Selections from international journals

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Factors associated with choice of biologic among children with Juvenile Idiopathic Arthritis: results from two UK paediatric biologic registers.

Kearsley-Fleet L, Davies R, Baildam E, Beresford MW, Foster HE, Southwood TR, Thomson W, Hyrich KL.

OBJECTIVE: The objectives of this study were to describe patients starting first-line biologics for JIA, to describe characteristics over time among patients starting etanercept, and to describe patterns of second biologic prescribing. METHODS: The British Society for Paediatric and Adolescent Rheumatology Etanercept Cohort Study, and the Biologics for Children with Rheumatic Diseases study are ongoing prospective observational cohorts, collecting data on patients starting biologic therapy for JIA. Patients registered from 1 January 2010 starting their first biologic were compared between therapies. Patients starting etanercept before 2010 were included to analyse changes in etanercept prescribing. The pathway of patients starting a second biologic was recorded in all patients. RESULTS: To 26 August 2014, 931 patients were recruited starting a first-line biologic (142 Biologics for Children with Rheumatic Diseases; 789 British Society for Paediatric and Adolescent Rheumatology Etanercept Cohort Study). From 2010, patients with systemic JIA (sJIA) were almost exclusively prescribed anakinra or tocilizumab. Choice between anti-TNF therapies was largely driven by history of chronic anterior uveitis (CAU). When investigating trends in patients starting etanercept over time, disease duration at etanercept start, patients with sJIA, a history of CAU, and those who received concomitant oral corticosteroids decreased over time. Patients who started a second biologic from 1 January 2010 showed a similar stratification. CONCLUSION: Although etanercept remains the most common biologic prescribed for JIA, there has been a clear shift towards the use of alternative biologics, largely driven by disease subtype and history of CAU. This channeling of children towards specific therapies should be considered carefully in future studies and in clinical guidelines and ongoing research.

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Airway lipoxin A4/formyl peptide receptor 2-lipoxin receptor levels in pediatric patients with severe asthma.

Gagliardo R, Gras D, La Grutta S, Chanez P, Di Sano C, Albano GD, Vachier I, Montalbano AM, Anzalone G, Bonanno A, Riccobono L, Gjomarkaj M, Profita M.

BACKGROUND: Lipoxins are biologically active eicosanoids with anti-inflammatory properties. Lipoxin A4 (LXA4) signaling blocks asthmatic responses in human and experimental model systems. There is evidence that patients with respiratory diseases, including severe asthma (SA), display defective generation of lipoxin signals despite glucocorticoid therapy. OBJECTIVE: We investigated airway levels of formyl peptide receptor 2-lipoxin receptor (FPR2/ALXR), LXA4, and its counterregulatory compound, leukotriene B4 (LTB4), in patients with childhood asthma. We addressed the potential interplay of the LXA4-FPR2/ALXR axis and glucocorticoids in the resolution of inflammation. METHODS: We examined LXA4 and LTB4 concentrations in induced sputum supernatants from children with intermittent asthma (IA), children with SA, and healthy control (HC) children. In addition, we investigated FPR2/ALXR expression in induced sputum cells obtained from the study groups. Finally, we evaluated in vitro the molecular interaction between LXA4 and glucocorticoid receptor-based mechanisms. RESULTS: We found that children with SA have decreased LXA4 concentrations in induced sputum supernatants in comparison with children with IA. In contrast to decreases in LXA4 concentrations, LTB4 concentrations were increased in children with asthma independent of severity. LXA4 concentrations negatively correlated with LTB4 concentrations and with exacerbation numbers in children with SA. FPR2/ALXR expression was reduced in induced sputum cells of children with SA compared with that seen in HC subjects and children with IA. Finally, we describe in vitro the existence of crosstalk between LXA4 and glucocorticoid receptor at the cytosolic level

mediated by G protein-coupled FPR2/ALXR in peripheral blood granulocytes isolated from HC subjects, children with IA, and children with SA. CONCLUSION: Our findings provide evidence for defective LXA4 generation and FPR2/ALXR expression that, associated with increased LTB4, might be involved in a reduction in the ability of inhaled corticosteroids to impair control of airway inflammation in children with SA.

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How to diagnose mould allergy? Comparison of skin prick tests with specific IgE results.

Kespohl S, Maryska S, Bünger J, Hagemeyer O, Jakob T, Joest M, Knecht R, Koschel D, Kotschy-Lang N, Merget R, Mülleneisen NK, Rabe U, Röseler S, Sander I, Stollewerk D, Straube H, Ulmer HM, van Kampen V, Walusiak-Skorupa J, Wiszniewska M, Wurpts G, Brüning T, Raulf M.

BACKGROUND: Diagnosis of mould allergy is complicated due to the heterogeneity of the test material and the decrease in the number of commercial mould skin test solutions that are currently available. OBJECTIVES: The aim of this study was to compare skin prick tests (SPT) from different manufacturers to one another and concurrently with sIgE tests for Aspergillus fumigatus (Asp f), Cladosporium herbarum (Cla h), Penicillium chrysogenum (Pen ch), Alternaria alternata (Alt a) and Aspergillus versicolor (Asp v) to ascertain a feasible diagnostic procedure for mould sensitization. METHODS: In this multi-centre study, 168 patients with mould exposure and/or mould-induced respiratory symptoms were included. Mould SPT solutions were analysed biochemically and tested in duplicate on patients' arms. Specific IgE (sIgE) concentrations to corresponding mould species and mould mix (mx1) were measured by ImmunoCAP. SPTs in accordance with one another and with sIgE were further considered. The test efficiency was calculated using receiver-operating characteristic (ROC) analysis. RESULTS: Mould sensitization was more frequently detected by the SPT (90 of 168) than by the sIgE tests (56 of 168). Concordances of double SPT positives were only sufficient (≥ 80%) for environmental allergens, two Asp f and three Alt a SPT solutions, whereas all other mould solutions revealed concordances < 80%. The antigen content of SPT solutions was positively associated with concordant SPT double values as well as with sIgE. Taking sIgE as the 'positive standard', all mould SPT solutions revealed test efficiencies > 80%, but varied up to 20% in sensitivity and positive predictive value with the exception of Alt a. CONCLUSIONS: SPT solutions are sensitive and essential diagnostic tools for the detection of mould sensitization. Our recommendation for diagnosis would be to test at least Alt a, Asp f and Pen ch using SPT and additional sIgE test to mx1.

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Differential response in allergen-specific IgE, IgGs, and IgA levels for predicting outcome of oral immunotherapy.

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BACKGROUND: Oral immunotherapy (OIT) induces desensitization and/or tolerance in patients with persistent food allergy, but the biomarkers of clinical outcomes remain obscure. Although OIT-induced changes in serum allergen-specific IgE and IgG4 levels have been investigated, the response of other allergen-specific IgG subclasses and IgA during OIT remains obscure. METHODS: A pilot study was conducted to investigate egg OIT-induced changes in allergen-specific IgE, IgG subclasses, and IgA levels and search for possible prediction biomarkers of desensitization. We measured serum levels of egg white-, ovomucoid-, and ovalbumin-specific IgE, IgA, and IgG subclasses by high-sensitivity allergen microarray in 26 children with egg allergy who received rush OIT. RESULTS: Allergen-specific IgE gradually decreased while IgG4 increased during 12-month OIT. Serum levels of IgG1, IgG3, and IgA increased significantly after the rush phase, then decreased during the maintenance phase. IgG2 levels changed in a manner similar to that of IgG4. In particular, significantly high fold increases in egg white-specific IgG1, relative to baseline, after the rush phase and high IgA levels before OIT were observed in responders, compared with low-responders to OIT. Patients who could not keep desensitization showed relatively small changes in all immunoglobulin levels during OIT. CONCLUSION: The response to OIT was associated with significant increases in serum allergen-specific IgG1 levels after rush phase and high baseline IgA levels, compared with small changes in immunoglobulin response in low-responders. The characteristic IgG1 changes and IgA levels in the responders could be potentially useful biomarkers for the prediction of positive clinical response to OIT.