

Enhanced portal flow velocity and volume following Iloprost treatment

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Abstract. *Objective:* We studied, with color Doppler sonography, portal flow velocity (PV) and volume (PFV) before and after Iloprost infusion. *Background:* Iloprost is a prostacyclin analogue with arterial vasodilator and platelet aggregation inhibitor properties. Recently, hemodynamic effects after treatment with Iloprost have been demonstrated in subjects with arteriopathy of lower limbs. *Methods:* We treated 10 subjects (2 males and 8 females; mean age 64 ± 8.2 years) affected by arteriopathy of lower limbs with intravenous infusion of Iloprost, at a dosage of 2 ng/Kg/min (16 hours/day) for 3 days. In all patients portal vein flow velocity (PV) (cm/s) and volume (PFV) (ml/min) were assessed. PV was directly determined by the Doppler system, whereas PFV was calculated using the formula "CSA x PV", after measuring the portal vein cross sectional area (CSA) (mm²). *Results:* The patients showed markedly increased PV and PFV after Iloprost infusion (pre-Iloprost vs post-Iloprost treatment mean portal flow velocity and volume values: 23.12 ± 3.89 cm/s vs 28.49 ± 3.90 cm/s, $p < 0.01$ and 1743.9 ± 241.7 ml/min vs 2271.7 ± 333.5 ml/min, $p < 0.001$, respectively). *Conclusions:* This study confirms our previous results about increased PV and PFV values after Iloprost treatment. In the light of these results we suggest some possible therapeutic implications in patients undergoing liver transplantation. However, further studies are necessary to confirm this hypothesis.

Key words: Iloprost, portal flow velocity, color Doppler ultrasound, hepatic circulation, liver transplantation

Introduction

Recently, we demonstrated significant hemodynamic effects of Iloprost infusion on portal flow velocity (PV) and volume (PFV) (1). Iloprost, a vasodilator and platelet aggregation inhibitor (2, 3), has been shown to improve clinical condition and survival of patients with primary pulmonary hypertension, Raynaud's phenomenon, scleroderma, severe chronic ischaemia of the lower limbs and thromboangiitis obliterans (Buerger's disease) (4, 5). In fact, it is able to significantly decrease pulmonary arterial pressure and

pulmonary vascular resistance and to favour arterial circulation. Thanks to these properties Iloprost, has been proposed as pretreatment for patients undergoing pulmonary thromboendarterectomy (6) and advantages have also been demonstrated by combining its inhalation and intravenous infusion in patients with primary pulmonary hypertension (7).

Recently, it has also been proved that Iloprost has hepatic cytoprotective effects (8).

In order to further evaluate the efficacy of Iloprost on hemodynamics of portal circulation also reducing the time of treatment, we have measured, with

color Doppler sonography, PV and PFV before and after only 3 days of infusion in 10 patients affected by arteriopathy of lower limbs.

Materials and methods

All patients, (10 patients, 2 males and 8 females; mean age 64 ± 8.2 years), after receiving a diagnosis of arteriopathy of lower limbs, were admitted to our hospital to be treated with intravenous infusion of Iloprost, according to the following protocol: 2 ng/Kg/min for 16 hours/day for 3 consecutive days.

The patients were studied by color Doppler sonography examination of portal vein before and after Iloprost treatment. In each subject, examined in a supine position, color Doppler sonography was performed by the same operator using a *General Electric* 500 equipment and a convex 3.5 MHz probe, after an 8-hour fast. PV was obtained, after positioning the caliper at the crossing point of the portal vein with the hepatic artery. In each patient, in order to diminish the variability of portal flow velocity, we determined the mean value of three Doppler sonography examinations performed at an angle of insonation lying between 50° and 60° . Furthermore, we measured the portal diameter (mm) and, by applying the formula " $r^2 \times \pi$ ", calculated the portal vein cross sectional area (CSA) (mm^2) and then obtained PFV (ml/min) by using the formula " $\text{CSA} \times \text{PV}$ ".

Only mild side effects, not requiring the treatment to be discontinued, were observed after Iloprost infusion.

The results are expressed as mean \pm SD. The mean difference of pre-Iloprost and post-Iloprost values of the PV and PFV, was compared using the t Test for

paired data. A p value <0.05 was considered sufficient to demonstrate statistical significance.

Results

Ten patients affected by arteriopathy of lower limbs, were studied to determine PV and PFV before and after 3 consecutive days of Iloprost infusion. As can be seen in table 1, PV and PFV significantly increased after 3 days of Iloprost treatment (PV mean value 23.12 ± 3.89 cm/s vs 28.49 ± 3.90 cm/s, $p < 0.01$, before vs after treatment, respectively and PFV mean value: 1743.9 ± 241.7 ml/min vs 2271.7 ± 333.5 ml/min, $p < 0.001$, before vs after treatment, respectively).

Discussion

We like to point out that the significant increase of PV and PFV already observed in patients with arteriopathy of lower limbs after 7 days of Iloprost infusion (1), is also obtained after only three days of therapy. This result seems to suggest that the increase of PV and PFV after Iloprost infusion is not related to the length of treatment but is rather linked to its pharmacological power. We believe that it is crucial to know the time needed to achieve a pharmacological effect especially in a new therapeutic approach. In fact, being aware that Iloprost confirms its ability to increase the hepatic perfusion also with a shorter treatment, is useful to further studies in this field.

We like to think that a possible field of therapeutic application of Iloprost might be the prevention of vascular complications occurring after liver transplantation. It is known that hepatic vascular thrombosis re-

Table 1. Mean of portal flow velocity (PV) and portal flow volume (PFV) in patients with Raynaud's phenomenon before and after Iloprost treatment.

Determinations	Number of patients	Pre-Iloprost mean value	Post-Iloprost mean value	Difference
PV	10	23.12 cm/s	28.49 cm/s	5.37
PFV	10	1743.9 ml/min	2271.7 ml/min	527.8

PV pre-Iloprost mean value vs post-Iloprost mean value in all patients; $p < 0.01$.

PFV pre-Iloprost mean value vs post-Iloprost mean value in all patients; $p < 0.001$.

presents a significant cause of graft loss (9, 10) and patient mortality and thus multidisciplinary treatment approaches are needed in these cases (10). Some asymptomatic patients with vascular complications may not require any treatment, while some of them may need a specific one; in this case, angioplasty, surgical reconstruction of the venous anastomosis and retransplantation are considered as a safe solution. It is true that vascular complications are the consequence of unresolved surgical technical problems requiring an invasive treatment and thus, on this basis, it would seem that Iloprost can not play a role in the treatment of the patients with hepatic vascular complications after liver transplantation. But we cannot rule out that Iloprost may have some efficacy in preventing the occurrence of vascular complications in these patients. In fact, Iloprost is a potent vasodilator with platelet aggregation inhibitor properties (2, 3) that might have some anti-thrombotic preventive usefulness after liver transplantation. Furthermore, the fact that Iloprost induces a better hepatic perfusion, as we have already observed, might play a role also after hepatic vascular thrombosis. For example, it is reported that in patients with pre-existing vascular alterations of portal vein, the occurrence of vascular portal complications, after liver transplantation, is more frequent than in subjects without (10). Literature also reports that, among vascular complications of portal vein after liver transplantation, there is not only occlusion, in which a treatment with Iloprost would have few possibilities of success, but also stenosis (10). In this latter case the potential advantages of the treatment with Iloprost are clear: it might not only display anti-aggregation properties but also relaxation and ability to improve the portal vein perfusion, thus favouring the patency of the portal vein. In addition, it might be crucial, after liver transplantation, to treat with Iloprost the subpopulation of patients in which, before liver transplantation, vascular alterations of portal vein (such as stenosis or occlusion) were detected to assess whether there is a reduction of incidence of stenosis or occlusion. Finally, these are only hypotheses at present that, however, we hope may be confirmed by further studies in this field.

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