Bosentan Therapy in a Patient with Failed Fontan Procedure: A Case Report

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ABSTRACT

Background: Increased pulmonary vascular resistance index (PVRI) leads to several complications in patients after a Fontan operation. This increase is mainly attributed to the overexpression of endothelin-1 for a long duration after the Fontan procedure. Here, we describe the case of a 3-year-old boy with a failed Fontan operation who was treated with bosentan, an endothelin-1 receptor blocker.

Case report: Cardiac catheterization was performed, which showed a main pulmonary artery pressure (MPAP) of 19 mmHg and PVRI of 5.6 woods/m². Oral bosentan regimen at a dose of 31.25 mg was initiated twice a day. The treatment was continued as pleural effusion and ascites persisted. No adverse events were observed, and the treatment was well tolerated. Pleural effusion disappeared, and ascites decreased markedly after 4 weeks, whereas the MPAP was 15 mmHg and the PVRI was 4.3 woods/m². After 3 months of bosentan therapy, the MPAP was 12 mmHg and the PVRI was 4.1 woods/m².

Conclusion: We observed that bosentan reduces the PVRI and complications such as pleural effusion and ascites after a failed Fontan procedure.

INTRODUCTION

The Fontan procedure, which has been used to treat patients with functional univentricular hearts since 1971, has markedly increased survival rates from 50% to 90% over the past decades. However, many patients still present with late complications such as arrhythmias, thromboembolizations, protein-losing enteropathy, and lower exercise capacity, which are believed to result from increased pulmonary vascular resistance index (PVRI). Studies have shown that high PVRI may result from either microembolization or pulmonary endothelial dysfunction, especially the overexpression of endothelin-1 after an extended Fontan circulation procedure.

DISCUSSION

In 1971, Fontan proposed a new surgical method for treating TA malformations, which involved connecting the superior and inferior vena cava to the pulmonary artery, resulting in a functional single ventricle. As the pulmonary flow is driven without support from the sub-pulmonary ventricle, this procedure was restricted by the PVRI. Bosentan was widely used to reduce the PVRI and the MPAP in patients with pulmonary artery hypertension due to congenital heart defects. However, only few studies on the utilization of bosentan in Fontan patients were reported. Keiichi Hirono showed that bosentan therapy reduced pulmonary artery pressure (PAP) and PVRI in SV patients who did not undergo the Fontan procedure. Since no significant changes in the PVRI and MPAP were observed after 4 weeks of bosentan therapy, 3 and 5 patients in this study underwent the Glenn shunt and
Fontan procedures, respectively [Hirono 2010]. Although sildenafil has been previously shown to reduce the PVRI after the Fontan circulation procedure [Goldberg 2011], it was not approved for use in children owing to the dose-dependent effects, which may increase the death rate of pediatric patients with pulmonary artery hypertension. In this case, the boy’s PVRI decreased from 5.6 to 4.1 wood/m$^2$ 4 weeks after therapy was initiated.

Because of the absence of the sub-pulmonary ventricle, poor cardiac function, pleural effusion, ascites, and protein-losing enteropathy were important early- and late-onset complications. A previous study found that bosentan might increase the cardiac output and the exercise capacity of Fontan patients [Schuuring 2013; Herbert 2014]. In this case, there were no significant changes in the 6MWD before and after bosentan therapy. Bowater SE suggested that since the 6MWD test has not been validated in Fontan patients, it might not be sensitive enough to measure changes when the baseline value is relatively high [Bowater 2012]. Pleural effusion and ascites were observed in the first 2 weeks. The pleural effusion disappeared, and ascites decreased after 4 weeks, whereas the PVRI and MPAP were reduced after 2 months of bosentan therapy, suggesting the need for a longer treatment duration, which is related to pulmonary hypertension. Since this study was limited to one patient and we did not have a longer follow-up period, we have no reason to believe that bosentan will not effectively improve exercise capacity after the Fontan procedure.

Many drugs are currently used to treat pulmonary hypertension. Bosentan use, which was approved for the treatment of pulmonary artery hypertension in adults, has resulted in possible abnormalities in hepatic and renal function tests. However, there are limited data on children undergoing the Fontan procedure. Bosentan therapy was well tolerated and adverse events were not observed in our patient.

We propose that bosentan therapy reduced the PVRI and occurrence of complications such as pleural effusion, ascites, and heart failure after a failed Fontan procedure. Because of limitations in our patient’s activity, the effects of bosentan on exercise capacity and cardiac output need to be confirmed in a future report.

**REFERENCES**


