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Association of prescription H1 antihistamine use with obesity: Results from the National Health and Nutrition Examination Survey

Joseph Ratliff[1], **Jessica Barber**[1], **Laura Palmese**[1], **Erin Reutenauer**[1], and **Cenk Tek**[1]
[1]Department of Psychiatry, Yale University School of Medicine, New Haven, CT, United States

Abstract

The incidence of obesity in the US has reached epidemic proportions. Previous research has shown several medications exert noticeable effects on body weight regulation. Histamine 1 (H1) receptor blockers commonly used to alleviate allergy symptoms are known to report weight gain as a possible side effect. Therefore, we investigated the association between prescription H1 antihistamine use and obesity in adults using data from the 2005–2006 National Health and Nutrition Examination Survey (NHANES). Adults taking prescription H1 antihistamines were matched by age and gender with controls; and compared on the basis of body measurements, plasma glucose and insulin concentrations, and lipid levels. Prescription H1 antihistamine users had a significantly higher weight, waist circumference, and insulin concentration than matched controls. The odds ratio (OR) for being overweight was increased in prescription H1 antihistamine users. H1 antihistamine use may contribute to the increased prevalence of obesity and the metabolic syndrome in adults given these medications are also commonly used as over the counter remedies.

Keywords

antihistamine; obesity; weight gain

Introduction

Approximately 68% of adults in the US are currently overweight or obese (1). Body weight is regulated by an intricate system of central and peripheral factors that determine energy intake and energy expenditure. One factor that plays a role in body weight regulation is histamine, a neurotransmitter released by the posterior hypothalamus. Intravascular administration of histamine reduces food intake in animal studies (2), while histamine antagonism stimulates food intake (3). Histamine receptors are divided into four different subclasses, with the histamine-1 (H1) and histamine-3 (H3) receptors expressed abundantly in the brain and implicated in appetite regulation (4). Histamine is also a crucial mediator of inflammation in allergic disease (5). H1 receptor antihistamines such as cetirizine, fexofenadine, and desloratadine are among the most commonly prescribed medications for the treatment of allergies and have been shown to stimulate appetite and weight gain as side effects of treatment (6). This analysis explores the relationship between prescription H1

Corresponding Author: Joseph Ratliff, Ph.D., Yale University School of Medicine, Department of Psychiatry, 34 Park St., Room 10, New Haven, CT 06519, Phone: (203) 974-7845, Fax: (203) 974-7691, joseph.ratliff@yale.edu.

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antihistamine use, obesity, and underlying risk factors in adults using data from the 2005–2006 National Health and Nutrition Examination Survey (NHANES).

Methods and Procedures

Study Population

The NHANES is a program of studies designed to evaluate the health and nutritional status of adults and children in the United States. The data from NHANES are used to assess the prevalence of major diseases and risk factors for diseases. A complete description of NHANES guidelines can be found online at http://www.cdc.gov/nchs/nhanes (7). All subjects provided written informed consent and the protocol was approved by the NCHS Research Ethics Review Board.

The NHANES uses a stratified, probability sampling design with oversampling of individuals thought to be at increased health risk. Weights are provided with the public use dataset so that estimates can be made to provide a nationally representative sample of the civilian, non-institutionalized population of the United States. Eligible persons 16 years or older are interviewed directly and all persons that complete the interview are invited to participate in the Medical Examination component of NHANES.

Prescription H1 antihistamine use

268 adults (174 female and 94 male) reported use of an H1 antihistamine and completed all outcome measure components. 599 age and gender matched controls (401 female and 198 male) were used as a comparison for body measurements, plasma glucose and insulin concentrations, and lipid levels (7).

Body measurements

All participants who attended the medical examination had their weights and heights measured according to a standard protocol. BMI was calculated as weight in kilograms divided by height in meters squared. Waist circumference was measured around the trunk in a horizontal plane just above the uppermost lateral border of the right ilium (7).

Plasma glucose, insulin, and lipids

Fasting plasma glucose concentration was determined by a hexokinase method and plasma insulin concentration was measured using an immunoassay. Fasting total cholesterol, LDL and HDL cholesterol, triglycerides, and apolipoprotein B levels accounted for lipid measurements. A detailed description of the laboratory method is listed on the 2005–2006 NHANES website (7).

Statistical Analysis

The association between prescription H1 antihistamine use with BMI, glucose concentration, insulin concentration, and lipid levels were determined using linear regression. Samples were weighted according to NHANES guidelines (7). Logistic regression was used to determine the odds ratio (OR) for prescription H1 antihistamine users in relation to overweight status (BMI > 25), as well as insulin and glucose concentration, and lipid levels. All analyses were performed using SPSS, version 17.0 for Windows (SPSS Inc., Chicago, IL).

Results

Table 1 shows the comparison of means between prescription H1 antihistamine users (n=268; mean age= 46.9) and adult controls (n= 599; mean age 45.6) on outcome measures associated with weight. The racial composition of the prescription H1 antihistamine users was; 80% Non-Hispanic white, 8% Non-Hispanic black, 8% Hispanic, and 4% other. The racial composition of the control group was; 72% Non-Hispanic white, 10% Non-Hispanic black, 13% Hispanic, and 5% other. The most prevalent H1 antihistamines used were cetirizine (50%) and fexofenadine (37%). After adjusting for gender, prescription H1 antihistamine users had significantly higher weight ($p < .001$), BMI ($p < .001$), waist circumference ($p < .001$), and insulin levels ($p < .005$) compared to healthy controls. There were no differences in fasting glucose levels, total cholesterol, LDL or HDL cholesterol, triglycerides, and apolipoprotein B levels between groups (data not shown). There were no significant differences based on gender or ethnicity for any of the outcome variables.

For both males and females using prescription H1 antihistamines, the odds of being overweight were significantly increased (OR, 1.70; 95% CI, 1.23–2.31 and 1.21; 95% CI, 0.98–1.49), respectively. After adjusting for age and gender, odds of being overweight were significantly increased for prescription H1 antihistamine users (OR, 1.55; 95% CI, 1.04–2.31). However, the OR for a greater waist circumference was not significantly increased (OR, 0.98; 95% CI, .984–1.011). Prescription H1 antihistamine use did not significantly increase the OR for elevated glucose, insulin, or lipid levels and there were no different effects among the antihistamines.

Discussion

We found a relationship between prescription H1 antihistamine use and an increased risk of obesity in US adults over the age of 18. Compared to age and gender matched controls; prescription H1 antihistamine users had significantly greater weight, BMI, waist circumference, and insulin levels.

Atypical antipsychotics with potent H1 antagonistic properties are strongly correlated with weight gain. New generation antipsychotics with high antihistaminic properties such as olanzapine induce weight gain (8). However, the current analysis excluded atypical antipsychotics and focused on H1 antihistamines prescribed for allergy relief. A previous study (9) found an association between obesity and allergy symptoms using the NHANES 2005–2006 dataset in children and adolescents, but did not explore this relationship in adults or the impact of prescription H1 antihistamine use. One possible reason for the increased weight observed with prescription H1 antihistamines may be due to an increased sedation accompanied by their use. While the second generation H1 antihistamines prescribed in this analysis are considered non-sedating, this may be mitigated by other factors. Cetirizine, the most commonly prescribed H1 antihistamine in the sample, is an active metabolite of hydroxizine, an older sedating antihistamine, so it still possesses minor sedative qualities (10). Second, these medications are deemed non-sedating at their prescribed dosage, however, the dosage and usage for these H1 antihistamines was not available for the NHANES 2005–2006 dataset. It is possible that prescription H1 antihistamine use provided some sedation that resulted in decreased energy expenditure and weight gain.

Prescription H1 antihistamine use was also associated with a higher waist circumference and insulin concentration compared to age and gender matched controls. Central obesity is highly associated with increased insulin levels and insulin resistance (11). Additionally, elevated waist circumference is one of the criteria for metabolic syndrome, a cluster of disorders that increase the risk for diabetes and cardiovascular disease. The mechanism

through which histamine modulates insulin function and energy expenditure has not been fully elucidated (12). Histamine promoted glucose uptake in rat, but not human adipocytes (13). In humans, insulin has been shown to up-regulate H1 receptor expression (14). H1 receptor expression is also modulated by leptin levels (15), which become elevated when insulin levels are increased. The 2005–2006 NHANES did not measure leptin levels. Perhaps the weight observed with prescription H1 antihistamine use is related to the disruption of H1 receptor expression and binding leading to impaired insulin and leptin signaling. More research is necessary to determine the extent of histamine's role in energy metabolism.

The OR for being overweight in prescription H1 antihistamine users was 1.55. ORs, as calculated in this study, tend to be an overestimation of the actual relative risk, but provide a worthwhile approximation. Since two-thirds of Americans are overweight or obese, it is crucial to further examine factors associated with weight gain.

Analysis of this nature provides some limitations. First, the analysis was conducted on twice as many women as men. According to the limited sample, the association between prescription H1 antihistamine use and obesity seems stronger in men compared to women so more research should be conducted to investigate this difference. Second, the 2005–2006 NHANES dataset only reports prescription medication use. Several H1 antihistamines are available without a prescription, so the actual number of individuals in the sample taking an H1 antihistamine is unknown. An estimated 50 people in the United States suffer from allergies, with approximately 35–50% of them using over the counter antihistamines, thus this analysis may be underestimating the impact of antihistamines. Since H1 antihistamines are increasingly accessible, they may be contributing to weight gain and increased development of metabolic syndrome. While causation cannot be attributed to prescription H1 antihistamine use only based on this cross-sectional analysis, it is imperative to explore the relationship between increased antihistamine use, obesity, and underlying risk factors.

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Table 1

Distribution of weight, BMI, waist circumference and insulin concentration in H1 antihistamine users and matched controls in adults using NHANES 2005–2006.

Measure	H1 Antagonist	Control	Significance
Weight (kg)			
Males	97.03 ± 24.40	87.52 ± 19.83	.000**
Females	79.96 ± 21.07	75.59 ± 23.82	.037*
BMI (kg)			
Males	30.87 ± 7.57	27.93 ± 5.56	.000**
Females	30.49 ± 7.70	28.75 ± 8.77	.024*
Waist Circumference (cm)			
Males	106.47 ± 15.92	98.49 ± 14.31	.000**
Females	96.81 ± 16.64	93.25 ± 17.90	.028*
Insulin (pmol/L)			
Males	113.52 ± 94.41	64.65 ± 60.23	.000**
Females	66.68 ± 47.58	66.48 ± 64.10	.981

Data are means ± standard deviations

** p<.01

* p<.05

H1, Histamine-1;
n= 268 (174 female, 94 male) for H1 antihistamine users; n= 599 (401 female, 198 male) for control.