

First experience of Tolvaptan therapy in patients with Failing-Fontan and diuretic resistance

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Introduction:

Up to 15% of all Fontan patients develop a so-called failing of the Fontan circulation. Symptoms are protein-losing enteropathy (PLE), which results in hypalbuminemia, hypogammaglobulinemia, lymphopenia, profound diarrhea, dystrophy and severe imbalance of the salt water homeostasis with serum-hyponatremia (negative predictor of morbidity and mortality in heart failure) pleural and pericardial effusions, ascites and edema. These patients need high doses of three- to fourfold diuretic therapy and electrolyte substitution. We report about our first experience of Tolvaptan treatment in patients with Failing-Fontan. Tolvaptan is a vasopressin receptor antagonist and has been demonstrated to be effective in patients with heart failure refractory to diuretic therapy.

Methods:

We treated four patients with Failing Fontan, three with PLE and one patient who suffered from congestive heart failure of his single ventricle. All patients showed signs of water overload with hyponatremia (<135 mmol/l), effusions and edema. Before and during Tolvaptan therapy we monitored laboratory parameters (electrolytes, neurohumoral parameters, liver enzymes, urinary sodium and osmolality) and clinical symptoms (weight, effusions, edema, abdominal girth, etc.). In one patient with PLE we performed serial experimental ²³Na-MRI (before and during therapy), to illustrate and quantify interstitial sodium and water in muscle and skin.

□ Results:

During Tolvaptan therapy all patients showed significant reduction of weight, pleural effusions, edema and ascites. Serum-sodium stabilized under Tolvaptan in the normal range (135-145 mmol/l). Tolvaptan reduced hepatic congestion and significantly decreased liver enzymes. Conventional three to fourfold diuretic therapy and electrolyte substitution could be considerably reduced under Tolvaptan therapy and therefore side effects of chronic conventional diuretic therapy. These effects were confirmed in long-term follow up. ²³Na-MRI showed a significant sodium overload in muscle and skin before Tolvaptan treatment which could be reduced and normalized under therapy.

□ Conclusions: □ Tolvaptan improves clinical state of health and symptoms of water overload in patients with failing Fontan. It reduces effusions, ascites, peripheral edema and normalized serum sodium and therefore eliminated the negative predictor of hyponatremia. Its value as rescue diuretic in patients with Failing Fontan, with water overload and diuretic resistance need to be discussed and further evaluated.