Prostacyclin improves symptoms, exercise tolerance, and survival in patients with pulmonary arterial hypertension. However, the difficulty of administration (whether intravenous, subcutaneous, or by inhalation) often causes side effects that can reduce the patient’s quality of life and which may sometimes be serious. Bosentan, an orally active endothelin receptor antagonist, improves functional class and exercise tolerance in these patients. We describe the successful transition from prostacyclin to bosentan in five patients with severe pulmonary arterial hypertension who suffered serious side effects with prostacyclin treatment.

**Key words:** Prostacyclin. Bosentan. Arterial pulmonary hypertension.
The mean duration of PC therapy was 57.4 months (range, 21-136).

The switch from PC to bosentan was done on an outpatient basis. Follow-up consisted of a clinical assessment, 6-min test, and echocardiogram. At the initial visit, the rate of PC tapering was established according to the severity of PH and total dose of PC (slower rate for more severe disease), and bosentan was initiated at 62.5 mg/12 h. Clinical control was performed at one month to readjust the decrease rate and to double the bosentan dose if tolerance was good. In the third month, a 6-min test and echocardiogram were performed for clinical follow-up, and every 6 months thereafter to monitor the patients’ clinical stability. Transaminases were measured 15 days after starting bosentan and monthly thereafter.

RESULTS

The patients’ baseline characteristics are shown in Table 1. All were stable. The 3 patients with treprostinil (cases 1-3) presented considerable pain that was refractory to analgesics at the infusion site. Case 3, who had previously received epoprostenol and required withdrawal of the central catheter due to pneumococcal sepsis, was gradually switched to treprostinil. Case 4 had been under treprostinil therapy, but was unable to tolerate the drug due to local pain and therefore, was switched to iloprost. Both this patient and patient 5 required 6 inhalations per day, which notably affected their quality of life and jeopardized therapeutic compliance.

In all patients, the initial dose of bosentan was 62.5 mg/12 h. Treprostinil was discontinued simultaneously, decreasing 2 to 3 ng/kg/min a week. In the patients on iloprost, the number of inhalations was reduced to half over 3-7 weeks and then discontinued. In all patients, the dose of bosentan was doubled from 3 to 4 weeks after it was started. The mean time to switch to bosentan was 6.6 weeks (range, 3-10) after reaching doses of 125 mg/12 h. The mean follow-up with bosentan was 17.6 months (range, 4-29 months). No patient presented deterioration in clinical status, and the pulmonary pressures and echocardiographic parameters remained stable (Table 2).

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bosentan was discontinued and iloprost was initiated. No adverse effects were observed in the remaining patients, including the patient with HIV infection who presented hepatitis C-related liver disease and a slight baseline transaminase elevation (always below three times the upper normal limit).

**DISCUSSION**

The evolution of our patients shows that the switch from PC to bosentan can be attempted in stable patients, with good long-term progress.

Although PC results in a significant change in the clinical progress and survival of patients with PH, it cannot be considered an ideal treatment, given the complexity of administration. Continuous intravenous infusion (epoprostenol) is associated with serious complications related to the infusion system, including sepsis (0.1-0.6 cases per patient-year), catheter displacement, and catheter thrombosis. The subcutaneous form of the drug (treprostinil) eliminates the risk of serious complications associated with the central catheter. However, 85% of patients present pain at the infusion site, with 8% requiring discontinuation of the treatment. Due to its short mean half-life, inhaled PC (iloprost) requires numerous inhalations per day (9), which interferes with the quality of life and affects therapeutic compliance.²

Bosentan is an oral endothelin receptor antagonist that decreases vascular resistance and improves cardiac output and exercise capacity in patients with idiopathic PH or PH associated with CD.³ An increased survival has recently been reported among these patients.³ The usefulness of bosentan has been shown in a study of TOS-associated PH with a mean follow-up of 9 months,⁴ and it is effective and safe for HIV-positive patients with PH; moreover, it can improve the hemodynamic and echocardiographic parameters at the mid-term.⁵ Bosentan is metabolized in the liver and causes a reversible, dose-dependent increase in transaminases in up to 3% of patients.⁶ Recent series⁷⁸ have shown bosentan to be an effective alternative to PC in stable patients. In fact, in our 5 patients we observed no clinical decline or pulmonary pressure deterioration, with a mean follow-up of almost 1.5 years. At month 4, 1 patient presented increased transaminases (5-fold the baseline values) that normalized when bosentan was discontinued. The HIV-positive patient experienced no deterioration in liver profile, despite the presence of hepatitis C virus infection.

In summary, bosentan is an effective alternative to PC. The transition can be attempted with some safety in stable patients. An invasive mode of administration is not required, thus decreasing the adverse effects secondary to the pharmaceutical form and noticeably improving the patients’ quality of life. More extensive studies are needed to confirm these results.

**REFERENCES**