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ORAL ABSTRACTS

332.THROMBOSIS AND ANTICOAGULATION: CLINICAL AND EPIDEMIOLOGICAL

Clinical Characteristics, Treatment, and Outcomes of Provoked Acute Cerebral Sinovenous Thrombosis in Patients <21 Years Old: Findings from the Kids-DOTT Multinational Trial

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Background

Cerebral sinus venous thrombosis (CSVT) is a rare pediatric condition with an estimated incidence of 0.7 per 100,000 children. However, amongst pediatric venous thromboembolism (VTE), the proportion of CSVT is high, at about 10% of all pediatric VTE. Key risk factors include perinatal stressors in cases of neonatal CSVT and acute infections, especially head and neck infections, in older children. To date, few multinational trials of pediatric VTE treatment have reported findings specifically among CSVT patients.

Aims

We sought to describe the clinical characteristics, treatment strategies, and outcomes of the patients with provoked acute CSVT enrolled in the Kids-DOTT trial and to compare these features to those of Kids-DOTT participants with non-CSVT VTE.

Methods

Kids-DOTT was an NIH-sponsored multinational randomized clinical trial (RCT) comparing 6 weeks vs. 3 months of anticoagulation for provoked acute VTE treatment in patients <21 years, with two non-randomized cohort arms run in parallel to the RCT for patients with persistent antiphospholipid antibodies or complete veno-occlusion at 6 weeks post-diagnosis of the index VTE. The primary RCT findings were recently published. In the present analysis, descriptive statistics were used to summarize patient and thrombus characteristics, treatments, and outcomes, and variables were compared between CSVT and non-CSVT VTE groups using Mann-Whitney U test for continuous variables and Chi-squared or Fisher's exact test, as appropriate, for categorical variables. All statistical analyses were performed using R Core Team, 2021. A P-value of <0.05 was considered statistically significant.

Results

Among 532 patients enrolled in the Kids-DOTT trial, the index VTE was a CSVT in 75 (14%). Age distribution differed significantly (P=0.002) between CSVT and non-CSVT VTE patients, with the CSVT more likely to occur in neonates and children, compared to non-CSVT VTE more likely to occur in adolescents. CSVT was less likely to be CVC-related compared to non-

CSVT VTE. The frequency of any infection (56.9% vs 26%, p<0.001) and specifically infection of the head/neck (35.4% vs 2%; P<0.001) as a provoking factor was significantly higher for CSVT vs. non-CSVT VTE. Non-head and neck infections were less likely to be associated with CSVT compared to non-CSVT VTE. One-third of CSVT patients received 6 weeks, while two-thirds received > 3 months, of anticoagulation (Table 2). No patients developed ISTH-defined symptomatic recurrent VTE or clinically relevant bleeding.

Conclusions

These multinational trial findings substantiate those of retrospective studies implicating head/neck infection as an important provoking factor for CSVT in young patients. The absence of recurrent VTE or clinically relevant bleeding among CSVT patients managed with anticoagulation in Kids-DOTT serve to augment recent RCT findings of CSVT treatment in children involving direct oral anticoagulants, demonstrating the safety and efficacy of therapeutic anticoagulation for pediatric CSVT.

Disclosures Kucine: *Protagonist Therapeutics:* Consultancy; *PharmaEssentia:* Consultancy. **Ahuja:** *TraumaChek:* Patents & Royalties; *ClotChip:* Patents & Royalties; *XaTec Inc:* Research Funding; *CSLBehring:* Honoraria; *NovoNordisk:* Honoraria; *Genentech:* Honoraria; *Sanofi:* Honoraria; *State of Ohio Rare Disease Advisory Council:* Membership on an entity's Board of Directors or advisory committees. **Goldenberg:** *Bayer:* Consultancy; *Astra Zeneca:* Consultancy; *Boehringer-Ingelheim:* Consultancy; *Chiesi:* Consultancy; *Daiichi Sankyo:* Consultancy; *University of Colorado-affiliated Academic Research Organization CPC Clinical Research:* Other: Serves on clinical trials oversite committees for pharma studies; *Novartis:* Other: Data and Safety Monitoring Committee; *Anthos Therapeutics:* Consultancy.

Table 1: Baseline characteristics of the Kids-DOTT study population

Variable	Overall, N = 532[1]	Patients with CSVT at enrollment, N = 75[1]	Patients with Non-CSVT VTE at enrollment, N = 457[1]	p-value[2]
Age (years)	8.0 (1.0, 15.0)	6.6 (2.3, 11.3)	8.5 (0.9, 15.6)	0.10
Age group				**0.002**
Neonate	23 (4.3%)	6 (8.0%)	17 (3.7%)	
Child	326 (61.3%)	55 (73.3%)	271 (59.3%)	
Teen	183 (34.4%)	14 (18.7%)	169 (37%)	
Sex (% male)	283 (53.2%)	47 (62.7%)	236 (51.6%)	0.076
Overweight/Obese	123/342 (36%)	20/57 (35.1%)	103/285 (36.1%)	0.9
Provoking Factors				
Central venous catheter	235/472 (49.8%)	4/64 (6.3%)	231/408 (56.7%)	**<0.001**
Hospitalization within previous 30 days	6/472 (1.3%)	0/64 (0%)	6/408 (1.5%)	>0.9
Trauma or surgery within previous 30 days	91/472 (19.3%)	9/64 (14.1%)	82/408 (20%)	0.2
Autoimmune/chronic inflammatory condition	14/472 (3.0%)	1/64 (1.5%)	13/408 (3.2%)	0.7
Estrogen/other prothrombotic medication use	29/472 (6.1%)	5/64 (7.8%)	24/408 (5.9%)	0.6
Congenital or acquired cardiac disease	3/472 (0.6%)	0/64 (0%)	3/408 (0.7%)	>0.9
Infection	143/472 (30.3%)	37/65 (56.9%)	106/407 (26%)	**<0.001**
Head/Neck	31/472 (6.6%)	23/65 (35.4%)	8/407 (2%)	**<0.001**
Non-Head/Neck	35/472 (7.4%)	0/65 (0%)	35/407 (8.6%)	**0.009**
Unknown Site	77/472 (16.3%)	14/65 (21.5%)	63/407 (15.5%)	0.2

[1]Median (IQR); n (%)

[2]Wilcoxon rank sum test; Fisher's exact test; Pearson's Chi-squared test

Table 2: CSVT anatomic sites, treatments, and outcomes in the Kids-DOTT study CSVT subpopulation (n= 75)

Variable	Frequency
CSVT Anatomic Site	
Sigmoid sinus: left-sided	7/44 (15.9%)
Sigmoid sinus: right-sided	6/44 (13.6%)
Superior sagittal sinus	10/44 (22.7%)
Transverse sinus: left-sided	10/44 (22.7%)
Transverse sinus: right-sided	10/44 (22.7%)
Involvement of Internal Jugular Vein	30/75 (40%)
Duration of Anticoagulation	
6 weeks	25/75 (33%)
≥3 months	50/75 (67%)
Symptomatic Recurrent VTE	0/75 (0%)
Clinically Relevant Bleeding	0/75 (0%)
Acetazolamide Use	6/41 (14.6%)
CSF Shunt/Drainage Intervention	4/40 (10%)
Anticonvulsant Administration	12/38 (31.6%)

Figure 1

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