Vancomycin to Prevent Clostrioides difficile Infection in Children

Oral vancomycin is used as a treatment for Clostrioides difficile infection (CDI), and adult studies suggest that vancomycin can be used as a preventative therapy to stop recurrence of CDI in patients receiving antibiotics for other reasons. However, no relevant data exists in children, and the authors of this study looked at the effectiveness of this intervention in children at a single academic health system.

This retrospective study occurred over 6 years and included all children with CDI diagnosed by polymerase chain reaction. Patients were identified who had a prior CDI, had a subsequent outpatient or inpatient encounter, and then required intravenous antibiotic usage during the encounter. This group was then divided into patients who did or did not receive oral vancomycin prophylaxis. Patient demographics were obtained on all patients including the identification of NAP1 (North American pulsed-field gel electrophoresis type 1) strains, use of acid suppression medication, and use of probiotics. Oral vancomycin prophylaxis was defined as dosing of 10 mg / kg every 12 hours during antibiotic administration and for 5 days afterwards.

A total of 148 patients were initially identified; however, the final study patient number after utilizing exclusion criteria consisted of 74 patients (30 receiving oral vancomycin prophylaxis; 44 not receiving oral vancomycin prophylaxis). Patients were statistically similar regarding demographics and comorbidities although more males received oral vancomycin prophylaxis (not significant). Most patients had a history of malignancy or immune suppression. There was no difference between groups in regard to acid suppression use or probiotic use. Hospital length of stay was longer in patients who received oral vancomycin prophylaxis. Most patients had only one prior CDI, and most patients had received antibiotics within 3 months of CDI. Oral vancomycin prophylaxis was more common in patients who had received fluoroquinolones and carbapenems. Oral vancomycin prophylaxis also was significantly more common in patients receiving 2 or more classes of antibiotics and receiving a longer duration of antibiotics. Patients who did not receive oral vancomycin prophylaxis were statistically more likely to have CDI recurrence. No vancomycin-resistant enterococci infection occurred in any patient within 8 weeks of vancomycin exposure. Univariate and multivariate analysis demonstrated that receiving oral vancomycin prophylaxis was the only significant factor associated with a reduced risk of CDI.

Oral vancomycin prophylaxis shows the potential of reducing CDI in at-risk pediatric patients with prior CDI. This is a retrospective study, and prospective data is needed to determine optimal timing and duration of oral vancomycin use. Additionally, the risk of vancomycin resistant enterococci infection still remains a concern in such patients.

Bao H, Lighter J, Dubrovskaya Y, Merchan C, Siegfried J, Papadopoulos J, Shin-Pung J. Oral vancomycin as secondary prophylaxis for Clostrioides difficile infection. Pediatrics 2021; 148: e2020031807.

Determining Genetic Variants in Pediatric Acute Liver Failure

A large number of pediatric acute liver failure (ALF) cases occur with no diagnosed etiology, and there is concern that potential genetic mutations affecting outcome may be present in such patients. Techniques such as next generation sequencing (typically defined as fast massively parallel sequencing) can determine a human genome in less than one day, and the authors of this study looked at the capacity of such screening techniques to determine genetic causes of ALF in children. This retrospective study of pediatric patients seen in a tertiary pediatric hospital in London looked at all cases of ALF over an 18-year period in which stored blood was available. Included study patients had no evidence of chronic liver disease. Additionally, such patients needed to have laboratory evidence of ALF defined as having an international normalized ration (INR)

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≥ 1.5 not corrected by Vitamin K with associated hepatic encephalopathy or having an INR ≥ 2 with or without hepatic encephalopathy. Clinical characteristics were obtained for all patients, and children with ALF were determined to have an indeterminate cause of disease if no known cause of ALF could be found. Additionally, blood samples underwent next generation sequencing to evaluate for 64 mutations causing genetic and metabolic liver disease in children, exome sequencing to evaluate the entire genome of the affected child and unaffected parents, or sequence variant filtration to determine potential disease-causing variants.

Next generation sequencing occurred in 41 patients while 4 patients underwent exome sequencing. Next generation sequencing identified eight children with either heterozygous or homozygous ALF-causing mutations of *NBAS*, *TWINK*, *CPT1A*, *MPV17*, *DLD*, *POLG*, and *SUCLG1*. Exome sequencing found mutations in all four children including mutations in *LARS1*, *FAH1*, *NPC1*, and *DLD*. Interestingly, those children with biallelic variants of such mutations presented with ALF at a significantly younger age and were significantly more likely to die from liver failure. Thus, this study shows that using genetic testing to diagnose unknown causes of ALF in children is beneficial in elucidating primary causes of hepatic disease. This aspect is especially important since liver transplantation for mitochondrial DNA mutations is controversial depending on the mutation as other organs besides the liver can be affected. This study shows that sequencing the genome for pediatric ALF is important to determine causality and outcome, and more work is urgently needed to make such testing easily available and affordable.

Hegarty R, Gibson P, Sambrotta M, Strautnieks S, Foskett P, Ellard S, Baptista J, Lillis S, Bansal S, Vara R, Dhawan A, Grammatikopoulos T, Thompson R. Study of acute liver failure in children using next generation sequencing technology. Journal of Pediatrics 2021; 236: 124-130.

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Answers to this month's crossword puzzle:

1 A	M	2 O	X	3 I	C	4 I	L	5 L	I	6 N	■	7 P	U	8 S
N	■	S	■	L	■	S	■	E	■	Y	■	O	■	I
9 A	C	H	A	L	A	S	I	A	■	10 C	O	L	O	N
L	■	A	■	N	■	U	■	11 K	12 G	■	■	Y	■	U
■	■	■	13 F	E	C	E	S	■	14 E	15 N	16 E	M	A	S
17 M	■	18 A	■	S	■	■	■	19 P	R	O	N	E	■	■
20 E	N	D	O	S	C	21 O	P	E	■	22 D	E	R	M	23 A
T	■	D	■	■	■	H	■	P	■	■	■	A	■	B
24 A	B	■	25 H	26 A	E	M	A	T	E	27 M	E	S	I	S
P	■	28 A	■	C	■	■	■	I	■	U	■	E	■	C
29 L	A	S	E	R	■	30 E	■	31 C	E	C	A	■	32 H	E
A	■	P	■	O	■	T	■	■	■	I	■	■	■	S
33 S	T	E	A	T	O	H	E	34 P	A	T	I	35 T	I	S
I	■	C	■	I	■	Y	■	E	■	I	■	E	■	E
36 A	R	T	I	C	U	L	A	R	■	37 S	C	A	R	S