Late-breaking abstract: Urinary leukotriene E4/exhaled nitric oxide ratio as a predictor of exercise-induced bronchoconstriction control by oral montelukast or inhaled corticosteroid

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Background: Exercise-induced bronchoconstriction (EIB) is associated with vigorous physical exertion in 45 to 85% of children with asthma. A fractional exhaled nitric oxide (FeNO) and urinary leukotriene E4 (LTE4) have been used as the non-invasive markers of airway inflammation in asthmatic children. This study aimed to prove the association between LTE4/FeNO ratio and the effectiveness of therapeutic trial by leukotriene receptor antagonist or inhaled corticosteroids.

Methods: We studied 24 asthmatic children aged from 6 to 18 years with EIB, and randomized to a 4-week trial by oral montelukast (n=12) or an inhaled fluticasone propionate (FP) (n=12). A spirometry and standardized exercise challenge were performed before and after therapeutic trials. Urinary LTE4 and FeNO were measured prior to exercise challenge and 30 minutes after exercise challenge. After 4-week treatment, the same studies were conducted.

Results: After 4-week treatment, post-exercise percent maximum fall in FEV1, baseline and post-exercise LTE4 and baseline FeNO were significantly diminished both study groups; (1) %ΔFEV1: montelukast (21.00 vs 16.54; p = 0.001), FP (23.54 vs 16.54; p = 0.002). (2) AUC20: (503.4 vs 374.9; p = 0.012), FP: (527.7 vs 374.9; p = 0.012). LTE4/FeNO ratio and EIB improvement were associated with greater response to montelukast (p < 0.042, r = 0.326) than FP for EIB treatment (p = 0.478, r = 0.274).
Conclusion: These data indicate that LITE/FeNO ratio was associated with greater response to montelukast than FP for EIB therapy, and is applicable for a predictor of EIB control in children with asthma.

P4250
Demographics, clinical course and outcome of children with status asthmaticus treated in a pediatric critical care unit: 8 year review
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Background: This retrospective study was done to understand demographics and clinical course of children who presented with status asthmaticus treated in a tertiary care pediatric intensive care unit (PICU).

Methods: The medical charts of all patients above 5 years of age admitted to the PICU with status asthmaticus, at Nationwide Children's hospital, Columbus, OH, between 2000-2007 were reviewed. Two hundred and forty seven (247) children were admitted on 281 occasions. Patients with significant co-morbidities were excluded. Final analysis was done using 222 encounters in 183 patients.

Results: The mean age was 11 years (range, 2-50 years). The mean PICU stay was 2.1 days (range, 1-15 days) and mean hospital stay was 3.6 days. Male: Female 109:74. Eighty nine (49%) were on no asthma controller medications. Adherence to therapy was noted in 124 of whom only 41 (33%) claimed compliance. 191 were known asthmatics. Asthma severity noted in 75 patients revealed 22 (29%) had mild intermittent, mild persistent 23 (30%), moderate persistent 17 (23%) and severe persistent 13 (17%). Sixty seven (37%) had a positive family history of asthma. Smoking exposure was noted in 140 (76%). Among 222 encounters, 203 received continuous albuterol, 216 received i.v/salbutamol, 113 receive Terbutaline, 57 received MgSO4, 8 received non-invasive ventilation (CPAP/BiPAP) and16 received intubation. All patients received corticosteroids. Complications included bronchopneumonia in 25 and atelectasis in 25 patients.

Conclusion: Asthmatics with any level of disease severity are at risk for asthma exacerbations requiring PICU stay especially if they are not compliant with their medications.

P4251
The outcome of asthma among Greek children
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Introduction: The natural history of childhood asthma is not fully clarified. This is the first study in Greece on asthma outcome among children.

Aims: To investigate asthma outcome and prognostic factors of severity among children.

Methods: The study included 148 adults with childhood asthma, diagnosed and monitored at the outpatient clinic of a tertiary university hospital. All subjects completed a focused questionnaire on current asthma and atopy and asthma symptoms at the ages of 10 and 16 years. The subjects were invited for evaluation with clinical history, spirometry, exercise and metacholine challenge and skin prick tests.

Results: 78 subjects (52.7%) with a mean age of 17 years agreed to participate in the reevaluation. Free of symptoms were 18/78 (23.1%). Almost half of the symptomatic adults (31/60) had intermittent symptoms. 20/29 (69%) with persistent symptoms had mild asthma. The mean age of remission was 15 years. 23 subjects (29.4%) relapsed after a period of remission. FEV1/FVC < 80% had 29/78 (37.1%), irrespective of severity level. Asthma severity in childhood was associated with FEV1/FVC in adulthood (p=0.007). The persistence of asthma up to the age of 16 years was an unfavourable predictive factor (p=0.04). Bronchial hyperreactivity demonstrated by 27/76 (35.5%) and was associated with current severity and pulmonary function 59/72 (82%) had positive skin prick tests. Atopy in childhood or in adulthood was not associated with current severity. Atopy in adulthood was associated with bronchial hyperreactivity (p=0.012).

Conclusions: Although 60/72 (76.9%) subjects of our sample continued to have asthma on reevaluation, the majority (51/60= 85%) had rather mild symptoms.

P4252
Asthma care community program focusing on primary care (PC) education: Train the trainer
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Objectives: To determine if asthma education intervention aimed at primary care practices can improve asthma care for children in a community and if the results vary by intervention duration of 6 or 12 months.

Methods: Ten practices were selected and were randomly assigned to one of 2 intervention groups. Group 1 (12 month intervention) and Group 2 (6 month intervention). Both groups included 5 pediatric PC practices. Inclusion criteria: voluntary participation, ability to identify one specialized non-physician designee for asthma care provider/practice. Program included visits from asthma educator every 2 weeks. Group 1 received early intervention for 12 months and was then monitored for 6 additional months and Group 2 was observed for 12 months and then intervention for 6 months and then monitoring for 6 additional months. Baseline survey and blinded chart review determined adequacy of documentation. Targeted questionnaire was done at 6 month intervals.

Results: In group 1, 6 month, 12 month and 18 month data (mean and exact 95% binomial confidence intervals) revealed significant improvement in documentation of asthma severity level, education, action plan, management according to NIH guidelines, day time and exercise related symptoms compared to baseline. Improvement was significant compared to group 2 at 6 and 12 month interval. In group 2, intervention started at 12 months and improvement in all of the above endpoints was noted at 18 months. At end of intervention and end of the follow-up evaluation, there was no significant difference in any end point between group 1 and 2.

Conclusion: In- office support for asthma education improves asthma care during and following the intervention.

P4253
Assessment of inhalation technique: Reliability and validity of a checklist in preschool children with asthma
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Background: Incorrect use of inhaler devices has a major influence on asthma control. Assessment of the inhalation technique of asthma patients is important. For this purpose the Dutch Asthma Foundation has developed a 7-points checklist. This checklist has not been validated in young children.

Objective: To assess reliability and validity of the checklist in preschool children with asthma using a metered dose inhaler with spacer.

Methods: 20 children (6m-6y). All patients were treated with daily inhaled corticosteroids (ICS). The inhalation technique was recorded on video tape and independently assessed by 6 observers using the Dutch asthma checklist (6-7 points) and a general impression of the inhaler technique (0-10). This assessment was repeated after 2 weeks.

Results: Inter-observer-agreement (IOA) was fairly good for the checklist (Intra-class Correlation ICC: 0.70, range 0.42-0.87) and the general impression (ICC: 0.64, range 0.50-0.90). IOA however was moderate with ICC 0.48 for the checklist and ICC 0.50 for the general impression.

Conclusion: Reliability and validity of assessment of inhalation technique in young children is suboptimal. IOA in assessment of inhalation technique in young children using metered dose inhaler with spacer is moderate. No difference was observed when a general impression was given or a checklist was used.

P4254
Prevalence and control of current asthma in Portuguese paediatric population
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Objective: To estimate the prevalence and control of asthma-like symptoms in children in the general Portuguese population.

Methods: Nationwide, two-phase, list-assisted random-digit-dialling telephone survey (Portuguese National Asthma Survey). The first phase questionnaire was based on the GA\LEN survey. Current asthma was defined as self-reported asthma and, in the last 12 months, wheezing and/or awaking with breathlessness and/or having an asthma attack. Participants identified as having “current asthma” in first phase were re-interviewed. In addition, other children with asthma living in the same residence were also interviewed.

Results: Of the 6,003 participants in the first-phase, 716 were children (0-17 years old); 143 (20.0%) had wheezing in the last 12 months; 240 (33.5%) awakened with cough or breathlessness in the last 12 months and 89 (12.4%) had an asthma diagnosis in the past.
P4255
Adolescent undiagnosed- wheeze: an unrecognised state associated with significant morbidity, tobacco and paracetamol use
Malak Shaheen, Emad Mohamed, Mona El Ganzory.
Malak Shaheen, Samer Mostafa, Eman Zaki.
Malak Shaheen, Samer Mostafa, Eman Zaki.

Background: Adolescents with undiagnosed wheeze disproportionately visit ED and are hospitalised for asthma. Non-tobacco use and no paracetamol use were significantly lower in undiagnosed- wheeze. Aims: To explore quality of care (QoC) as perceived by children with asthma and their parents in a randomized controlled study. Treatment, either by general practitioners (GP), paediatricians (PP) or asthma nurses (AN). Methods: Children (6-16 yrs) with stable asthma were recruited from hospital practice (n=62) and from general practice (n=45). Subjects were allocated to three follow up arms (GP, PP, AN). At baseline and after 1 and 2 years, QoC was measured, by parents completing the QUOTE-CNSLD-questionnaire. By factoranalysis an adapted version was derived. Children also completed a 5-item Likert scale, independently and if needed assisted by the research nurse.

Results: A comparative study of patients' and parent's perspective in three paediatric asthma settings; a randomised controlled study in children with stable asthma

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Aims: To explore quality of care (QoC) as perceived by children with asthma and their parents in a randomized controlled study. Treatment, either by general practitioners (GP), paediatricians (PP) or asthma nurses (AN). Methods: Children (6-16 yrs) with stable asthma were recruited from hospital practice (n=62) and from general practice (n=45). Subjects were allocated to three follow up arms (GP, PP, AN). At baseline and after 1 and 2 years, QoC was measured, by parents completing the QUOTE-CNSLD-questionnaire. By factor-analysis an adapted version was derived. Children also completed a 5-item Likert scale, independently and if needed assisted by the research nurse.

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Results: Two dimensions measured significant differences between children recruited from hospital care and from primary care at baseline. No difference during follow-up indicates that from a quality perspective a specialized asthma nurse is cost effective.

P4259
Quality of Life in Asthmatic Children: A Comparative Study of Patients’ and Parents’ Perceptions
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Background: Pediatric asthma is one of the most important public health problems. Pediatric pulmonologists are not only responsible for clinical relief of children’s symptoms but also for ensuring a better quality of life for them and their families.
P4260
Effects of exposure to parental smoking on pulmonary function and symptoms in children with asthma
Polytimi Panagiotopoulou-Gartagán1, Panagiotis Nikolau2, Efthimia Kalampoula1, Emmanouela Karavankili1, George Kavadas1, Maria Chatzisimeon1, Athanasios Kaditis1, Chryssa Bakoula1, George Charousou1. 1First Department of Pediatrics, University of Athens School of Medicine and Aghia Sophia Children’s Hospital, Athens, Greece; 2Department of Forensic Medicine and Toxicology, University of Athens School of Medicine, Athens, Greece
Exposure to parental smoking (EPS) has been associated with increased asthma symptoms and airway hyper-reactivity. Aim of the present study was to evaluate prospectively the effects of EPS on pulmonary function and symptoms in children with asthma.
Methods: Urine cotinine-to-creatinine ratio (UCCRR) was used as an indirect measure of EPS, while FEV1 and asthma exacerbations were the main outcome variables. Subjects were evaluated at baseline and 2 years after an intervention to eliminate EPS.
Results: 78 children (6-14 y.o.) were recruited. Subjects with history of EPS (n=38) had significantly lower FEV1 and higher UCCRR compared to those without such history (90.6±11.1 vs 96.4±12.6%, predicted, p<0.046; and 25.3±2.1 vs 14.1±1.1 ng/mg; p=0.005). Two years later, 31 children were re-evaluated; subjects with a decrease in UCCRR were similar regarding FEV1 compared to those with an increase in UCCRR (100.1±9.4 vs 105.4±14.7% predicted, p=0.399). However, there was a trend for reduced frequency of asthma exacerbations: from 3.2±2.1/yr to 0.7±1.1 yr in children with reduced UCCRR.
Conclusions: History of EPS is associated with decreased airway function. Reduction in urinary cotinine levels within 2 years is accompanied by a trend for improvement in asthma exacerbations but not in airway function.

P4261
Perinatal weight gain and early development of recurrent wheeze and asthma in term children
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Rationale: Perinatal growth and asthma may share origins
Objectives: We explored the association between growth in the perinatal period and the development of recurrent wheeze and asthma.
Methods: The analysis included 398 of a birth cohort of 411 Danish neonates and the development of recurrent wheeze and asthma. Weight gain in the peri-natal period was significantly associated with the development of recurrent wheeze or asthma in young-at-risk children born at term suggesting peri-natal mechanisms as a common link.

P4262
Relation of asthma and body mass index in children
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Background: The prevalence of obesity and asthma has increased in past decades. Most prospective studies suggest that obesity increases the risk of asthma but some did not find this association.
Aims and objectives: The purpose of this study was to determine the association between asthma and Body Mass Index
Method: This case-control study was conducted on 200 asthmatic children aged 6-15 years and 200 healthy controls. The criteria for asthma diagnosis and its classification were on the basis of National Asthma Education and Prevention Program (NAEPP). BMI of patients and controls were also measured and BMI was defined as overweight and obese respectively. The data was analyzed by SPSS software.
Results: The BMI among the asthmatic children (17.9 kg/m²) was higher than the BMI among the non-asthmatic (16.5 kg/m²), p value <0.0001. This relationship was significant in both males and females. 18% of asthmatic children were classified as overweight and 13.5% of them were obese. The frequency of overweight and obesity in control group was 5.6% and 6%, p value <0.001. However, there was no significant relationship between severity, duration of asthma and kind of medication and BMI in asthmatic children, p value >0.05.
Conclusion: Result of this study showed that there is an association between asthma and obesity and symptoms and obesity in children. Therefore, attention to weight control in asthmatic children might be effective.

P4263
Influence of obesity on pulmonary function (PF) in severe asthmatic children
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While there have been reports in adults evaluating the effects of obesity on PF tests, in severe asthmatic children studies are scarce.
Aim: To evaluate the influence of obesity on PF in children with asthma.
Methods: 39 children (41% male) with controlled severe asthma with and without obesity, and 22 non-obese asthmatic patients (59% male) were included. Patients were divided according to asthma diagnosis (NIH guidelines) and to Body Mass Index (BMI) cut off (IOTF): Group 1 asthma with normal weight, G2 asthma with obesity and G3 obesity without asthma. Spirometry and plethysmography were performed in all patients. Considered parameters were FVC, FEV1/FVC, FEPF50, FEF25-75, TLC (total lung capacity), FRC (functional residual capacity), RV (residual volume) and sGaw (specific airway conductance). BMI corrected for age and sex and BMI z-score were assessed. PF between G1, 2 and 3 were compared.

<table>
<thead>
<tr>
<th>Table 1. Pulmonary Function</th>
<th>Values</th>
<th>Mean±SD</th>
<th>G1(n=16)</th>
<th>G2(n=23)</th>
<th>G3(n=22)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFC</td>
<td>%</td>
<td></td>
<td>112.2±16</td>
<td>115.1±14</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>FEV1</td>
<td>%</td>
<td></td>
<td>96.6±18</td>
<td>103.4±15</td>
<td>114±15</td>
<td>0.003**</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td></td>
<td></td>
<td>80.3±10</td>
<td>88±6</td>
<td>0.001*</td>
<td></td>
</tr>
<tr>
<td>PEF</td>
<td>L/sec</td>
<td></td>
<td>77.2±8</td>
<td>93.5±29</td>
<td>132±11</td>
<td>0.001*</td>
</tr>
<tr>
<td>FVC</td>
<td>L</td>
<td></td>
<td>114.9±9</td>
<td>115.7±16</td>
<td>107.4±11</td>
<td>NS</td>
</tr>
<tr>
<td>TLC</td>
<td>L</td>
<td></td>
<td>118±20</td>
<td>118±20</td>
<td>107±15</td>
<td>0.002*</td>
</tr>
<tr>
<td>FRC</td>
<td>L</td>
<td></td>
<td>156±52</td>
<td>126±43</td>
<td>85±34</td>
<td>0.001*</td>
</tr>
<tr>
<td>RV</td>
<td>%</td>
<td></td>
<td>0.11±0.7</td>
<td>0.12±0.7</td>
<td>0.17±0.6</td>
<td>0.04*</td>
</tr>
</tbody>
</table>

A significant inverse correlation between BMI z-score and FVC (r = -0.5, p = 0.001) and RV (r = -0.4, p = 0.006) was found between asthmatic patients.
Conclusion: Obesity might influence PF decreasing FVC and RV despite of asthma diagnosis.

P4264
Assessment of physical activity with accelerometer in Brazilian asthmatic children
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Background: Although it is widely accepted that asthmatic children are physically unconditioned, however there are few reports quantifying the level of physical activity, especially in developing countries.

Thematic Poster Session
Hall 2-36 - 12:50-14:40
TUESDAY, SEPTEMBER 27TH 2011

783s
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Objective: To evaluate the level of physical activity in asthmatic children and to compare among asthma severities.

Methods: Sixty-nine children (50M/19F, 18.8±3.3 kg/m^2) with persistent mild (n=27), moderate (n=20) and severe (n=22) asthma were evaluated. Children wore an accelerometer for 6 days (4week and 2weekend) and the total steps per day (TStp) and steps walked at either moderate or vigorous intensities (>10 steps/minute) were evaluated.

Results: Our results show that 71% of all asthmatic children were considered physically active (male>12,000 and female>10,000 steps per day). The level of activity at moderate or vigorous intensities in physically active children represented around 45% of total step counting and they showed higher activity levels during week compared with weekend days (p<0.05). The level of physical activity in asthmatic children was not related to either gender or weight. Interesting, children with mild persistent asthma were physically less active during week days than those with moderate and severe asthma (p<0.05), however no difference was observed in the weekend days (p>0.05).

Conclusion: Contrary to popular belief, most asthmatic children were considered physically active and those patients with moderate and severe asthma are still more active.

P4265 Relationships between body mass index and clinical and functional characteristics in childhood asthma: A cross-sectional analysis
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Background: Overweight is a risk factor for subsequent asthma in children and obesity in adult represents a unique phenotype of asthma, with more severe disease.

Objectives: To assess the relationships between body mass index and clinical and functional characteristics of childhood asthma in a cross-sectional design.

Methods: The z-scores of BMI were evaluated according to the level of control (severity) and atopy. The same analyzes were repeated for other variables (waist circumference, body mass index) obtained from the adolescents' records. All the analyses were performed using the Statistical Package for Social Sciences (SPSS) version 14.0.

Results: Data from 506 children (178 girls, 10.8±2.6 years, min-max [6-15]) of whom 92 (18%) with overweight were analyzed. The z-scores of BMI were not significantly different according to atopy (p=0.31), recent exacerbation (p=0.24) or optimal control (p=0.94). There was no correlation between z-score and ICS dose (r=0.05). The correlation between z-score and ICS dose (p=0.07). Z-scores of BMI did not correlate with indices directly obtained from spirometry, but negatively correlated with pre- and post-bronchodilator FVC/TLC and RV/TLC ratios (Rho = -0.25, p < 0.0001; Rho = -0.22, p < 0.0001, and Rho = -0.25, p < 0.0001; Rho = -0.26, p < 0.0001, respectively). These results were confirmed when comparing children with or without overweight.

Conclusions: This cross-sectional analysis suggests that overweight does not influence asthma control in asthmatic children, but alters lung volumes proportions.

P4266 The influence of overweight/obesity on asthma symptoms among Dutch children
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Background: Overweight has been identified as a risk factor for the development and the severity of asthma in children. The prevalence of overweight in children had been increasing more rapidly in certain areas of Southern Limburg compared to the other Dutch provinces. The aim of this study was to assess the influence of overweight and obesity on the prevalence of asthma symptoms in Southern Limburg, the Netherlands.

Methods: Parents of 39,316 children (6 - 16 years) in Southern Limburg were invited to complete an online questionnaire. The questionnaire consisted of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire (Asher, MI. et al. Clin Exp Allergy 1998; 28 Suppl 5: 52-66), and additional questions about anthropometric variables, risk factors for asthma, and social environment. Corrections were made for the following confounders: sex, age, ethnic background, tobacco smoke exposure, birth delivery, family history of asthma, birth weight and breast feeding of the mother during pregnancy.

Results: The response rate was 23.7% (n=9,309). The prevalence of asthma, overweight and obesity was respectively 7.7%, 15.2% and 2.5%. A high Body Mass Index Standard Deviation Score (BMI-SDS) was significantly related to the prevalence of current asthma (adjusted OR= 1.10, 95%CI= 1.03-1.18, p<0.01). Also “current wheezing symptoms” were related to a high BMI-SDS, (adjusted OR= 1.40, 95%CI= 1.02-1.91, p<0.02). Dry cough at night was not associated with BMI-SDS (adjusted OR=1.01, 95%CI= 0.97-1.07, p=0.53).

Conclusion: There is a slight but statistically significant positive association between BMI SDS and asthma in children in Southern Limburg, the Netherlands.

P4267 Leptin levels in obese and non-obese children with asthma
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Objective: The aim of the study was to evaluate the serum leptin levels in children with asthma and to compare it with healthy controls and to determine the relationship of leptin, systemic inflammation and lung function in asthmatic children.

Method: The study included 62 patients with stable asthma (47 obese and 15 non-obese) and 15 healthy controls, mean age 11.2±2.85 years. All subjects were prospectively and consecutively evaluated. A skin prick test and blood sampling for assessing serum leptin levels and C reactive protein were performed in all subjects. Body mass index was calculated using height and weight, waist circumference and waist to hip ratio measured on the same day that pulmonary function test performed.

Results: Leptin concentrations were significantly higher in obese asthmatic patients than in non-obese asthmatics and healthy controls (4.20±3.06 vs. 1.74±1.12 vs. 1.76±0.97 mg/l; p<0.001). The correlation between leptin and CRP was negative in group obese asthmatics, but without significance. The correlations of leptin with indices of pulmonary function in the study group (FEV1/FVC, PEF and PEF50%) were negative (p<0.001; p<0.05).

Conclusion: High level of serum leptin in obese asthmatic children probably is marker of exacerbated airway inflammation and influence the control and disease severity.