STRONG CHILDREN'S RESEARCH CENTER

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ABSTRACT

Title: **Elevated Liver Enzymes and Rate of Body Mass Index Z-Score Rise in Pediatric Inflammatory Bowel Disease Patients Receiving Infliximab**

Background:
In the pediatric population, we are seeing a rising incidence of elevated liver enzymes that are directly related to weight and rising body max index. When pediatric patients with Inflammatory Bowel Disease (IBD) are initiated on Infliximab treatment, it is common to see a significant upward trend in BMI over the first 1-3 years of treatment. (IBD) is a chronic, inflammatory condition affecting the gastrointestinal (GI) tract. Subtypes include Crohn's Disease (CD), Ulcerative Colitis (UC), and indeterminate colitis. About 1% of the United States population lives with IBD; up to 25% of cases onset in pediatric age. Various factors contribute to IBD development including genetic inheritance, environment (e.g. diet), immune dysregulation, and microbial dysbiosis. These factors cause immune cells to inappropriately secrete inflammatory proteins including tumor necrosis factor-alpha (TNF-a). This leads to production of other biomolecules, which cause further damage to the gastrointestinal tract. There are multiple medications that are used to treat IBD. One of the first FDA approved, and most effective biologic therapies in pediatric IBD, is Infliximab. This drug targets TNF-a and is administered as an infusion. There are numerous potential side effects reported with Infliximab, including liver transaminase elevation. However, there is limited pediatric data exploring possible etiologies.

Many children are underweight or have experienced weight loss leading up to their diagnosis of IBD due to underlying inflammation of the gastrointestinal tract. To our knowledge, the rate of rise of BMI in this initial treatment period and its effect on liver enzymes has not been investigated in pediatric patients. While rises in liver enzymes have historically been attributed to medications or confounding autoimmune hepatitis, it would be important to know if weight gain, especially rapid weight gain, may be having an impact on the liver, and if so, are these changes sustained. If this is found to be a potential etiology of liver dysfunction in pediatric IBD patients, we would intervene earlier with dietary or behavioral changes which could have positive impacts on the inflammation caused by fat accumulation in the liver.

Objective:
This study sought to describe the incidence of transaminase elevation in pediatric patients with IBD on Infliximab and to understand if there is a correlation between rate of rise of BMI z-score and sustained elevation of transaminases.

Methods:
This was a retrospective, chart review study. Subjects were those aged 6 months to 21 years, with a diagnosis of IBD (UC, CD or indeterminate) who were prescribed Infliximab between Jan 1, 2010-July 1, 2025. The researchers reviewed the electronic medical chart of each patient that was identified and obtained age at first Infliximab infusion, sex, and Inflammatory Bowel Disease subtype. Other data collected included Infliximab dosing, weight, length, BMI, and z-score at time of first Infliximab infusion and one year in addition to AST at 0, 3, 6 and 12 months after initiation of treatment. Statistical analyses were performed with this data.

Results:
After reviewing charts of approximately 300 patients, 128 met the criteria for this study. They had all received infliximab infusions at consistent rates of every 4-8 weeks on average. Of these, 19.53% had sustained elevated ALT levels for at least 3 months and 11.52% had sustained elevated AST levels for at least 3 months. When looking at the patients with sustained ALT and AST there was no correlation in rate of rise of BMI z-score using pearson partial correlation coefficients for analysis. It was also noted that anywhere between 10-25% of patients had elevated ALT or AST levels at the time of their infusions.

Conclusion:
Over the first year of Infliximab therapy, less than twenty percent of patients had a sustained elevation in transaminases. There was no correlation found between sustained transaminase elevation and rate of rise of BMI z-score. This information is helpful for clinicians to provide reassurance to families that rate of rise of BMI z-score will not impact transaminases, implying that liver health will be maintained.
Limitations to the study included that liver enzymes could have spiked or decreased at times not measured per the timeline, there was missing data due to hemolysis of blood sample, potential impact of steroids on transaminases and BMI z-score, and inability to fully analyze the full complement of IBD patients due to some initiating infusions at other institutions.
Future directions involve looking at trends of liver enzymes with every Infliximab infusion for the first year of therapy, following the liver enzymes and BMI z-score for a longer duration, evaluating the impact of dosage or changes in dosages to changes in BMI, as well as performing similar studies for patients on other biologics used to treat IBD.

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