Differences in IBD Care Between Adult and Pediatric Gastroenterologists

There has been a significant discussion about the transition of pediatric patients with inflammatory bowel disease (IBD) to adult gastroenterology care. The authors of this study attempted to evaluate for IBD clinical practice differences between adult and pediatric gastroenterologists and to compare these patterns of care with established clinical guidelines. A clinical questionnaire was administered to adult and pediatric gastroenterologists in Israel consisting of 21 questions pertaining to IBD diagnostics and medical management. A total of 200 adult gastroenterologists and 65 pediatric gastroenterologists were given the questionnaire, and 60% and 75% completed the survey, respectively.

Pediatric gastroenterologists had significantly more and longer clinic visits compared to their adult counterparts, and they were significantly more likely to follow thiopurine methyltransferase (TPMT) metabolite levels for those patients with IBD treated with thiopurines. Pediatric gastroenterologists were more likely to recommend the varicella vaccination while adult gastroenterologists were more likely to recommend the pneumococcal vaccine. Pediatric gastroenterologists also were significantly more likely to order fecal calprotectin testing for IBD diagnosis and follow-up testing.

In regards to therapy, pediatric gastroenterologists were significantly more concerned with thiopurine-related lymphoma as a side effect of thiopurine use. Thus, significantly more pediatric gastroenterologists utilized exclusive enteral nutrition or methotrexate as initial therapy for Crohn disease compared to adult gastroenterologists. Pediatric gastroenterologists also were more likely to combine thiopurine and anti-TNF alpha agents short term as a treatment of Crohn disease compared to adult gastroenterologists who were more likely to combine these medications for longer periods of time. Finally, adult gastroenterologists were significantly more likely to use once daily aminosalicylate therapy for treatment of ulcerative colitis compared to pediatric gastroenterologists; however, there was no difference between physician groups using infliximab or cyclosporine / other as rescue therapy in ulcerative colitis.

This study demonstrates that adult and pediatric gastroenterologists appear to treat IBD differently, and both groups in this study did not necessarily follow established treatment guidelines. More research is needed in determining why such discrepancies in care exist so that problems arising in patient care transition from the pediatric to adult world can be minimized.

Assa A, Avni I, Ben-Bassat O, Niv Y, Shamir R. "Practice variations in the management of inflammatory bowel disease between pediatric and adult gastroenterologists." Journal of Pediatric Gastroenterology and Nutrition. 2016; 62: 372-377.

Probiotics and Protection Against Type I Diabetes Mellitus

Alterations in the infant intestinal microbiome potentially can lead to an increased risk of autoimmune disease, such as Type 1 Diabetes Mellitus (T1DM), and animal models have already suggested a link between increased gut biodiversity and a reduced risk of autoimmune diabetes. The authors of this study used data from The Environmental Determinants of Diabetes in the Young (TEDDY) study, an international prospective cohort study attempting to identify causes of T1DM. Over a 6-year period, 434,788 newborns were screened for T1DM high-risk HLA genotypes, and 7473 of these children with eligible genotypes were included in this study when they were older with an age range of 4-10 years. Blood samples were obtained every 3 months between 3 and 48 months of age, and then blood samples were obtained every 6 months. Persistent islet antibody positivity was considered if antibodies to insulin, glutamic acid decarboxylase, or insulinoma antigen 2 were detected on at least 2 consecutive tests. An infant screening form was used to determine maternal medication use, history of maternal smoking, probiotic use during pregnancy, mode of delivery, infant diet, and infant probiotic use.

The percentage of probiotic use for infants varied between countries, and more probiotic use was seen toward the end of the study period. Kaplan-Meier curves demonstrated that the risk of islet autoimmunity was decreased in infants exposed to probiotics early in life (27 days of age or younger) compared to infants exposed to probiotics later in life (after 27 days of age) or in infants not receiving any probiotics when patients were controlled for first-degree relatives with T1DM, HLA-DR-DQ genotype, sex, order of birth, delivery mode, maternal age, maternal probiotics use, smoking during pregnancy, breastfeeding duration, year of birth, antibiotic use by the infant, and diarrhea. In particular,

the risk of developing T1DM was significantly reduced in those children who received probiotics at 27 days or younger and had HLA-DR3-DQ and HLA-DR4-DQ genotypes which are known genotypes considered high risk for development of T1DM.

This study suggests that certain at-risk infants for T1DM may benefit from receiving probiotics in early life. However, the specific strain of probiotic as well as dosing to achieve such potential protection is unknown.

Uusitalo U, Liu X, Yang J, Aronsson C, Hummel S, Butterworth M, Lermark A, Rewers M, Hagopian W, She J, Simell O, Toppari J, Ziegler A, Akolkar B, Krischer J, Norris J, Virtanen S, for the TEDDY Study Group. "Association of early exposure of probiotics and islet autoimmunity in the TEDDY study." JAMA Pediatrics. 2016; 170: 20-28.

Are There Biochemical Markers for Necrotizing Enterocolitis?

Necrotizing enterocolitis (NEC) is an intestinal inflammatory disease leading to bowel necrosis, and it is a significant cause of death in premature infants. Its cause is unknown although intestinal permeability and bacterial translocation likely are contributing causes. The authors of this study considered if the proteome (the entire protein amount expressed by the genome) and the metabolome (the entire set of small molecules found in a biologic sample) of patients could predict severity of NEC. The authors of this study performed proteomic and metabolomic profiling of 10 patients with either NEC or late-onset sepsis (typically defined as sepsis diagnosed after three days of age) and 9 control patients. Serum samples were obtained 14 days before or after disease diagnosis (if possible) and at the time of disease diagnosis. Proteomic analysis was performed using shotgun proteomics which combines high performance liquid chromatography with mass spectrometry while metabolomic analysis was performed using ultra performance liquid chromatography-tandem mass spectrometry, for which both techniques allow for relatively rapid results.

A total of 447 unique proteins and 24,153 metabolites were isolated. Proteins, including alpha-2-macroglobulin, alpha-1-antitrypsin, serotransferrin, complement C3, and fibrinogen (alpha and beta chains), were most commonly isolated in all study patients which matches prior studies in which alpha-2-macroglobulin and alpha-1-antitrypsin have been demonstrated to be the most common proteins in pre-term infants in the first 6 months of life. Two patients with NEC who had undergone surgery (one of whom subsequently died) had uniquely increased transforming growth factor beta induced protein. Proteins, including C-reactive protein, Ig alpha-2 chain C region, isoform 2 of annexin A2, lithostathine-1-alpha, macrophage migration inhibitory factor, serum amyloid A-2 protein, and transforming growth factor beta induced protein, were increased in patients with NEC; however, these proteins were not always increased at diagnosis and, at times, were less abundant compared to control patients. C-reactive protein levels were increased in all NEC patients at the time of diagnosis and were higher than compared levels in control patients.

No unique proteome/ metabolome profile could predict the occurrence of NEC or late-onset sepsis in this patient group. The finding of C-reactive protein elevation in NEC patients has been described previously and likely indicates increased inflammation as C-reactive protein is an acute phase reactant. The association of macrophage migration inhibitory factor and Ig alpha-2 chain C region with NEC has not been noted in prior studies and may have some association with NEC pathogenesis. However, such protein expression was not always higher in the patients with NEC compared to control patients suggesting an incomplete understanding of the inflammatory pathways associated with NEC. The authors conclude that there is no specific biomarker that currently can predict NEC and late-onset sepsis in premature infants although the proof of concept of combining analysis for the proteome and metabolome in such patients is intriguing.

Stewart C, Nelson A, Treumann A, Skeath T, Cummings S, Embleton N, Berrington J. "Metabolomic and proteomic analysis of serum from preterm infants with necrotising enterocolitis and late-onset sepsis." Pediatric Research. 2016; 79: 425-431.

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