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The Impact of the Parental Smoking in the Absolute Lung Volumes of Asthmatic Tunisian Children

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Abstract

Background: Exposure to parental smoking is one of the most threating life problem in the word during childhood and it is unfortunately in increasing. Previous studies have shown a high association between this condition and uncontrolled asthma. To the best to our knowledge, the impact of this association on the body plethysmographic parameters is rarely described.

Objective: To determine the impact of parental smoking on the lung volumes of asthmatic children.

Methods: We carried out a cross sectional study at the department of Functional Explorations Sfax (Tunisia) between January 2017 and January 2018, including 133 asthmatic children. Regarding to their parental smoke status, we divided our population into two groups exposed GI and none exposed children GII.

Results: The two groups were composed respectively of 62 and 71 asthmatics children. A predominance of male gender was observed. The measurement of routine spirometric values, and the body plethysmography were performed by the participants. No statistical significant differences were reported in term of forced expiratory volume in the first second (FEV1s) (L) (%Th), forced vital capacity (FVC) (L), total lung capacity (TLC) (L) (%Th) and FEV1s/FVC ratio between the two groups. Nevertheless, the residual volume RV (L) (%Th) was significantly higher in exposed asthmatic children respectively 252.52 ± 59.32% in GI versus 228.86 ± 57.28% in GII ($p<0.05$).

Conclusion: Body plethysmography is a sensitive tool to detect pulmonary changes due to smoke exposure that are not currently detected by spirometry.

Keywords: Body plethysmography; Children; Parental smoking; Asthma

Introduction

Asthma is the most prevalent chronic lung disease of childhood [1]. It is treatable, preventable but at sometime associated with a burden quality of life if it is not well controlled [2]. Over the two last decades, its prevalence is in increasing and it was estimated around 7% of Tunisian children [3]. Previous studies have shown that early bronchiolitis [4], parental asthma [4], atopic dermatitis [5], so smoke exposure [6] are the major predictor factors of asthma in children. Exposure to outdoor and indoor passive smoking was associated with worsening asthma, increasing of exacerbations, wheezing symptoms and acute bronchial constriction [7]. The International Consultation on Environmental Tobacco Smoke recognizes therefore smoke exposure as a high risk of developing uncontrolled asthma [7]. Parents are aware of both of the hazards of active and passive smoking [6] but no change in parental smoking behaviour has been reported. Yet, asthmatic children continue to be exposed to smoking [6,8-11].

Ideally, the follow up of asthma should take into account this factor "smoke exposure", but now there are no clear recommendations on how monitoring these children. Obviously, asthma monitoring of exposed children can be assessed using clinical scales, symptoms and therapy use but lung function tests and measure of inflammatory biomarkers are more objective and rigorous [12]. Hassanzad, et al. [11] had shown that cotinine level is associated with a decreased forced expiratory volume in the first second (FEV1s) in asthmatic children. Traditionally, spirometry and particularly (FEV1s), is indicated regarding the clinical course in asthmatic children (risk factors, lung impairment function). But, it is well known that spirometry is the gold test to assess airway obstruction and reversibility (features of asthma). Most of respiratory societies (The global initiative for Asthma (GINA), the American National Asthma Education and Prevention Program (NAEPP), British thoracic society (BTS)) recommended its use to monitor asthma in children aged more than 5 years at least annually and more frequently in uncontrolled asthma. There are several reasons to perform this test in smoke exposed asthmatic children [13]. Studies had shown a strong association between smoke exposure and reduced forced vital capacity (FVC, l); and FEV1 (l) [14]. Besides, a higher risk of developing proximal obstructive ventilator defect (POD) was observed [15].

Nevertheless, there is a lack of appropriate data about the impact of passive smoking in the total lung volumes of asthmatic children. Body plethysmography is not a routine test to monitor asthma. Its indications are restricted particularly in obese asthmatic children. Although body plethysmography measurements have a potential role in monitoring and diagnosing difficult and severe cases of asthma, no

clear guidelines about its indication was provided. Recently, studies had shown a correlation between the lung residual volume (RV), total lung capacity (TLC) and asthma severity [16]. While in others studies, FEV1s wasn't a good indice to assess asthma severity [17]. Such findings, suggested that both of spirometry and plethysmography can be required to test the impact of passive smoking in asthmatic children. With this background, we hypothesized in our study that parental smoking can affect the lung volumes even before the drop of spirometric parameters in asthmatic children. Such results, may encourage parents to quit smoking, because controlling passive smoking is still the greatest way to manage asthma [18]. We aimed in this study to assess whether parental smoking affects the lung function of asthmatic children.

Methods

Subjects

We carried out a cross sectional study at the laboratory of Functional Explorations Sfax (Tunisia) between January 2017 and January 2018. This study included asthmatic children aged between 6 and 13 years old and who were addressed to perform plethysmography test. Asthma diagnosis was confirmed according to GINA guidelines [3]. All asthmatic children responding to the inclusion criteria were eligible to participate. Children with other chronic respiratory disease or intellectual deficiency or an acute exacerbation in the last two weeks or congenital myopathy or others diseases associated with respiratory complications were not included. Children with whom cooperation is difficult were excluded.

Sample size

To obtain satisfactory results, sample size was calculated. Comparison between two proportions p1 and p2 in two equally sized groups requires the following equation: n = ([p1× (1 – p1) + p2 × (1 – p2)]/ (p1 – p2)2) × cp power [4].

Where n is the number of subjects required in each group and cp power characterized by a specific confidence interval and a specific P value. According to Suárez López de Vergara et al. [19], spirometry abnormalities were seen for FEV in 64% of the exposed asthmatic children against to 36% in those non-exposed [1] Plugging this observed value into the predictive equation, and requiring 80% power and a significant p value fixed at 0.05, the sample size was thus 92 children.

Medical questionnaires

Standard questionnaire were asked by a doctor with whom children and parents were not familiar. Questionnaire included data about clinical symptoms, history of the asthma, and Tabaco status. Asthma duration (years) was determined by the answer to this following question "how long your son or/ daughter is suffering from asthma?

Physical examination

Weight (kg) and height (cm) was measured and used to calculate the body mass index (BMI) according to the following equation: weight divided by the square height (kg/ m^2).

Plethysmography function test

All Plethysmography tests were realized, at the same place according to the ATS/ERS 2005 recommendations [20] with a plethysmograph Body Box 5500. All tests were performed by two qualified investigators. The following parameters were measured or calculated: FVC (l); FEV1s (l), FEF: forced expiratory flow, forced expiratory flow from 25% to 75% of FVC (FEF25–75%, l sec1), FEV1/ FVC ratio (absolute value) [21]. Functional residual capacity (FRC, L), total lung capacity (TLC, L) and residual volume (RV, L). The: FEV1s, FVC, FEF and FEF25–75, were expressed as percentages of the predicted values according the local Tunisian reference values (%Th) [22]. The European Respiratory Society/European Community for Steel and Coal (ERS/ECSC1983) references were used to express RV, TLC and FRC in percentages (%Th).

POD is defined by FEV1/FVC ratio below the lower limit of normal [20]. The following POD classification severity based on FEV1 (%) was applied [20]: mild (>70%), moderate (60 to 69%), moderately severe (50 to 59%), severe (35 to 49%) and very severe (<35%).

Reversibility test was performed by administration of 400 micrograms of bronchodilator [3]. The bronchodilator response was evaluated according to the proportional post-bronchodilator increase in FEV1 in relation to the baseline value all evaluations were performed at baseline and 10-15 min after reversibility test.

Lung hyperinflation is defined by an increase of FCV or RV above 130% of the predicted value.

Statistical analysis

The statistical analyses were carried out using the Statistical Package for Social Sciences (SPSS) version 20.

The analyses of data distribution was performed by Kolmogorov-Smirnov test. Continuous variables were expressed by means ± standard deviation SD or by medians (1st-3rd quartiles). Categorical variables were expressed by frequencies.

The Student t test for independent sample test for parametric data and Mann-Whitney test for nonparametric data were used to compare the following continuous measures between the two groups (age, height, weight, BMI, FEV1 (L)(%Th), FVC (L) (%Th), FEV1/FVC (absolute value), FEF25–75% (l sec1,%)) ,VR (L)(%Th), TLC (L)(%Th), and FRC (L)(%Th), Correlations between asthma duration (years old) and FEV1 (L)(%Th), (L)(%Th), FEV1/FVC (absolute value), FEF25–75% (l sec1) (%Th), VR (L)(%Th), TLC (L)(%Th)and FRC (L) (%Th)were carried out using Spearman or pearson correlation coefficient. p Values under 0.05 were considered none significant :NS.

Results

Children data

A total of 159 asthmatic children were recruited. Among them, 26 children didn't fulfill the inclusion criteria (difficult cooperation, inacceptable results) and were therefore excluded.

Of the 133 participants, 61 (53%) were smoke exposed (GI) and 72 (47%) were smoke exposure free (GII). None of the investigated children was active smoker.

Significantly, the prevalence of boys was higher than girls (64% of the participants were males versus 36% were Females). Their demographics and clinical characteristics are shown in the Table 1.

	GI	GII	P
Age (years)	9.88 ± 2.09	9.26 ± 1.96	NS
Sex ratio (M/F)	43/18	41/31	<0.05
Weight (Kg)	35.08 ± 9.49	33.73 ± 10.72	NS
BMI (kg/m2)	17.42 ± 3.64	17.52 ± 3.63	NS
Asthma duration (years)	5.70 ± 3.85	4.90 ± 3.38	NS
FEV1 (%Th)	86.75 ± 15.41	92.25 ± 16.55	NS
FEV1(l)	1.78 (1.572.07)	1.75 (1.422.07)	NS
FVC (%Th)	98.00 (88.00102.00)	100.5 (91.00111.70)	<0.05
FVC (l)	2.29 (1.902.62)	2.15 (1.772.50)	NS
FEV1/FVC	0.80 (0.740.86)	0.8 (0.750.84)	NS
FEF (%Th)	82.04 ± 19.18	85.87 ± 22.21	NS
FEF25-75(Th)	85.08 ± 22.14	89.22 ± 23.47	NS
RV (%Th)	252.52 ± 59.32	228.86 ± 57.28	<0.05
RV (1)	1.85 ± 0.48	1.60 ± 0.44	<0.05
VGT (%Th)	190.89 ± 38.17	179.22 ± 37.48	NS
VGT(l)	2.68 ± 0.60	2.38 ± 0.56	NS
TLC(l)	4.19 ± 0.81	3.85 ± 0.81	NS
TLC (%Th)	136.00 (123.00149.00)	128.00 (124.00138.00)	NS
Inc of FEV1 post%(baseline)	10.00 (4.0014.00)	9.00 (4.0014.00)	NS
Inc of FVC post%	4.00 (1.7511.00)	3.50 (2.007.50)	NS

GI: exposed asthmatic children, GII: non-exposed asthmatic children, M: male. F: female, (%Th): percentage of theoretical value, P<0.05: significant result, NS: non-significant, FVC: forced vital capacity.FEV1:1st second forced expiratory volume. FEF25–75%: forced expiratory flow from 25% to 75% of FVC, RV: residual volume. FEF: forced expiratory flow.

Results are expressed by medians (1st-3rd quartiles), Results are expressed by mean ± SD, Inc of FVC post: increase of FVC post Bronchodilator, Inc of FEV 1 post : increase of FEV 1s post bronchodilator, Test Man Withney used for non-parametric values , Test T used for parametric values

Table1: Clinical, demographic and plethysmographic characteristics of the smoke exposed and none exposed children.

Baseline and post bronchodilator spirometric results

At baseline, the FVC (%) was significantly lower in Exposed asthmatic children by 2.5% compared to those non-exposed whereas no difference in the FEV1s (L) (%Th), FEF25 – 75(%Th), and FEF (%Th), were observed.

72% of children of GI had POD versus 74% of GII (p: NS). Gender factor didn't affect the POD distribution.

Bronchodilator responses were similar between the two groups with complete reversibility in 50% of children of GI versus 48% in GII.

Baseline plethysmography results

The plethysmography test was performed by 113 children. The RV (L) (%Th) was significantly higher in exposed asthmatic children respectively 252.52 ± 59.32% in GI versus 228.86 ± 57.28% in GII (p<0.05). Nevertheless, no difference have been identified in term of TLC (L)(%Th) and FRC (L)(%Th) (Table 1). None of these children had developed restrictive ventilatory defect.

Lung hyperinflation (LH) reported in 86% of children of GI and 73% in GII, were associated with normal simple spirometry respectively in 22% in GI and 11% in GII (p=NS). The risk of developing isolated LH (with normal spirometry) was higher for girls in GI than GII (4 girls in GI versus 1girl in GII (p<0.05).

Analysis of the effect of asthma duration on lung function

There is no significant correlation between Asthma duration and RV (L) (%Th) in both two groups. However, it was negatively

correlated with the FEV1/FVC ratio in both GI and GII (GI (r=0.382, p<0.05) versus GII (r=0.302, p<0.05)).

Only in none exposed children (GII), FRC (L) and FVC (%Th) increased with the increase of asthma duration with a coefficients of correlation respectively (r=0.291, p<0.05), (r=0.305, p<0.05).

Paradoxically, while FEF (%Th) decreased with the increase of asthma duration in GI (r=0.321, p<0.05), they were reciprocally positively correlated in GII (r=0.311, p<0.05).

Discussion

Methodological discussion

Our sample size appeared to be valid since the calculated one is 92 children. Gill R et al.. [23], conducted a study composed of 40 asthmatic children. According to international recommendations [20], a number of subjects more than 100 ensures valid findings.

However, larger cohorts composed of 3187 and 484 asthmatics children were reported in others studies [14,19].

Principal results

Our results point towards the importance of the use of the body plethysmography to assess the impact of smoke exposure in the respiratory function of asthmatic children. In difference to the previous studies, no differences had been identified in the FEV1s (L) (%Th) [14,24,25], FEF(%Th), FEF25 – 75(%Th) [14,24,25] between smoking exposed and none exposed children. Nevertheless, we found a strong association between passive smoking and higher values of RV (L) (%Th) and lower FVC (%Th).Absolute lung volumes measurement are not indicated in current recommendations in asthmatic children according to the GINA 2017. However, investigators showed that their measurement may reveal lung impairment more readily than spirometry [26]. Lung hyperinflation or high RV were frequent in asthmatic children, even in those with a normal spirometry [26] .Besides, RV was considered as a sensitive inflammatory index [27]. Peroni, et al. [27] showed a significant relationship between the RV with the allergen avoidance or exposure. Thus, the significant increase of RV(%Th) in asthmatic exposed children, in our study, could be probably the consequence of tobacco exposure inflammation. Vasconcelos et al. supported this hypothesis and highlighted in their experimental study, the role of smoke exposure in airway inflammation [28]. Passive smoking even during a short period lead to an increase of inflammatory cells, mucus accumulation; tracheal hyperresponsiveness [28] and then air trapping.

The significant decrease of FVC (% Th) in exposed asthmatic children, in our study, may provide further evidence of persistent inflammation due to smoke exposure. Such findings have been reported in several studies [8,14,19]. 64% of exposed children in the study of Lopez et al. [19] developed FVC decrease against 36% of those none exposed. And this decline was associated with increasing number of smokers at home [14].

Besides, this decrease suggested the presence of high lung volumes particularly RV in exposed asthmatic children. According to Sorkness et al. [29], FVC is the best spirometry predictor of lung hyperinflation and air trapping.

Our study showed that passive smoking had an adverse effect on lung function in infancy but these hazards still longer and continue even in long term. A significant association has been identified between asthma duration and decreased FEV1s/FVC ratio and FEF (%Th) in exposed children compared to those controls. It has been established, by previous investigators that smoke exposure during childhood and prenatally, disturbs lungs growth and accelerates spirometry drops [14]. The immunological system of children and particularly the asthmatic ones are immature and more susceptible to environmental and Tobacco toxins [30].

Moreover, increased lung volumes were linked to worse respiratory evolution. They were considered as sensitive tools in detecting epithelial remodelling and were the marker of poorly controlled asthma.

In difference to the previous studies [15], proximal obstructive ventilatory defect (POD) and lung hyperinflation (LH) had a high prevalence in both exposed and none exposed asthmatics groups respectively 72% versus 74% and 86% versus 73%. According to the literature their prevalence varied between studies respectively 21% [15] for POD, and 4% [15] to 40% [26] for LH. For exposed asthmatic children, distal obstructive ventilatory defect was the most common abnormality [8].

Such outcomes can be related to the differences between studies, in the age of subjects, the equipment and the methods of interpretation.

While POD was defined in our study by FEV1/FVC ratio below the lower limit of normal, the cut off was the 80% of predicted value in both of the study of RG Suarez Lopez de Vergara et al. [19] and Labbe et al. [26], and 0.85 in the study of Mahut et al. [15]. Besides, LH was defined in our study by an increase of RV or FVC above 130% of the predicted value. Yet, it was retained by Labbe, et al. [26] when the RV/TLC was above 30% while it was 33% in the study of Mahut, et al. [15].

Furthermore, we referred in our study to the local Tunisian norms [22] for flows and to (ERS/ECSC1983) norms for absolute lung volume while Labbé et al. used the references of Zalaptel, et al.

Besides we preferred in our study to restrain the age between 6 and 13 years old. Because in this period, children are less exposed to the hormonal and pubertal fluctuation that may interfere on the respiratory function. However, most of investigators used to study the impact of smoke exposure in children aged between 6and 16 years old [14,23]. While invasive methods are difficult to perform, we just relied on subjective questionnaire to determine the passive smoking status and isolated body plethysmography to assess the respiratory function. Nevertheless, in this situation it would be better to measure the Urine cotinine [11]. The indication of body plethysmography in asthma during infancyMay clarifies the physiopathology of the interaction between smoke exposures and respiratory function drops. Further investigations as nasal biomarkers, airway biopsy, and sputum cells count may improve our comprehension of this pathogenesis.

Conclusion

In our study, there is obviously evidence of the harmful effect of the passive smoking on the respiratory function of asthmatic children. The body plethysmography is able to detect pulmonary changes due this smoke exposure that are not currently detected by spirometry.

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Ethics

This study respect to the rules of the Tunisian country.

Conflict of Interest

None.

References

1. Centers for Disease Control and Prevention (CDC) (2011) Vital signs: asthma prevalence, disease characteristics, and self-management education: United States, 2001-2009. MMWR Morb Mortal Wkly Rep 60: 547-552.
2. Sennhauser FH, Braun-Fahrländer C, Wildhaber (2005) The burden of asthma in children: a European perspective. Paediatr Respir Rev 6: 2-7.
3. Global Strategy for Asthma Management and Prevention (2017) Global Initiative for Asthma (GINA).
4. Törmänen S, Lauhkonen E, Riikonen R, Koponen P, Huhtala H, et al. (2017) Risk factors for asthma after infant bronchiolitis. Allergy 73: 916-922.
5. Hyvärinen M, Piippo-Savolainen E, Korhonen K, Korppi M (2007) Teenage asthma after severe infantile bronchiolitis or pneumonia: Asthma after infantile pneumonia and/or wheezing. Acta Paediatr 94: 1378-1383.
6. Hatoun J, Davis-Plourde K, Penti B, Cabral H, Kazis L (2018) Tobacco Control Laws and Pediatric Asthma. Pediatrics 141: S130-S136.
7. World Health Organization (1999) International Consulation on Environmental Tobacco Smoke and Child Health. Geneva.
8. González BFJ, Takkouche B, valdes L, Temes E, Leis R. et al. (2007) Parental smoking and lung function in healthy children and adolescents. Arch Bronconeumol 43: 81-85.
9. Crone MR, Nagelhout GE, van den Burg I, HiraSing RA (2010) Passive smoking in young children in the Netherlands sharply decreased since 1996. Ned Tijdschr Geneeskd 154: A1658.
10. Kumar GS, Roy G, Subitha L, Sahu SK (2014) Prevalence of bronchial asthma and its associated factors among school children in urban Puducherry, India. J Nat Sci Biol Med 5: 59.
11. Hassanzad M, Khalilzadeh S, Elsampanah NS, Bloursaz M, Sharifi H, et al. (2015) Cotinine level is associated with asthma severity in passive smoker children. Iran J Allergy Asthma Immunol 14: 67-73.
12. Ayuk AC, U waezuoke SN, Ndukwu CI, Ndu IK, Iloh KK, et al. (2017) Spirometry in Asthma Care: A Review of the Trends and Challenges in Pediatric Practice. Clin Med Insights Pediatr 11: 117955651772067.
13. Thacher JD, Schultz ES, Hallberg J, Hallberg U, Kull I, et al. (2018) Tobacco smoke exposure in early life and adolescence in relation to lung function. Eur Respir J 51: 1702111.
14. Fernández-Plata R, Rojas-Martinez R, Martinez-Briseno D, Garcia-Sancho C, Perez-Padilla R (2016) Effect of Passive Smoking on the Growth of Pulmonary Function and Respiratory Symptoms in School children. Rev Investig Clin Organo Hosp Enfermedades Nutr 68: 119-127.
15. Mahut B, Bokov P, Delclaux C (2010) Abnormalities of plethysmographic lung volumes in asthmatic children. Respir Med 104: 966-971.
16. Luo J, Liu D, Chen G, Liang B, Liu C (2017) Clinical Roles of Lung Volumes Detected by Body Plethysmography and Helium Dilution in Asthmatic Patients: A Correlation and Diagnosis Analysis. Sci Rep 18: 40870.
17. Bacharier LB, Strunk RC, Mauger D, White D, Lemanske Jr RF, et al. (2004) Classifying Asthma Severity in Children: Mismatch Between Symptoms, Medication Use, and Lung Function. Am J Respir Crit Care Med 170: 426-432.
18. Rosen LJ, Noach MB, Winickoff JP, Hovell MF (2012) Parental smoking cessation to protect young children: a systematic review and meta-analysis. Pediatrics 129: 141-152.
19. Suárez López de Vergara RG, Fernandez CG, Hernandez CO, Aguirre-Jaime A, et al. (2013) Environmental tobacco smoke exposure in children and its relationship with the severity of asthma. An Pediatr Barc Spain 78: 35-42.
20. Miller MR, Hankison J, Brusasco V, Burgos F, Casaburi R (2005) Standardisation of spirometry. Eur Respir J 26: 319-338.
21. Criée CP, Sorichter S, Smith HJ, kardos P, Merget R, et al. (2011) Body plethysmography – Its principles and clinical use. Respir Med 105: 959-971.
22. Trabelsi Y, Ben Saad H, Tabka Z, Gharbi N, Buvry AB, et al. (2004) Spirometric Reference Values in Tunisian Children. Respiration 71: 511-518.
23. Gill R, Krishnan S, Dozor AJ (2014) Low-level environmental tobacco smoke exposure and inflammatory biomarkers in children with asthma. J Asthma Off J Assoc Care Asthma 51: 355-359.
24. Haby MM, Peat JK, Woolcock AJ (1994) Effect of passive smoking, asthma, and respiratory infection on lung function in Australian children. Pediatr Pulmonol 18: 323-329.
25. Chen Y, Rennie DC, Lockinger LA, Dosman JA (2005) Environmental tobacco smoke, and pulmonary function in rural children and adolescents: the Humboldt study. J Agric Saf Health 11: 167-173.
26. Labbé G, Merlin E, Kauffman C, Fauquert JL, Heraud MC, et al. (2010) Merlin E, Kauffman C, et al. Intérêt de la mesure des volumes pulmonaires par pléthysmographie corporelle dans le suivi de l'asthme de l'enfant. Rev Mal Respir 27: 42-48.
27. Peroni DG, Piacentini GL, Costella S, Pietrobelli A, Bodini A, et al. (2002) Mite avoidance can reduce air trapping and airway inflammation in allergic asthmatic children. Clin Htmlent Glyphamp Asciiamp Exp Allergy 32: 850-855.
28. de Vasconcelos TB, de Araújo EYR, de Pinho JPM, Saores PMG, Bastos VPD (2016) Effects of passive inhalation of cigarette smoke on structural and functional parameters in the respiratory system of guinea pigs. J Bras Pneumol 42: 333-340.
29. Sorkness RL, Bleecker ER, Busse WW, Calhoun WJ, Castro M, et al. (2008) Lung function in adults with stable but severe asthma: air trapping and incomplete reversal of obstruction with bronchodilation. J Appl Physiol 104: 394-403.
30. Duramad P, Tager IB, Holland NT (2007) Cytokines and other immunological biomarkers in children's environmental health studies. Toxicol Lett 172: 48-59.