Central venous catheter-associated thrombosis in children with congenital hyperinsulinism

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Introduction

- Congenital Hyperinsulinism (CHI), a heterogeneous condition caused by dysregulated insulin secretion, is the most common cause of hypoglycaemia in neonates and infants
- Central venous access is often required to deliver high rates of glucose to achieve and maintain euglycaemia
- Central venous cathether (CVC) placement is the single most significant risk factor for thrombosis development in infants and children
- Development of severe CVC-associated thrombosis has been noted in some of our patients with CHI

Objectives

- Determine the incidence of CVC-associated thrombosis in patients with CHI
- Analyse for potential risk factor associations
- Evaluate outcomes of CHI patients receiving enoxaparin prophylaxis

Methods

- Retrospective 3 year review (2014-2017)
- Patients with CHI requiring CVC placement at a specialist centre for CHI
- Incidence of CVC-associated thrombosis: clinically suspected, confirmed by ultrasound
- Potential risk factors
  - Patient & CHI characteristics
  - CVC characteristics
  - Fluids infused via CVC (dextrose, glucagon)
- Outcome of enoxaparin prophylaxis: select patients requiring high concentration dextrose for the majority of fluid intake and/or sustained glucagon infusion
- Statistical analysis:
  - Mann-Whitney U test (continuous data); Chi-squared & Fisher’s exact tests (categorical data)
  - Stepwise backward logistic regression for correlation of variables with thrombosis

Results

Incidence

- 6/33 (18%) patients requiring CVC developed thrombosis over a 3-year period
- 4.2 thromboses/1000 catheter days

Case Detection

- Thrombosis detected at a median of 12 days (range 2-118) days after CVC insertion
- Median age 24 days of life (range 6-139)
- 4 symptomatic (swelling, redness, warmth, reduced limb mobility, catheter blockage), 2 asymptomatic (routine echo, USS to identify sites for CVC insertion)

Patient Characteristics

- 3 with genetically-confirmed CHI requiring surgery (1 focal, 2 diffuse)
- 3 with negative genetics and responsive to diazoxide

Potential Risk Factors

- Trend towards higher thrombosis frequency in patients with homozygous & compound heterozygous ABCC8/KCNJ11 mutations (p=0.29)
- Compound heterozygous mutations correlated with thrombosis \( R^2=0.40, p=0.001 \)
- No association with other patient, CVC or fluid characteristics (table 1)

<table>
<thead>
<tr>
<th>Presence of any ( K_{ATP} ) mutation</th>
<th>Thrombosis (n=6)</th>
<th>No thrombosis (n=27)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 (50%)</td>
<td>12 (44%)</td>
<td>0.80</td>
<td></td>
</tr>
<tr>
<td>Maximum glucagon, mcg/kg/hr</td>
<td>15.0 (IQR 11.0)</td>
<td>10.0 (IQR 5.0)</td>
<td>0.37</td>
</tr>
<tr>
<td>Maximum dextrose, %</td>
<td>20.0 (IQR 16.9)</td>
<td>20.0 (IQR 10.0)</td>
<td>0.91</td>
</tr>
<tr>
<td>Catheter days</td>
<td>15 (IQR 39)</td>
<td>24 (IQR 75)</td>
<td>0.41</td>
</tr>
</tbody>
</table>
* Interquartile range; \( * \) Shorter duration in patients with thrombosis reflects earlier removal due to thrombosis

Enoxaparin prophylaxis (N=7)

- No differences between prophylaxis vs. thrombosis groups
- None developed thrombosis
- No bleeding complications during 109 patient-days of prophylaxis

Conclusions

- Significant incidence of CVC-related thrombosis in patients with CHI (18% vs. 9.2% in neonatal population [1])
- Association between thrombogenesis and CHI severity? Evidence of impaired fibrinolysis in hyperinsulinaemic states [2-5]
- Preliminary outcomes in patients on prophylaxis suggests its efficacy and safety – requires on-going evaluation

References