477. Clinical and diagnostic markers and management of paediatric allergic diseases

P4566

Intensive oil baths from six weeks of age reduce xerosis and possibly atopic eczema in infancy

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Background: Atopic eczema (AE) is often the first step of the allergic march, with onset early in life, followed by asthma and allergic rhinitis. AE affects up to 20% of children, and is characterized by dry, itchy skin. AE is a complex genetic and environmental disease, with alteration of skin barrier. Restoration of the barrier by emollients and/or oil baths is an important part of AE treatment, but its role in preventing AE is not known. Theoretically reducing prevalence of AE could prevent later allergy and asthma development.

The present pilot study aimed to evaluate whether frequent oil baths of infants with dry skin could reduce xerosis and eczema at the age of six months.

Patients and methods: A randomized controlled intervention study of six weeks old infants with dry skin, followed to six months by monthly assessment. They were randomized by well baby clinics (1 vs 5, respectively) to either daily oil bath (0.5 dl) and fat cream in the face (n=24) or observation (normal procedures) (n=31). The outcome was skin quality at six months.

Results: Normal skin was observed at six months in 18 children (75%) with skin treatment, compared to 12 (38%) in the observation group (p<0.001). Frequency of oil baths was 5-7/week (n=19) and 2-4/week (n=5) in the intervention group. Skin care varied in the observation group. AE was reported in one child versus five children in the intervention versus the observation group. No adverse reactions reported.
Conclusion: The present pilot study showed that regular oil baths of infants were feasible, reduced xerosis, and also possibly eczema. If verified in further studies, one might speculate if this would reduce development of allergy and asthma.

P4567
Problematic severe asthma in children: A nationwide study in The Netherlands
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Introduction: Epidemiological data on problematic severe asthma in children are sparse.
Methods: A 3 year (2008-2011), nationwide survey on PSA in children 4-18yrs old in the Netherlands through a national surveillance system among all paediatricians.
Results: In this cross sectional study 328 children, aged 4-18yrs with PSA, were identified. A prevalence of at least 0.01% of children with asthma. PSA is more frequent in boys than in girls under 12yrs old. This sex ratio reverses >12yrs old. Eighty-five% had allergic asthma and in 85% symptoms started before they were 4yrs old. Investigations included lung function, FeNO, trials of steroids, chest radiographs, sweat tests, immunodiagnostics, HRCT, bronchoscopy in various percentages of patients. Over 10% had 5-13 exacerbations requiring prednisolon in the past year. ICU admittance in 11%. Fifty% had exacerbations with no symptoms in between, 40% suffered from very acute asthma attacks and 30% were continuously symptomatic. All despite up-to-date intensive surveillance and treatment. Seventy-five% received psycho diagnostics and 50% psychotherapy. FEV1 was normal in 85% of patients. Persistent airflow limitation in the past year was present in 13%. Daily prednisolon, omalizumab or antiTNFalfa was used in resp 5%, 1% and 0,08%.
Conclusions: PSA in a country with a high standard medical system and coverage of medical cost for all, is rare. Asthma symptoms in children with PSA start <4yrs old. Children have severe symptoms despite intensive treatment and follow-up. Daily ICS doses are high with additional frequent oral steroids courses. Follow-up of this cohort into adulthood will yield the natural course of symptoms, lungfunction and psychosocial problems.

P4568
Bronchodilation with mometasone furoate/formoterol fumarate administered by metered-dose inhaler with and without a spacer in children with persistent asthma
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Rationale: The bronchodilatory effect of mometasone furoate/formoterol fumarate (MF/F) administered by metered-dose inhaler (MDI) with or without spacer has not been evaluated previously in children.
Methods: This was a randomized, multicenter, placebo (PBO)-controlled, single-dose 4-period crossover study. Children with persistent asthma aged 5-11y participated in this study. Subjects used inhaled corticosteroids with/without long-acting beta-2 agonists for ≥12wk before enrollment, and at screening had FEV_1 ≥70% predicted. Subjects received MF/F-MDI 100/10μg with/without spacer, F-DPI 10μg, and PBO-MDI with/without spacer in separate treatment periods. The primary endpoint was FEV_1 AUC (0-12 h) for the comparison of MF/F with spacer vs PBO. Secondary measurements included MF/F without spacer vs PBO, as well as MF/F with spacer vs MF/F without spacer, and F-DPI vs PBO. Analysis was performed with an ANCOVA model for a crossover study.
Results: Data from 87 subjects were analyzed. MF/F with spacer demonstrated a larger change in mean FEV_1 AUC (0-12h) vs PBO (115 vs −9mL), with a treatment difference of 124mL (95% CI 94 to 154, $P<.001$). Similarly, MF/F without spacer vs PBO resulted in a 102mL difference in mean adjusted FEV_1 $AUC_{0\text{-}12h}$ (95% CI 73 to 131, $P<.001$), whereas the difference between MF/F with spacer vs MF/F without spacer was 22 mL (95% CI –8 to 52, $P=.144$). The difference between F-DPI vs PBO was 106 mL (95% CI 77 to 135, $P<.001$). No unexpected adverse events were observed.
Conclusions: In this trial, MF/F-MDI 100/10μg demonstrated significant bronchodilation in children aged 5-11y regardless of the use of a spacer.

P4569
Vitamin D receptor and vitamin D binding protein polymorphisms are associated with asthma control in children
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Introduction: Vitamin D levels have been associated with the onset of asthma and are suggested as a marker of disease severity in asthmatic children. Furthermore, polymorphisms in vitamin D pathway genes have been associated with vitamin D levels.
Aims and methods: 111 children with asthma and 96 healthy controls of Greek origin were analyzed for the VDR ApaI, VDBP rs7041 and rs4588 polymorphisms using PCR-RFLP method. Asthma control level was assessed according to Childhood Asthma Control Test (C-ACT) and Global Initiative for Asthma guidelines (GINA).
Results: Genotype distribution for all studied polymorphisms did not differ significantly between asthmatic patients and healthy controls. Frequencies of VDR ApaI AA, AC and CC genotypes were 38.4%, 40.7% and 20.9% in the controlled group and 28%, 72% and 0.0%, respectively, in the uncontrolled group according to C-ACT (p=0.008). This association was verified when we analyzed the VDR ApaI genotypes in asthmatic group according to GINA classification (p=0.002). For the VDBP rs7041 polymorphism, the frequency of variant G allele was significantly higher in children with controlled asthma according to C-ACT (66.9% vs 50.0%, p=0.030) and GINA guidelines (62.8% vs 52.8%, p=0.027). For the VDBP rs4588 polymorphism the frequency of variant A allele was significantly lower in children with controlled asthma according to C-ACT (23.3% vs 40.0, p=0.019) and GINA (23.3% vs 37.5%, p=0.048) guidelines.
Discussion: VDR ApaI and VDBP rs7041 and rs4588 polymorphisms were associated with asthma control according to C-ACT and GINA classification in asthmatic children.

P4570
Role of vitamin D in asthma severity and control in children
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In addition to its role in bone physiology and autoimmune disease, recent data suggest a potential role of vitamin D in asthma since it has immunomodulatory properties. The aim of this study is to determine the relationship between serum vitamin D levels and the severity and control of asthma in children. We measured vitamin D levels in serum collected from 38 asthmatic children in winter and summer,compared to those of 30 healthy children. The mean age is 9.8 years and Sex-ratio was 2.16. Asthma was mild persistent in 60.5% of cases, moderate in 36.8% of children, and severe in 2.7%. The average vitamin D level was significantly lower in asthmatics in summer despite abundant sun exposure (20.74 ng/ml vs 26.77 ng/ml p = 0.001) and levels of vitamin D were significantly lower in winter than in summer in both groups (in asthmatics 17.37ng/ml vs 20.74ng/ml; p=0.036 and 18.97ng/ml vs 26.77ng/ml; p<0.001 in controls). Subjects with well-controlled asthma had higher serum levels of vitamin D than children with partially controlled or non-controlled asthma in summer (24.28ng/ml vs 13.9ng/ml; p<0.001) but not in winter (17.28ng/ml vs 17.67ng/ml). In the same way, children with more severe asthma had lower serum vitamin D levels than children with mild asthma in winter (12.07ng/ml vs 20.80ng/ml; p<0,001) and in summer (13.8ng/ml vs 25.26ng/ml; p<0,001). Our study indicates that vitamin D deficiency is more common among children with asthma and lower vitamin D levels are associated with a greater disease severity and probably with worse disease control. Randomized interventional trials on vitamin D supplementation will be needed to confirm its role in treatment and eventually in prevention of asthma.

P4571

WITHDRAWN

P4572

Comparison of bronchodilator effect of salbutamol delivered via MDI + spacer and DPI in children with asthma

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Background: Inhaled short acting beta2-agonists are widely used in asthma treatment. Studies comparing the efficacy of salbutamol containing pressurized metered dose inhalers (pMDI) and dry powder inhalers (DPI) in the paediatric asthma population are limited.
Aim: This study aimed to compare the bronchodilator response to a salbutamol pMDI plus spacer and to a salbutamol DPI by children and adolescents with asthma related bronchoconstriction.
Methods: 80 patients aged 5 to 18 years with physician diagnosed asthma with a forced expiratory volume in one second (FEV1) < 85% were enrolled in a single centre, randomized, open label study. Patients were randomized to salbutamol 200 ug via pMDI (Ventolin HFA Inhalation Aerosol, GlaxoSmithKline, UK) plus large volume spacer (Volumatic, GlaxoSmithKline, UK), or salbumatol 200 ug via DPI (Buventol Easyhaler, Orion Pharma, Finland). The primary variable was FEV1 change from baseline, the co-primary endpoint was forced expiratory flow 25–75% (FEF25-75%) change from baseline 20 minutes after administration of salbutamol.
Results: FEV1 change from baseline was 19.77% (SD: 15.519) and 13.93% (SD: 12.828) in the PMDI + spacer group and in DPI group respectively. The difference was not significant (p=0.069, 95% CI: -12.149, 0.472). FEF25-75% change from baseline 37.11% (SD: 35.293) and 30.20% (SD: 31.241) in the PMDI + spacer group and in DPI group respectively. The difference was not significant (p = 0.3564, 95% CI: -21.75, 7.923).
Conclusion: The present study shows that salbutamol DPI is a valid alternative for relieving bronchoconstriction in children (5 to 18 years of age) with asthma.

P4573

Serum level of specific IgG antibody for aspergillus and its association with severity of asthma in asthmatic children

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Background: Aspergillosis is one of the frequent causes of exacerbation of asthma depending on the geographical regions. The specific serum IgG level for aspergillus is a major diagnostic criterion in aspergillosis.
Methods: Ninety six asthmatic patients, with mean age of 5.4±3.0 years who were referred to the asthma clinic of the Mofid Children's Hospital, were enrolled in this study. Serum specific IgG for aspergillus was measured and its association with severity of asthma was evaluated.
Results: Nineteen asthmatic patients (10 females and 9 males) had aspergillus IgG antibody. Among them, severe persistent asthma and moderate persistent asthma were detected in 5 and 13 cases, respectively, whereas only one patient suffered from mild persistent asthma. A total of 36.5% of the 96 patients had a history of atopy, while 26% had allergic rhinitis. There was an association between the severity of asthma and the presence of aspergillus IgG antibody. Moreover, the positivity for aspergillus IgG antibody was higher in older patients.
Conclusion: Our results indicated an association between aspergillus antibody level and severity of asthma. It could be recommended that the IgG titer for aspergillus is measured in pediatric patients with asthma, whereas co-morbidity of aspergillosis and asthma increases the risk of asthma exacerbation.

P4574

Diagnostic value of flexible bronchoscopy in persistent and recurrent wheezing of infancy

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Persistent or recurrent wheezing are common problems in infancy.The aim of this study is to evaluate the diagnostic value of flexible broncoscopy(FB) and analyze its results in infants with persistent or recurrent wheezing.
Material and method: Ninety-six wheezy infants who had been performed FB between 1999 and 2011were included in this study. Demographic features, radiological, laboratory and bronchoscopic findings were analyzed.
Results: Sixty-six patients were male and the median age at FB date was 0.9 (0.6-1.5) years. Median age at symptom onset was 3 (1-6) months.Twenty-one patients had persistent and 75 had recurrent wheezing. Fifty-five patients had regular asthma therapy before the procedure.Thirty patients had atelectasis on radiological imaging.FB revealed a diagnosis in 64 patients.Functional abnormalities in 43 patients (13 tracheobronchomalacia, 10 bronchomalacia, 7 tracheal dyskinesia, 6 tracheomalacia, 4 laryngotracheomalacia, 3 laryngotracheobronchomalacia), structural abnormalities in 8 patients (5 bronchial stenosis, 2 tracheal stenosis, 1 abnormal bronchial anatomy) and foreign body in the airways in 1 patient were determined.Microbiological investigations of the bronchoalveolar lavage (BAL) fluid revealed CMV PCR positivity in 8 patients and bacterial infections in 4. BAL fluid microbiological investigations demonstrated various bacterial agents in 37 patients.Also, accompanying gastrooesophageal reflux in 28 shown by lipid laden macrophages in BAL fluid.
Functional and structural airway abnormalities must be kept in mind in the differential diagnosis of infants with persistent or recurrent wheezing.FB is a diagnostic tool in these patients and avoids redundant medications.

P4575

Paradoxical effect of salbutamol in asthmatic children

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Paradoxical bronchospasm is defined as the rapid onset of bronchoconstriction after administrating β2 agonist. Few studies published suggest that it is due to tensiactive chlorofluorocarbons in the metered dosis inhaler (MDI). Although bronchodilator test (BT) with salbutamol is a usual aim of control in asthma, there are no studies in these children.
Objective: To set the characteristics of paradoxical bronchospasm after standard BT with MDI salbutamol in asthmatic children.
Methods: Asthmatic children (2006-2011) in whom FEV1 decreases ≥9% after conventional BT with MDI salbutamol. Age, sex, body mass index, atopy, pharmacological treatment, level of asthma severity and control, percentage of FEV1 decrease and brochodilator response after terbutaline dry powder were collected. Statistical analysis with SPSS.
Results: 32 patients,mean age 8.3 years (56% males).History of allergy in 65.6% (68.4% Dermatophagoides) and obesity in 34.3%. 81.3% patients had controlled asthma at the time of testing, following treatment with montelukast (42.9%), inhaled corticosteroids (28.5%), both of them (4.8%) or immunotherapy (9.5%). 14.3% patients had moderate to severe asthma, treated with corticosteroids and long acting beta-agonist. 46.9% showed a fall in FEV1 >15%. In this group 40% were obese and 60% allergic, with no differences among asthma severity or pharmacological therapy (p>0.05). 27 patients underwent bronchodilation with terbutaline dry powder being positive in 81%.
Conclusion: In controlled asthmatic children, especially obese and allergic, MDI salbutamol can produce paradoxical bronchoconstriction that reverts with terbutaline drypowder. Although not a usual situation, it should be considered for the symptomatic management of the disease.

P4576

Evaluation of lung function in children with asthma and gastroesophageal reflux disease association

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Aim: The aim of study was to assess the lung function disorders using spirometric measurements in a group of children with asthma and gastroesophageal reflux disease (GERD) associated.
Materials and methods: The study included 58 children with moderate asthma aged from 5 to 16 years. The main group entered 38 children with association of asthma with GERD; controls included 20 GERD-free asthmatic children.
Results: Analysis of the mean FVC values showed restrictive character of lung function changes in both groups that partially develop in children with long-term asthma: 64.0±2.4% in main group comparing with 69.1±2.5% in controls ($p>0.05$). Obstructive type changes differed between study groups and were characterized by decreased levels of lung function variables (FVC, FEV1, PEF and MEF25-75): FEV1 in children from the first group was significantly lower comparing with controls (61.7±2.6% vs. 72.4±2.1%, $p<0.01$), also PEF (46.6±2.5% vs. 56.0±3.3% in controls, $p<0.05$) and MEF25-75 (58.3±3.8% vs. 71.0±3.4%, respectively, $p<0.05$). Noticeably, significantly more expressed obstructive changes of distal airways and lung function variables were observed in children with associated asthma and GERD: 56.7±2.9% vs. 67.7±3.2% in controls for MEF75 ($p<0.05$), 59.9±3.9% vs. 75.8±3.6% for MEF50 ($p<0.01$) and 68.8±5.6% vs. 87.9±6.2% for MEF25 ($p<0.05$).
Conclusions: Analysis of spirometric variables denotes more severe obstructive changes of lung function in children with association of asthma and GERD, that is showed by lower values of FEV1, PEF, MEF25-75, MEF75 and MEF25, comparing with asthmatic children who are GERD-free.

P4577

Exhaled nitric oxide and serum IgE in children admitted to a pediatric department

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Background: Exhaled nitric oxide (FeNO) is a noninvasive marker to assess airway inflammation in adults and children, but the clinical evidence is still equivocal.
Methods: We aimed to assess the FeNO levels in children admitted to our pediatric department and to correlate the results with other diagnostic tools. We enrolled two groups of children aged 5 to 16 yrs: first (149 cases, M/F 89/60) - admitted for asthma, and the control group (100 cases, M/F 55/45), without known history of atopy. We measured the FeNO (using Niox Mino, Aerocrine, Sweden), total and specific serum Ig E. The statistical analysis was done using the Chi-squared test.
Results: We found a statistical significant difference in specific IgE levels between the two groups: p = 0,01; RR = 3,76 (0.99 - 14,25), but similar values for FeNO (p = 0,19) and the total serum IgE (p = 0,59). Total IgE over 300 kU/l was correlated with high FeNO levels recorded in the asthmatic children: p = 0,009; RR = 4,28 (1,37 – 15,44), but the exhaled NO was not correlated with stage, gender nor controller therapy (corticoids and/or leucotriene inhibitors or none).
Discussions: In our patients the role of FeNO in monitoring asthma is still uncertain. The correlation with high total serum Ig E (also nonspecific) may be a future approach in increasing the value for the clinical use.

P4578

The relationship between exhaled nitric oxide and compliance/adherence in patients with bronchial asthma using inhaled corticosteroids

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Background: The measurement of FENO is the important index to evaluate the control of the patients with bronchial asthma using inhaled corticosteroids (ICS). When FENO in the patients using ICS is high, we often try to increase the dose of ICS. However, it is necessary to take compliance/adherence of the patients into consideration before that.
Objectives: The aim of this study was to examine whether the measurement of FENO is useful as the index of compliance/adherence to asthma treatment by ICS.
Methods: One hundred forty-seven subjects (4 to 23 years of age; 82 male, 65 female) with bronchial asthma using ICS were recruited from the outpatient division at the Department of Pediatrics at Fukuoka National Hospital between January-August in 2011. We measured their FENO and asked them to complete a questionnaire regarding the use of ICS. We asked them how often they inhaled ICS for a month, and classified them into five groups categorized as the grade of compliance. Additionally, we made a questionnaire about adherence. The patients answered that they inhaled ICS by themselves were defined as good adherence group, and otherwise as poor adherence group. We compared FENO in 5 groups categorized as the grade of compliance. Likewise, we also compared FENO in good and poor adherence groups.
Results: FENO in the patients of good compliance groups were significantly lower than that of poor compliance groups ($p<0.0001$). However, there was no significant difference in the good adherence group and the poor adherence group.
Conclusions: It was indicated that the measurement of FENO could be useful as the index of compliance to asthma treatment by ICS.

P4579

Carboxyhemoglobin as a marker for chronic carbon monoxide exposure in school-age children with persistent asthma

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Introduction: When inhaled, carbon monoxide (CO) reacts very rapidly with hemoglobin in the blood and forms carboxyhemoglobin (COHb), decreasing the oxygen delivery to vital organs, leading to free-radical production and cytokines releasing.
Aims: To investigate the adverse effects of CO on the respiratory system using COHb as a marker for chronic CO exposure and forced expiratory volume in one second (FEV1) as a marker for the lung airflow obstruction.
Methods: We examined blood COHb concentrations in school-age children who suffer from moderate and easy form of asthma (n=52), ages 8-16 years, living in urban and suburban areas. COHb was measured in patient's blood immediately after obtaining by spectrophotometric method and expressed as a percentage of blood hemoglobin. FEV1 parameter was measured using Schiller-spirovit SP-1 spirometer.
Results: Our study show that school-age children, with moderate and easy form of persistent asthma have statistically significant elevation of COHb concentration (3.53% ±0.97) in relation to control group (2.03% ± 0.28, $p<0.001$) and decrease of FEV1 parameter compared to control group, ($p< 0.001$). We also studied the influence of environmental factors: air pollution, secondhand smoking, wood-heating, heavy traffic, aspect of living in urban and rural areas. There are positive associations between air pollution concentrations and asthma aggravation in children.
Conclusions: Our results sugests that blood COHb concentration above safe level of 2.5% can be involved in pathogenesis of many respiratory diseases, especially asthma and trigger asthma attacks and allergies. The most important factor in prevention is reducing of air pollution.