CORRELATION BETWEEN ADALIMUMAB TROUGH SERUM CONCENTRATION, ANTI-ADALIMUMAB ANTIBODIES AND TNF-ALPHA LEVELS WITH CLINICAL OUTCOME IN PATIENTS AFFECTED BY CROHN'S DISEASE

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INTRODUCTION/OBJECTIVES:

Few data are available on the role of Adalimumab (ADA) trough serum concentrations and anti-ADA antibodies (AAA) in influencing the therapeutic response of Crohn’s Disease (CD), and even less, on the importance of analyzing TNF-α serum levels in ADA-treated patients during long-term follow-up.

AIMS & METHODS:

To evaluate the course of ADA trough serum concentrations, AAA formation and TNF-α serum levels and their clinical relevance during a long-term follow-up period of patients with CD.

In this prospective study, 21 consecutive CD patients (13M/8F; mean age 41), who achieved remission and in maintenance treatment with ADA, were included in a 2-years follow-up program. Blood samples were drawn at standardized time points (at 6, 12, 18, 24 months and in case of CD relapse) just before ADA injection. Trough ADA serum concentrations and AAA were measured using an enzyme-linked immunosorbent assay (Matriks biotek). Moreover, TNF-α serum levels were measured using a human TNF-α ELISA (DIACLONE). Disease activity was assessed at the same time points by means of the Harvey-Bradshaw Index (HBI; remission <5, mild disease 5-7, moderate disease 8-16, severe disease >16) and CRP blood level (normal if <5 mg/L).

RESULTS:

During follow-up, 16 (76%) patients maintained clinical remission and continued ADA therapy until 96 weeks, while 5 (24%) patients withdrew ADA because of perianal abscess development (n=1) and lack of response despite escalation of ADA administration (n=4). At the time of recurrence, patients who relapsed had lower median ADA serum concentrations compared to those in remission [3.7 mcg/ml (range 0.0-6.1) vs. 7.8 mcg/ml (6.8-9.1), (p=0.0001)]. There was a good correlation between ADA serum concentration and disease activity expressed by HBI (r2=0.6583, p<0.001). Values of CRP were higher in patients who relapsed than in those in remission [(3.3 mg/l (0.8-4.8) vs. 8.3 (3.3-36.2)] (p=0.0018). In addition, median TNF-α serum levels were not different between these two groups (51.4 pg/ml [1-143.2] vs. 28.1 [3.3-72.9], p=0.1). No correlation was found between ADA serum concentrations and TNF-α levels (r2=0,0084, p<0.692). AAA were found in only 2 (9%) patients and did not affect ADA serum concentrations (8.8 mcg/ml before and after AAA development) and outcome.

CONCLUSION:

Earlier ADA therapy discontinuation and disease relapse correlated well with lower ADA serum concentrations during a 2 year follow-up period. The measurement of TNF-α serum levels seems of limited value in the management of CD patients and ADA efficacy. Development of AAA does to not influence ADA serum concentrations and good outcome.