Background: Tumour necrosis factor (TNF) receptor-associated periodic syndrome (TRAPS) is one of the best-known monogenic auto-inflammatory disorders resulting from an autosomal dominant variation in the TNF superfamily receptor 1A (TNFRSF1A) gene (1).

Objectives: To define best treatment approach in patients with TRAPS and effect on long-term outcomes.

Methods: We reviewed data on patients with TRAPS enrolled in the Eurofever International registry according the INSIGHD gene variant classification and the new Eurofever/PRINTO classification criteria (EPCC).

Results: Data on 226 patients were available. Patients not fulfilling the EPCC carrying likely benign/benign variants (40 patients, 18%) or pathogenic/likely pathogenic variants (38 patients, 17%) or VOUS/not classified variants (21 patients, 9%) or VOUS/not classified variants not fulfilling the EPCC.

Conclusion: Anti-IL-1 drugs are the best maintenance treatment in TRAPS with potential to reverse the most serious disease complications of AA amyloidosis and infertility. The diagnosis of TRAPS should be considered very carefully in patients carrying VOUS/not classified variants not fulfilling the EPCC.

References

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Background: Juvenile dermatomyositis (JDM) is a systemic, autoimmune inflammatory muscle disorder and vasculopathy that affects children younger than 18 years. Although the cause of JDM remains unknown it is clear that genetic and environmental influences play a role in the aetiology. New treatments are becoming available and being tested through international multicentre trials. Increasing evidence suggests a role for types I and II IFN in juvenile and adult dermatomyositis, including elevated IFN-response gene signatures in the muscle, skin and blood. It has recently been reported that patients with refractory JDM responded well to treatment with tofacitinib, a JAK inhibitor, with corresponding downregulation in selected IFN-response genes.

Objectives: In this study, we evaluated our cases with resistant JDM who received tofacitinib treatment.

Methods: Six patients who received tocifatinib because of severe skin involvement of JDM were included in the study. The data were obtained retrospectively from the hospital records.

Results: The age ranges of the cases were between 7-17 years and the ratio of girls and boys was 1 (3/3). The age of diagnosis was between 2-13 years, and the follow-up period was between 3-9 years. Calcinosis cutis in 5 cases, decreased muscle strength in 3 cases, joint involvement in 4 cases were detected. Systemic steroids, methotrexate, and non-steroid anti-inflammatory drugs were given in all cases before tocifatinib treatment. Pamidronate was used in 4 cases because of severe skin calcinosis, high dose intravenous immunoglobulin in 4 cases, mycophenolate mofetil in 3 cases, rituximab in 3 cases and cyclophosphamide in 1 case previously. Tofacitinib treatment (10mg/day) was started in six cases with treatment-resistant JDM. Five cases had been treated with tocifitinib for 6-24 month intervals. The treatment was discontinued in one case because of severe allergic reaction. Variable level of improvement were detected in the skin findings of all cases during the therapy period. The treatment was interrupted for 1 month in only one case due to neutropenia.

Conclusion: Tocifitinib seems to be an effective and safe treatment option in patients with JDM who are resistant to conventional treatments. More studies are needed on this subject.

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SAFETY OF BIOLOGICAL AGENTS IN JUVENILE IDIOPATHIC ARTHRITIS: A META-ANALYSIS OF OBSERVATIONAL STUDIES


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Background: Follow-up cohorts (observational studies) were initiated consecutively or simultaneously to the development of randomised controlled trials (RCTs) in JIA patients 1-2. They help to identify many complications observed only in clinic or simultaneously to the development of randomised controlled trials (RCTs) with withdrawal and parallel designs was performed by meta-analysis.

Objectives: To estimate the incidence of serious adverse events (SAEs) including serious infections, malignancies, and death in patients with juvenile idiopathic arthritis (JIA) treated with biological agents (BAs) in daily clinical practice 3.

Methods: We systematically searched, up to May 2019, Medline and Embase databases for observational studies performed in JIA disease under BAs treatment. Outcomes were SAEs, serious infections, malignancies and all-cause mortality. Complementary, the incidence of SAEs in randomised controlled trials (RCTs) with withdrawal and parallel designs was performed by meta-analysis.

Results: A total of 31 observational studies were included (6811 patients totalizing 17530 patients-years [PY] of follow-up). The incidence rate of SAEs was similar in observational cohorts and withdrawal RCTs (4.46 events per 100 PY, 95% CI 2.85-6.38, I2= 95%) and 3.71 events per 100 PY (95%CI 0.0-13.34, I2= 56%), respectively. The incidence of SAE was lower in parallel RCT. The incidence rate of serious infections, malignancies and death in observational cohorts was estimated at 0.74 events per 100 PY (95%CI 0.32-1.30, I2=83%) 0.10 events per 100 PY (95% CI 0.06-0.16, I2=0%) and 0.09 events per 100 PY (95% CI 0.05-0.14, I2=0%), respectively. Infections were the known cause of death in 8 of the 14 deaths. In meta-regression and subgroup analysis, variation of serious infections rates were partially explained by follow-up time (R2 = 30.3%, p = 0.0008), JIA categories (all JIA versus polyarticular versus systemic JIA categories, p= 0.001) and cohort quality (Newcastle-Ottawa score ≥ 6 versus ≤ 5 stars, p= 0.0025).

Conclusion: Our results suggest that the incidence rate of SAEs related to BAs in JIA disease is similar to those observed in randomised withdrawal trials. The overall incidence remained low. However, unsatisfactory description of SAEs prevents analysis of hospitalisation causes. Infection and, to a lesser extent, cancer and death, explain only part of burden of BAs.

References:

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THE ANTI-VACCINE ANTIBODY AGAINST MEASLES, PAROTITIS, RUBELLA, DIPHTHERIA AND HEPATITIS B IN 170 JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

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Background: Patients with juvenile idiopathic arthritis (JIA) may have lower protective levels of anti-vaccine antibodies due to high inflammatory activity, interrupted or incomplete vaccination schedule, and due to using immune-modulating drugs, e.g. systemic corticosteroids (CS), methotrexate (MTX) and biologics.

Objectives: The aim of our study was to find the predictors of low levels of anti-vaccine antibodies in patients with JIA.

Methods: In the present study were included data 170 JIA (55 boys and 115 girls) aged from 2 to 17 years, who received scheduled vaccination before the age of 2 years and before JIA onset against measles, parotitis, hepatitis B, diphtheria and rubella. In all patients the Ig G anti-vaccine antibodies levels were detected with ELISA. In each patient we evaluate the type of the disease (oligoarthritis - 73, polyarthritis - 61, systemic-16 and enthesis-related arthritis - 20), onset age, presence of uveitis, duration of JIA, treatment with corticosteroids (CS), methotrexate (MTX) and biologics.

Results: The main demographic characteristics: age of inclusion in the study 11.4 (7.14-18.4) years, disease onset – 6.0 (3.7-9.0) years, disease duration – 3.8 (1.9-6.5) years. Treatment with CS was in 43 (25.3%), MTX in 154 (90.6%) and biologics 82 (48.2%) patients, among them 53 had TNFα-inhibitors. More than 1 biologic consequently received 16/82 (19.5%) patients. Protective levels of anti-measles antibodies was in 98 (57.6%) of all JIA population, anti-parotitis – 136 (80.0%), anti-hepatitis B – 85 (50.0%), anti-diphtheria – 88 (51.7%), anti-rubella – 167 (98.8%). Data of vaccination status and anti-vaccine antibodies levels in the table. In univariate and multivariate regression analysis the main risk factors for anti-measles antibodies were MTX using (p= 0.0045), more than 1 biologics (p= 0.0004); for anti-hepatitis B – MTX (p= 0.03), for anti-diphtheria antibodies: onset age (p= 0.0002), JIA duration (p= 0.00007), number vaccine doses (p= 0.02), more than 1 biologics (p= 0.01); combined treatment with biologics and other drugs (MTX or CS).