Central venous cathether-associated thrombosis in children with congenital hyperinsulinism

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Fetal, neonatal endocrinology and metabolism (Abstract 341)

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 1. Selected CHI & treatment characteristics and association with thrombosis.

	Thrombosis (n=6)	No thrombosis (n=27)	P value
Presence of any K_{ATP} mutation	3 (50%)	12 (44%)	0.80
Maximum glucagon, mcg/kg/hr	15.0 (IQR[a] 11.0)	10.0 (IQR 5.0)	0.37
Maximum dextrose, %	20.0 (IQR 16.9)	20.0 (IQR 10.0)	0.91
Catheter days	15 (IQR 39)[b]	24 (IQR 75)	0.41

[a] Interquartile range; [b] 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

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