Use of Biologics in Pediatric Crohn's Disease

Biologic therapy using anti-tumor necrosis factor alpha (anti-TNF alpha) agents is part of the arsenal of care for children with Crohn's disease (CD), but it is difficult to obtain data on the effectiveness of this drug class in the pediatric age range. In 2007, a United States national quality improvement collaborative, known as ImproveCareNow, was developed as a learning health system for pediatric inflammatory bowel disease (IBD).

In particular, the ImproveCareNow patient registry was utilized to make a dataset over a 5-year period that included 4130 patients with CD. This study included those pediatric patients in which anti-TNF alpha therapy was or was not initiated in order to determine effectiveness of the medication. The study evaluated if biologic therapy affected both clinical remission and corticosteroid-free remission in pediatric CD patients. The authors compared results to the prior REACH study in which patients were included who had received anti-TNF alpha therapy within 3 months of a CD diagnosis, although this pediatric study allowed remission to be assessed as late as 16 weeks after starting anti-TNF alpha therapy, as opposed to 10 weeks in the REACH study. The authors also used methods from the prior SONIC trial to look at 26-week corticosteroid-free remission rates for patients receiving anti-TNF alpha therapy versus those not receiving such therapy, as well as comparing anti-TNF alpha therapy response to anti-TNF alpha therapy with the addition of thiopurines. The Short Pediatric Crohn's Disease Activity Index (sPCDAI) and the Physician Global Assessment were used to assess CD clinical severity at each clinic visit.

Using these methodological limitations, 1814 CD patients received anti-TNF alpha therapy with 603 patients beginning therapy during the study. No anti-TNF alpha therapy occurred in 2316 CD patients. CD was described as inflammatory in 89% of patients, stricturing in 3.9% of patients, and penetrating in 7.1% of patients. Physician-rated disease severity was higher for patients receiving biologic therapy although sPCDAI was comparable between patient groups. At 26 weeks, patients undergoing initiation with anti-TNF alpha therapy had a 54.4% chance of reaching remission compared to 41.2% change of patients who had not started this drug class which was significant. Patients receiving anti-TNF alpha therapy also had a 47.3% chance of having corticosteroid-free remission at 26 weeks compared to 31.2% of patients who had not started this drug class which also was significant. These clinical response rates to anti-TNF alpha therapy were comparable to the REACH and SONIC studies.

This study provides further evidence that anti-TNF alpha therapy is effective for treatment of pediatric CD, and this drug class appears to match efficacy of adult biologic drug trials. More importantly, use of a comparative effectiveness registry, commonly used for quality improvement measurements, can be used to produce data regarding efficacy of pediatric IBD therapy.

Forrest C, Crandall W, Bailey C, Zhang P, Joffe M, Colletti R, Adler J, Baron H, Berman J, del Rosario F, Grossman A, Hoffenberg E, Israel E, Kim S, Lightdale J, Margolis P, Marsolo K, Mehta D, Milov D, Patel A, Tung J, Kappelman M. "Effectiveness of anti-TNFa for Crohn disease: research in a pediatric learning health system." Pediatrics. 2014; 134: 37-44.

Nutritional Outcomes and Pancreatic Enzyme Replacement in Cystic Fibrosis

Nutrition in a cornerstone for cystic fibrosis (CF) care as good nutritional outcome correlates with pulmonary function in the pediatric population. Pediatric enzyme replacement therapy (PERT) is needed in CF patients to help overcome exocrine pancreatic insufficiency, improve fat absorption, and improve weight gain. The authors of this study evaluated PERT dosing as a potential marker of pediatric CF nutritional status.

Data from this study came from the Cystic Fibrosis Foundation (CFF) Patient Registry which is a large patient data site which monitors patient care and quality improvement through all recognized CFF centers in the United States. All pediatric CF patients taking PERT were included over a 3-year study period, and the highest dose of PERT for each patient during that study period was included in the analysis. Body mass index (BMI) means for each program were placed into quartiles for comparison. Mixed affect modeling using BMI, ethnicity, age, acid suppression medication use, forced expiratory volume in 1 second percentage (FEV1%), presence of *P. aeruginosa* infection, supplemental tube feed status, growth hormone supplementation, and presence of CF-related diabetes were utilized as covariates.

A total of 179 programs consistent of 14,482 patients were evaluated. Although there was no significant

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difference in age at time of CF diagnosis, patients in the top quartile for BMI were statistically younger and had less problems with failure to thrive, malnutrition, and history of meconium ileus. The patients in the top BMI quartile also were statistically more likely to have been diagnosed with CF by newborn screening, had higher FEV1%, were more likely to be receiving supplemental tube feeds (nasogastric or gastric route), and were more likely to be receiving acid suppression therapy. Lowest quartile BMI programs had significantly more patients with CF-related diabetes, more patients requiring insulin, and more patients with osteoporosis. Mean PERT dosing in the top quartile programs (1755 lipase units /kg/meal) was significantly higher compared to lowest quartile programs (1628 lipase units/kg/meal), even after adjusting for the multiple covariates included in this study.

This study suggests that higher PERT dosing is associated with better pediatric CF BMI, and regular assessment of PERT dosing in these patients is essential as part of pediatric CF care. Also, other factors were noted to be associated with improved BMI including newborn screening, use of acid suppression therapy, and use of supplemental tube feeds suggesting these factors need to be considered as well in any pediatric CF patient with poor BMI. Finally, it should be remembered that excessive PERT dosing is associated with distal intestinal obstruction syndrome (DIOS), and PERT dosing should be maintained below 10,000 International Units / kilogram /day to prevent DIOS complications.

Haupt M, Kwasny M, Schechter M, McColley S. "Pancreatic enzyme replacement therapy dosing and nutritional outcomes in children with cystic fibrosis." The Journal of Pediatrics. 2014; 164: 1110-1115.

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