HHS Public Access

Author manuscript

Ann Allergy Asthma Immunol. Author manuscript; available in PMC 2021 June 01.

Published in final edited form as:

Ann Allergy Asthma Immunol. 2020 June ; 124(6): 626–627.e1. doi:10.1016/j.anai.2020.03.005.

Exposure to violence, chronic stress, asthma, and bronchodilator response in Puerto Rican children

Jeremy Landeo-Gutierrez, MD[1], **Anna L. Marsland, PhD**[2], **Edna Acosta-Pérez, PhD**[3], **Glorisa Canino, PhD**[3], **Juan C. Celedón, MD, DrPH**[1]

[1]Division of Pulmonary Medicine, Department of Pediatrics, UPMC Children's Hospital of Pittsburgh, University of Pittsburgh, Pittsburgh, Pennsylvania

[2]Department of Psychology, University of Pittsburgh, Pittsburgh, PA

[3]Behavioral Sciences Research Institute, University of Puerto Rico, San Juan, PR

Keywords

violence; stress; asthma; bronchodilator response

Exposure to violence (ETV) and chronic stress may cause or worsen asthma (1). Among Puerto Rican school-aged children, we previously reported that lifetime ETV at the individual or community level is associated with increased risk of asthma (2). In a separate analysis (not accounting for ETV), we showed that high levels of chronic stress are associated with reduced response to short-acting bronchodilators among Puerto Rican children with asthma (3). Based on these findings, we hypothesized that ETV and high chronic stress have joint detrimental effects on asthma and bronchodilator response (BDR). We tested this hypothesis in the same cohort of Puerto Rican children as in our prior studies (2)(3).

Subject recruitment and study procedures have been previously described (4). In brief, 678 children (aged 6 to 14 years) with four Puerto Rican grandparents were recruited from randomly selected households in the metropolitan area of San Juan and Caguas (Puerto Rico) from March 2009 through June 2010, using a multistage probabilistic sampling design. Of the 678 participants, 472 were aged 9 years and older, and thus eligible to complete questionnaires on ETV and chronic stress, along with spirometry. Written parental consent and assent were obtained for participating children. The study was approved by the

Corresponding author: Juan C. Celedón, MD, DrPH, Division of Pediatric Pulmonary Medicine, UPMC Children's Hospital of Pittsburgh, 4401 Penn Avenue, Pittsburgh, PA 15224, Phone: 412.692.8429; Fax 412.692.7636, juan.celedon@chp.edu.

Disclosures of Interest: Dr. Celedón has received research materials from Merck and GSK (inhaled steroids) and Pharmavite (vitamin D and placebo capsules), in order to provide medications free of cost to participants in NIH-funded studies, unrelated to the current work. The other authors have no conflicts of interest to declare.

institutional review boards of the University of Puerto Rico (San Juan, PR), Brigham, and Women's Hospital (Boston, MA), and the University of Pittsburgh (Pittsburgh, PA).

The Checklist of Children's Distress Symptoms (CCDS) (5), a 28-item scale, was administered to participants to assess stress symptoms in the previous six months, as a result of ETV. Answers for each question in the CCDS range from 1 to 5. An overall score is obtained by summing the scores for all 28 questions, and then dividing by the number of questions, so that the final score ranges between 1 and 5 (5). As in previous work, high chronic stress was defined as the upper quartile [≥2.6 points] of the CCDS score (3). Participants also completed a modified version of the ETV Scale (6), which measures both witnessing and direct victimization for five specific events: (a) shoving, punching or kicking; (b) knife attacks; (c) shootings; (d) hearing gunshots; and (e) witnessing verbal abuse of the child's primary caregiver.

Spirometry was conducted with an EasyOne spirometer (NDD Medical Technologies, Andover, MA), following American Thoracic Society recommendations for children (7). The best FEV_1 and FVC values were selected for data analyses. After completing spirometry, subjects were given 200 μg of inhaled albuterol using a spacer, and spirometry was repeated after 15 minutes.

The main aim of this study was to examine whether: 1) high chronic stress modifies the estimated effect of ETV on asthma (defined as physician-diagnosed asthma and ≥1 episode of wheeze in the previous year), and 2) ETV modifies the estimated effects of high chronic stress on BDR. Our outcomes of interest were asthma (as defined above) and BDR ([(post-bronchodilator FEV_1 − prebronchodilator FEV_1)/prebronchodilator FEV_1] × 100) in subjects with asthma.

Bivariate statistical analyses were conducted using the Fisher's exact test for categorical variables, and two-tailed *t* tests for pairs of binary and continuous variables. Logistic or linear regression was used for the multivariable analyses of asthma and BDR. All models included the ETV Scale score and/or high chronic stress, and were adjusted for age, sex, and household income (< vs. ≥$15,000 [near the median income for households in Puerto Rico in 2008–2009]) (8). Other variables considered for inclusion in the models were body mass index (BMI) z-score, and current exposure to second-hand smoke (SHS); such variables remained in the final models if they were associated with the outcome of interest at $P < 0.05$ or if they changed the effect estimate (odds ratio [OR]) by ≥10%. After the final models were built, we tested for an interaction between ETV and chronic stress on asthma or BDR.

Compared with control subjects, subjects with asthma (cases) were younger and more likely to be male and currently exposed to SHS, and to have higher ETV and chronic stress but lower FEV_1 and FEV_1/FVC (Supplementary Table 1). There were no significant differences in BMI Z-score, household income, or BDR between cases and controls.

Models 1 and 2 in Table 1 show the results of the multivariable analysis of ETV, high chronic stress, and asthma. In an analysis adjusting for age, sex, household income, and current exposure to SHS, each one-point increment in the ETV scale was significantly associated with 1.12 times increased odds of asthma (Model 1). After adding high chronic

stress to the model, the ETV scale remained significantly associated with asthma but there was no significant association between high chronic stress and asthma (Model 2). Moreover, there was no significant interaction between ETV and high chronic stress on asthma, either on the multiplicative or additive scale (data not shown). Models 3 and 4 in Table 1 show the results of the multivariable analysis of high chronic stress and BDR. In this analysis, high chronic stress was significantly associated with 4.0% lower BDR (Model 3). In a model additionally adjusted for ETV, high chronic stress remained significantly associated with lower BDR, but there was no significant association between ETV and BDR (Model 4). Moreover, we found no significant interaction between high chronic stress and ETV on BDR, either on an additive or multiplicative scale (data not shown).

We recognize several limitations. First, we cannot assess temporal relationships in this cross-sectional study. Second, we only assessed the child's stress symptoms in the prior six months, and thus cannot exclude an association between persistent pre- and/or post-natal chronic stress and asthma at school age. Third, we have limited statistical power to assess interactions with modest effects. Fourth, lifetime ETV is correlated with poverty and other risk factors for asthma. Although we accounted for household income (a measure of socioeconomic status that is highly correlated with health insurance in our cohort) and current SHS, we cannot exclude confounding by other variables such as access to and adherence with medications. Despite these limitations, our results and prior findings suggest that one potential mechanism for the observed association between current or recent high chronic stress and reduced BDR may be persistent secretion of catecholamines leading to down-regulation of the $ß_2$-adrenergic receptor (3).

To our knowledge, this is the first study to jointly examine ETV and chronic stress in relation to both asthma and BDR in school-aged children. We show that lifetime ETV is associated with asthma, independently of high chronic stress, in Puerto Rican children. Among Puerto Rican children with asthma, we report that high chronic stress is associated with reduced BDR, independently of ETV.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding:

This work was supported by grants HL117191, HL119952, and MD011764 from the U.S National Institutes of Health (NIH). Dr. Landeo-Gutierrez is supported by training grant T32 HL129949 from the U.S. NIH.

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Table 1.

Multivariable analysis of lifetime exposure to violence, chronic stress, and asthma and bronchodilator response

Variables	Asthma				Bronchodilator response[Ψ]			
	Model 1 ETV only		Model 2 ETV + high chronic stress		Model 3 High chronic stress only		Model 4 High chronic stress + ETV	
	Odds ratio (95% confidence interval)	P value	Odds ratio (95% confidence interval)	P value	Beta (standard error)	P value	Beta (Standard Error)	P value
Each 1 point increment in ETV[¥] scale	1.12 (1.02, 1.22)	0.02	1.10 (1.00, 1.22)	0.04	---	---	0.46 (0.34)	0.18
High chronic stress[†]	---	---	1.19 (0.73, 1.94)	0.48	−4.01 (1.47)	<0.01	−4.63 (1.60)	<0.01
Age	0.87 (0.78, 0.96)	<0.01	0.87 (0.78, 0.97)	0.01	0.24 (0.35)	0.49	0.12 (0.36)	0.73
Male sex	1.30 (0.89, 1.91)	0.18	1.31 (0.89, 1.92)	0.17	1.18 (1.32)	0.37	1.09 (1.35)	0.42
Household income (≥$15,000/ year)	0.88 (0.58, 1.32)	0.53	0.87 (0.58, 1.31)	0.50	0.16 (1.41)	0.91	0.22 (1.44)	0.88
Current second-hand smoke exposure	1.40 (0.93, 2.11)	0.10	1.41 (0.94, 2.11)	0.10	1.15 (1.35)	0.39	0.96 (1.39)	0.49

[¥] Exposure to Violence (ETV)

[†] Checklist of Children's Distress Symptoms (CCDS) score in the upper quartile.

[Ψ] In children with asthma.

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