The Impact of Ambrisentan Therapy on Protein-Losing Enteropathy in Patients After Fontan Procedure

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【Background】
- PLE, defined as the abnormal loss of serum proteins into the lumen of the gastrointestinal tract, was a serious complication after Fontan procedure.  
- There were many treatment options, but the outcome was generally poor.

<table>
<thead>
<tr>
<th>Fontan (n)</th>
<th>Incidence of PLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Martens, L et al. JTCS 1999;115:1063-1073</td>
<td>3029</td>
</tr>
<tr>
<td>Feldt, R et al. JTCS 1999;112:872-80</td>
<td>427</td>
</tr>
</tbody>
</table>

【Aim】
- To investigate the efficacy of ambrisentan in patients with PLE after Fontan operation.

【Subject】
- PLE, proteinlosing PN pulmonary vasodilator IS immunosuppressant MMF/mycophenolate mofetil eTCPC Extracardiac total cav-pulmonary bypass

【Treatment goal】
1. dose reduction of steroid  
2. reduction of supplementation of albumin or gamma-globulin

【Treatment protocol】
- Ambrisentan was added at starting dose of 0.1mg/kg per day.
- Case3: up-titrated dose 0.2mg/kg per day.

4 years male, Tricuspid valve dysplasia, p-TCPC

【Result】

<table>
<thead>
<tr>
<th>No</th>
<th>The observation period</th>
<th>Steroid reduction</th>
<th>Interval of supplement</th>
<th>Adverse effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case1</td>
<td>4.3</td>
<td>+</td>
<td>+ (0→22day)</td>
<td>+ (puffy)</td>
</tr>
<tr>
<td>Case2</td>
<td>3.8</td>
<td>+</td>
<td>+ (off)</td>
<td>+ (3→28day)</td>
</tr>
<tr>
<td>Case3</td>
<td>4.0</td>
<td>+</td>
<td>+ (off)</td>
<td>+ (puffy)</td>
</tr>
<tr>
<td>Case4</td>
<td>3.4</td>
<td>+</td>
<td>+ (off)</td>
<td>-</td>
</tr>
</tbody>
</table>

- No severe adverse effect but transient puffy face (2pts) was found.
- All case could reduce PSL dose.
- 2 of 4 cases could cancel supplement of Alb, all cases can extend.
- All cases could extend interval of supplement IgG.

【Discussion】
The pathological mechanism of PLE after Fontan procedure is as follows:  
1. characteristics of Fontan physiology, especially low cardiac output and high central venous pressure  
2. increased mesenteric resistance  
3. systemic inflammation  
4. altered Glycosaminoglycan make-up in intestine

Pathological mechanism of PLE after Fontan

【How dose ambrisentan work for PLE?】
Ambrisentan is a highly selective blocker of the endothelin receptor type A (ETA), which results in vasoconstriction of smooth muscle to reduce pulmonary resistance and decrease vascular permeability & proinflammatory cytokines.  

【Conclusion】
Ambrisentan is one of the treatment of the choice for the patients demonstrating steroid-dependent PLE after Fontan procedure

【Reference】(1) Jack ivych et al Congenital Heart Dis 2007 (2) Justin M et al.PEDIATRIC CARDIOLOGY and CARDIAC SURGERY 26  