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INFLUENCE OF ANTI-TUMOR NECROSIS FACTOR (TNF) DRUG IMMUNOGENICITY ON THE TREATMENT EFFECTIVENESS IN JUVENILE IDIOPATHIC ARTHRITIS (JIA) USING SERUM CALPROTECTIN AS A DISEASE ACTIVITY MARKER. MULTICENTER STUDY. ITACA STUDY

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Background: There is a lack of evidence about the loss of efficacy of anti-TNF agents in JIA and its possible relation to the immunogenicity generated. In the last years there has been interest in the role of serum calprotectin in children diseases, including JIA.

Objectives: To assess the immunogenicity and bioavailability of anti-TNF drugs, their relationship with disease activity and the clinical utility of serum calprotectin in monitoring JIA patients.

Methods: This is a 12-month prospective, multicenter, non-interventional, observational study. Patients from 2 to 18 years diagnosed with non-systemic JIA according to ILAR criteria and receiving treatment with IFX, ADA or ETN were included. The patients were evaluated using the CHAQ and the juvenile arthritis disease activity score (JADAS 71) and determination of anti-TNF drug, anti-drug antibody and calprotectina serum levels were performed.

Results: 222 patients were included. At month 12, 181 (81.5%) continued receiving treatment, and 205 (94.5%) had positive serum levels of anti-TNF drug (96.2% of ETN, 93.5% of ADA and 66.7% of IFX) at baseline and at 12 months serum levels were positive in 161 (95.3%) patients (97.5% ETN, 93.2% ADA and 100% IFX). In total, 16 (7.3%) patients presented anti-drug A (1 of 106 anti-ETN, 13 of 109 anti-ADA, 2 of 3 anti-IFX) at baseline and 4 patients (2.4%) (0 of 81 anti-ETN, 4 of 88 anti-ADA, 0 of 1 anti-IFX) at 12 months. Regarding the relationship between anti-TNF levels or anti-drug Abs, disease activity, and functional disability overall, statistically significant differences were not observed between the groups. Patients with high levels of serum calprotectin at the baseline visit (16 of 216) showed higher JADAS-71 score [1.23 (2.06 SD) vs. 2.06 (3.44 SD)] and CHAQ [0.11 SD (0.28 SD)] vs 0.17 (0.40 SD)] compared with normal calprotectin group, although no statistically significant differences were observed ($p = 0.066$ and $p = 0.288$) between the groups with a normal and high level of serum calprotectin and the number of patients was small.

Conclusion: The low prevalence of anti-drug Abs observed was in consonance with the high proportion of patients with a positive serum level of anti-TNF drug. These data suggest an appropriate management of the long-term treatment of Spanish JIA patients, who showed a maintained inactive disease/low disease activity state and a very low functional disability state as a consequence of a low immunogenicity and good bioavailability of anti-TNF drugs.

Baseline patients' characteristics.

	Total
Sex	
Female, n (%)	156 (70.3)
Age (years)	
Mean (SD)	10.77 (4.27)
Age at onset of symptoms	
Mean (SD)	4.61 (3.65)
Age at diagnosis, Diagnosis	
Mean (SD)	5.01 (3.90)
Uveitis episode prior to the study	
N (%)	76 (34.7)
Antinuclear antibodies (+)	
N (%)	155 (69.8)
Rheumatoid factor(+)	
N (%)	10 (6.0)
Anti-cyclic citrullinated peptide antibody(+)	
N (%)	14 (6.4)
HLA B27(+)	
N (%)	5,01 (3,90)
JIA subtypes according ILAR	
oligoarthritis(%)	69 (31,1)
Oligoarthritis (%)	25 (11,3)
polyarthritis FR positive (%)	7 (3,2)
polyarthritis FR negative (%)	62 (27,9)
Psoriatic (%)	10 (4,5)
arthritis-enthesitis (%)	33 (15,3)
Undifferentiated (%)	15 (6,8)

Table 2. JADAS -71 score according to immunogenicity and bioavailability of anti-TNF drugs

	Serum anti-TNF (Negative)	Serum anti-TNF (Positive)	Anti-drug antibodies (Negative)	Anti-drug antibodies (Positive)	Total
Baseline					
N	22	197	200	19	221
Mean (SD)	1.52 (2.66)	1.35 (2.29)	1.30 (2.28)	1.99 (2.66)	1.38 (2.34)
p value	0.743		0.216		
Month 12					
N	20	178	182	16	199
Mean (SD)	2.19 (2.61)	0.94 (1.90)	0.98 (1.97)	2.06 (2.22)	1.08 (2.01)
p value	0.009		0.039		

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