood flow in ischemic ex-
tremities, as shown in previous studies4,5. Second, as in this case (n=5, 4 males and 1 female), blood flow did not change during and after alprostadil infusion. Finally, in one case (n=1, male), blood flow decreased only during and both during and after intravenous alprostadil infusion (so-called steal phenomenon and borrowing-lending phenomenon)6,7. The two latter types compared with the former type may have more serious symptoms and arteriographic findings. Indeed, our patient had rest pain (Fontaine stage III) in his lower right leg. Digital subtraction angiography showed avascular areas at the tip of the great toe and multiple occlusions of the distal arteries with collateralization around the area of occlusions in his lower right leg (Figure 2). It is expected that intra-arterial infusion of prostaglandin E1 is more effective compared with intra-venous infusion of prostaglandin E1. However, reproducibility and safety of intra-arterial infusion of prostaglandin E1 are not guaranteed yet. Future studies are needed to confirm the effectiveness and safety of intra-arterial infusion of prostaglandin E1 in patients with peripheral arterial diseases.

Conclusion

Although intra-arterial infusion of prostaglandin E1 is worth trying in patients for whom intravenous prostaglandin E1 infusion is not effective, we must keep in mind the preservation capacity of blood supply in collateral arteries when vasodilators are intravenously or intra-arterially administered in patients with severe peripheral arterial diseases. LDPI, a non-invasive approach for observation, is expected to play an important role in screening for safety and usefulness of the administration of vasodilators, including intravenous infusion of prostaglandin E1, in patients with peripheral arterial diseases.

Conflicts of Interest
None.

References