

## Evaluation of infliximabe through levels and detection of anti-infliximabe antibodies in Crohn's disease patients.

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### Abstract

We studied 40 patients with Crohn's disease (CD), 18 to 60 years of age, of both genders, who were followed up at the IBD outpatient clinic, Gastrocenter - UNICAMP, and who were under continuous and regular use of Infliximab (IFX). The peripheral blood collection was performed before the IFX application. Quantification of serum IFX levels and presence of anti-IFX antibody (ATIs) were performed by the ELISA method - Promonitor®. The endoscopic activity of the disease was defined as CDEIS > 5 or the presence of deep ulcers in at least one intestinal segment analyzed and according to the radiological activity. The study has been approved by the UNICAMP Research Committee CAAE 53097116.2.0000.5404.

### Key words:

Inflammatory bowel disease, Crohn's disease, biological therapy

### Introduction

Crohn's disease (CD) is characterized by recurrent chronic transmural inflammation, which can affect any segment of the digestive tube from the mouth to the anus, especially the ileal region. The introduction of biological agents into the treatment of inflammatory bowel diseases has modified the natural process of the disease with a tendency to decrease surgeries and hospitalizations<sup>(1)</sup>.

The objectives of the study were to evaluate the serum level of IFX and anti-IFX antibodies (ATIs) in patients with CD followed at the IBD outpatient clinic of Gastrocenter - UNICAMP and to correlate with the clinical activity of disease and with results of objective examinations (ileocolonoscopy or enterorrressonance) performed in the routine of these patients.

### Results and Discussion

The average time of using IFX was 53 (4 -192) months. The CDEIS among patients who were in remission (CDR) ranged from 0 to 3, with a median of zero, while in those in activity (CDA) ranged from 4.25 to 22.4, with a median of 9.6. Considering the serum level of IFX, there was no difference between the remission and the activity groups ( $p > 0.05$ ). Of the 22 active patients, 18 presented levels above the detectable value of the test, 2 at sub therapeutic levels and 2 at undetectable levels of IFX. Of the 18 in remission, 14 had IFX levels above the detectable test value and 4 undetectable levels of IFX. 80% of all patients were at levels above therapeutic concentrations (6-10  $\mu\text{g}/\text{mL}$ ). In the CDA group, 21 patients had negative ATIs ( $\leq 5\text{UA}/\text{ml}$ ) and only 1 had positive ATIs ( $> 5\text{UA}/\text{ml}$ ). In the CDR group, 15 patients had negative ATIs ( $\leq 5\text{UA}/\text{ml}$ ) and only 3 patients had positive ATIs, 2 in low and 1 in high levels (Image 1).

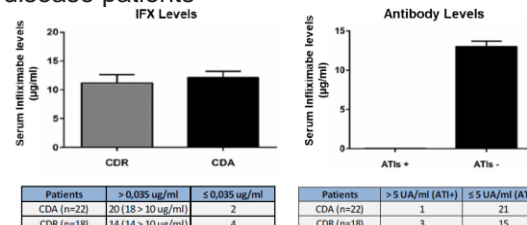
Combination therapy with immunosuppressant was present in 26 (68%) patients, and of these 17 (60%) presented positive ATIs, most of them with low levels ( $p > 0.05$ ) (Image 2).

The need for treatment monitoring, employing and quantitatively identifying the serum concentration of IFX and antibodies is extremely relevant for clinical practice<sup>(2,3)</sup>.

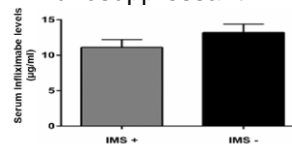
### Chart 1. Characterization of patients

Total of patients	40
Gender (M/F) - n (%)	22 (55%) / 18 (45%)
Average age (years)	37.5 (18 - 61)
Average duration of disease (months)	120 (2 - 360)
Smokers - n (%)	4 (10%)
Submitted to surgery	27 (67.5%)
Mg/kg of IFX	5.22 mg/kg (3.51 - 7.89)
Average time of using IFX (months)	53 (4 - 192)
Extraintestinal manifestations	5 (12.5%)
<b>PCR (reference 6 mg/l)</b>	
CDA	22 (0.09 - 103)
CDR	18 (0.37 - 36.80)

### Image 1. Serum IFX levels and antibodies in Crohn's disease patients



### Image 2. Serum IFX levels according the use of immunosuppressant



### Conclusions

Immunogenicity was not the main factor for the loss of response to the drug, because the minority (10%) had high levels of ATIs. The introduction of drug monitoring for anti-TNFs, including drug level and detection of ATIs, allow more personalized therapeutic management with better dose adjustment and possibly greater economy<sup>(2,3)</sup>.

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