ACE-inhibitors: useful in single ventricle physiology?

C.Blanche
Mrs R-N, 37 y.o

Right atrial isomerism
Complete AVSD with hypoplastic LV
VA discordance
Pulmonary atresia
Comorbidities

• Stroke in 1981 with mild residual neurological impairment
• Multiple ischemic stroke, likely cardioembolic in 2010
• Depressive disorder
• Difficult social and personal situation
No Fontan palliation: anatomy not favourable for a lateral tunnel

- 1979: LBTS
- 1981: Bidirectional Glenn (LBTS ligation)
- 1989: RBTS -> stenotic
- 1994: Central shunt (venous graft, AA to LPA origin, close to bifurcation)
- 1996: Stenting of the central shunt (LPA anastomosis)
- 2003: Large aneurysm of the central shunt

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2003-2007

- NYHA II
- Aneurysm: coiling? covered stent? -&gt; technically difficult
- TCPC:
  - RPA 13 mmHg  LPA 16 mmHg (mild stenosis) EDP: 8 mmHg
  - Mild to mod AR, mild AVVR, normal RVEF.
- MDT (many times):
  1. high risk for any surgery: cyanotic, a lot of collaterals
  2. TCPC: difficult, position of the left-sided IVC
  3. Heart transplant to be considered if more symptomatic
Palpitations with left arm weakness

MRI: multiple ischemic lesions, likely cardio-embolic.

Anticoagulation refused -> ASA

↑ dyspnea (NYHA III)
Using a wheelchair frequently

Dizzy spells, nausea and vomiting
↓ weight (37 kg)
• Medication: ASA 100 mg OD, Enalapril 5 mg BID (for years) Citalopram, Cerazette.

• SaO2 82%  BP 79/40 mmHg  HR 103  bpm
• Cachectic, no signs of heart failure.
• Appropriate secondary erythrocytosis, no anemia or iron deficiency.
• ProBNP  1989 ng/L (↑ but ↔)
Worsening functional capacity

No obvious change on imaging, bloods...

Discussed in GUCH meeting for heart transplant

NO

High risk of bleeding (cyanotic/collaterals)

Cachectic

Psychologically not stable
Dizzy spells likely due to orthostatic hypotension

Harm/benefit of ACE-inhibitors: Decreased ACE-I -> clinically improved, ↑ weight

2012

2013...

2015

NYHA IV

Wanted to get pregnant... -> strongly discouraged -> lost of FU
• On admission: stopped completely ACE-I in 2013.

• SaO2 76%      BP 89/60 mmHg   HR 115 bpm   RR 30/min
• Peripheral oedema of the upper limbs >>> lower limbs.
• Bilateral crackles, hepatomegaly. No clear ascitis on examination.

• Hb 204 g/L   Ht 61%   Platelets 272 G/l
• ProBNP 6048 ng/L ↑↑ (1989)
• Mild renal failure
• Abnormal liver tests.
Central shunt with aneurysm
Glenn

RBTS

Central shunt
Glenn and RBTS flows
BT 0.13
AOtop 0.78
Forward 3.3
FR 76%
AO-AP 1.62*
LPA 0.91
0.26*
RPA 1.3
Glenn 0.21
Ao root 3.5
FR 18%
DAO 0.49
IVC 1.02
0.89
0.33
0.97
0.51
Summary:

1. More symptomatic, signs of heart failure, peripheral oedema of the upper limbs >>> lower limbs.
2. Worsening ventricular EF (echo and CMR).
3. ↑ AVV regurgitation (moderate).
4. Stable AR (mild to moderate).
5. Reversal flow in the Glenn shunt.
• Put on diuretics and ACE-I.
• Discharged on Torasemid 5 mg OD and Enalapril 2.5 mg BID.
• 2016:
  – back to her baseline (NYHA III)
  – no signs of heart failure anymore.
What is the evidence of heart failure treatment in patients with congenital heart disease?
CONGENITAL HEART DISEASE

AT RISK OF HEART FAILURE

- Stage A: At high risk of HF but without structural heart disease or symptoms of HF
  - Therapy: Early identification of predisposing factors, Risk reduction

- Structural Heart Disease
  - Therapy: As in Stage A

Stage B: Structural heart disease but without signs of HF
  - Selected patients: ACEi, ARB, BB, AICD

Stage C: Structural heart disease with prior or current symptoms of HF
  - Therapy: As in Stages A and B
    - Routine use:
      - Diuretics if fluid retention
      - ACEi
      - BB
    - Selected patients:
      - Aldosterone antagonist
      - ARBs
      - Digitals
      - Hydralazine/nitrates
      - CRT-P
      - AICD

Refractory HF symptoms at rest
  - Therapy: Appropriate measures from Stages A, B and C
  - Decide appropriate level of care
  - Options:
    - Compassionate end-of-life care/ hospice
    - Extraordinary measures:
      - Heart transplant
      - Chronic inotropes
      - Permanent mechanical support
      - Experimental surgery or drugs

Stage D: Refractory HF requiring specialized interventions

HEART FAILURE

Congenital heart disease:
- Surgical/ Percutaneous repair of hemodynamic lesions
- Iron supplementation
- Exercise training

CHD-related Pulmonary Hypertension
- Targeted Pulmonary Hypertension Therapies (ERAs and/or PDE-5i and/or Prostanoids)
• Patients: heterogeneous population
• Studies: underpowered, retrospective, short-term follow-up
• Outcomes: very different
• Scarce evidence to prescribe HF treatment
Use of ACE inhibitors in Fontan: Rational or irrational?


The Australia and New Zealand Fontan Registry

National registry of Fontan (Aus/NZ): 36% on ACE-I
Table 6. Important Clinical Issues With Insufficient Data on Benefit or Harm

The routine use of standard HF medical therapies in:

- SV patients palliated with a Fontan repair with normal ventricular systolic function
- Asymptomatic systolic dysfunction of the systemic or subpulmonic RV
- Prevention of HF in asymptomatic patients with normal ventricular function, especially a systemic RV

Appropriate surrogate end points for clinically meaningful outcomes.

Predictors of prognosis in CHD, including but not limited to:

- The role of measurement of BNP and other markers of neurohormonal activation in patients with CHD
- HF scores
- CPE parameters
- Imaging parameters such as EF, ventricular size, and valvular function

Issues of liver dysfunction, cirrhosis, and hepatocellular carcinoma in patients with cardiac physiology that predisposes to congestive hepatopathy (i.e., Fontan physiology, failing subpulmonic ventricle), specifically:

- Morbidity and mortality associated with the development of liver dysfunction
- Screening strategy
- Effective medical or invasive therapies to prevent or treat liver dysfunction
- Timing of heart transplantation and/or heart-liver transplantation for optimal patient outcomes and organ use
- Timing and options for mechanical circulatory support or heart transplantation
- Sudden death risk stratification in patients with CHD
- The role of CRT
• Mrs R-N, 37 y.o...
• ACE-I:
  – Indicated?
  – Clinical deterioration related to the stop of Enalapril treatment?

Thank you!