International Journal for Pharmaceutical Research Scholars (IJPRS)

V-6, I-4, 2017 ISSN: 2277 - 7873

RESEARCH ARTICLE

Gender Specific Correlation between Obesity and Asthma

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Manuscript No: IJPRS/V6/I4/00088, Received On: 29/12/2017, Accepted On: 03/01/2018

ABSTRACT

The present study was designed to examine 1) whether continuous feeding with a palatable hypercaloric diet and cycling this diet with chow diet would affect the state of asthma or respiratory parameter; and 2) whether gender would be affected by these diet regimens. Male & Female Swiss albino mice were assigned to four groups: control & asthmatic mice fed with chow diet while obese & obese asthmatic mice fed with a palatable Hypercaloric diet, after 8 weeks of the diet, the animals were killed. The hypercaloric diet and food cycles schedules caused similar increases in body weight gain, total serum cholesterol, triglycerides as well as respiratory parameters. While in SOD as antioxidant parameter, its decline with hypercaloric diet intake. The data showed that the continuous intake of a hypercaloric diet for 8 weeks cause obesity and cause asthma or make existing asthma more severe.

KEYWORDS

Hyper Caloric Diet, Mice, Triglycerides, Obesity, Asthma

INTRODUCTION

Asthma is a major respiratory health outcome that is estimated to affect more than 300 million people of all ages worldwide. Epidemiologic study suggests that there is a higher risk of asthma in obese individuals and the reason behind is rapid economic development and urbanization, accompanied by changes in lifestyle, diet and decreased physical activity. In current decades, the prevalence of obesity has increased drastically. Obesity means by more than 30 kg/m^2 BMI. Obesity seems to be associated with a high risk of chronic diseases like diabetes and cardiovascular disease, and thus constitutes a major public health problem.

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Preliminary data suggest that obese patients with asthma demonstrate different asthma phenotypes compared with patients of normal weight.[1] The obese asthma phenotype can be reversed by weight loss with improvements in lung function and by that overall asthma control as well as proper medication utilization. The recent trend systematic review showed strong evidence that obesity precedes the onset of persistence and intensity of the symptoms of asthma in adolescence, but the role of sex is not clear.[2] The primary aim of this pre-clinical animal study is to determine whether gender modifies the association between asthma and obesity or not. However, results of clinical studies from the Genes-environments and Admixture in Latino Americans (GALA II) Study and the Study of African Americans, Asthma, Genes, and Environments (SAGE II) both reported that sex was indeed found to play a role in the relationship between BMI and

asthma but the direction of this difference varied by race.[3]

The mechanism of occurrence asthma in obesity has been widely discussed. Recent opinions have stressed over obesity´s primacy. Enfield et al.[4], explained that obesity and asthma with diabetes mellitus type II as a combination of mechanical and inflammatory effects of obesity. Other factors also contribute to the occurrence of asthma, e.g. Leadbitter et al.[5] found a relationship between fetal growth and the development of asthma and atopic in childhood. Delgado et al.[6] explained the coincidence of asthma and obesity as a result of various effects of high fat mass percentage and/or volume, e.g. reduced pulmonary volumes, diameter of peripheral respiratory airways and the lung's blood volume, as well as the ventilation-perfusion relationship. They also pointed out that the increase in the normal functioning of adipose tissue in the obese leads to a systemic proinflammatory state, which produces a rise in the serum concentrations of several cytokines, the soluble fractions of their receptors, and chemokines (adipokines), e.g. IL-6, IL-10, tumor necrosis factor-α, transforming growth factors-ß1, C-reactive protein, leptin, and decreased adiponectin. They also added that the specific regions of the human genome related to both asthma and obesity have been identified. Gruchala-Niedoszytko et al.[7] summarized with the following conclusions: 1) the associations between obesity and asthma can be not only causal but also accidental, 2) the levels of inflammation markers in obese asthmatics are related to the parameters of obesity, 3) asthma in obese subjects can differ from the obvious phenotype of this disease and their response to standard medication is reduced. Nevertheless, asthma and obesity can have another unknown common cause.[8]

MATERIAL & METHODS

Animals

Healthy female Swiss Albino mice, weighing 20-40 g, procured from Zydus Research Centre, Ahmadabad, India. The animals were housed in standard polypropylene cages in an environmentally controlled clean-air room and maintained under controlled room temperature (22 ± 2 ℃) and humidity (55±5%) with 12:12 h light and dark cycle. All the mice were fed with commercially available normal pellet diet (NPD) and water ad libitum, prior to the dietary manipulation. Hypercaloric diets were given fresh each day and food consumption was measured daily at the same time (9:00–10:00 h.). At the end of the experimental period (8 weeks), all animals were sacrificed by decapitation 24 h[9-10]. The protocol (DDU/FOP/01/2017) was approved by the Institutional (Faculty of Pharmacy, Dharmsinh Desai University, Nadiad) Animal Ethics Committee (IEAC) under the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) before carrying out the project.

Experimental Design

Study Groups: Mice were randomly divided into four groups (Table 1) (n=6)

Table 1: Group distribution

Groups	Details of group	No. of animals
I	Normal control group (Normal pellet diet)	6 male + 6 female
II	Asthmatic group (Ovalbumin induced asthma)	6 male + 6 female
III	Obese group (Hypercaloric diet)	6 male + 6 female
IV	Obese asthmatic group (Ovalbumin treatment followed by hypercaloric diet)	6 male + 6 female
Total		**48**

Induction of Obesity

Table 2: Composition of Hypercaloric diet[11]

Ingredients	Weight in gm	In kJ/g
Normal Pellet diet	300	17.03 kJ/g
Peanuts	200	1.02 kJ/g
Milk chocolate	200	2.35 kJ/g
Sweet biscuits	100	1.00 kJ/g
Total	800	21.4 kJ/g

A dietary fat constituent is rich in Saturated Fatty Acid (SFA). Subsequent Hypercaloric feeding increased adiposity and insulin resistance. All animals except group I (control) and group II (Asthmatic group) were fed with a Hypercaloric diet (Table 2) from day 0 to day 56. On day 57, ovalbumin challenge is given for induction of asthma in all groups expect group I (control). Mice of the control group were kept on normal pellet diet. The induction of obesity was confirmed by measuring the serum triglycerides level and % weight gain on day 56. Mice with 40-45% weight gain from initial were considered as obese and were included for further study.

Induction of Asthma

All the animals of group II and IV were challenged to ovalbumin from day 57 to day 64 (eight days) for induction of asthma. Tidal Volume, Airflow rate & Respiratory rate were measured to confirm the induction of Asthma.[12]

Sampling

Blood sample and tissue specimens (ling tissue) were collected at the end of the experiment on 11th week from all groups. (Control & experimental group)

Blood Samples

Blood samples for serum separation were collected by ocular vein puncture at the end of the experimental period in dry, clean and screw capped tubes and serum were separated by centrifugation at 5000 rpm for 15 minutes. The clean, clear serum was separated and received in dry sterile sample tubes and kept in a deep freeze at -20 °C until used for subsequent biochemical analysis. Parameters like triacylglycerol (TG), total cholesterol, SGPT & SGOT were determined by enzymatic method. (Test kit AUTOSPAN, CHOD-PAPP Enzymatic End Point essay).

Tissue Samples (Lung homogenate)

At the end of the experimental period, the animals were sacrificed by cervical decapitation. The lung was dissected out, quickly removed and were rinsed in ice-cold physiological saline, then blotted between two filter paper and quickly stored in a deep freezer at -20 °C for further biochemical analysis. Briefly lung tissue was subsequently minced into small pieces and 10% homogenate was prepared in cold phosphate buffer (pH 7.4). The homogenate was centrifuged at 1000 x g for 10 min at 4 °C and the supernant was used directly for the determination of SOD.

Biochemical Analysis

Serum total cholesterol (TC), Serum triglycerides (TG), SGPT & SGOT were analyzed.

Statistical Analysis

Values are presented as means ± standard error means. Statistical comparisons were carried out by one-way analysis of variance, in conjunction with Dunnet's test to compare the disease groups with control. The probability of 0.05 was chosen as the significant level (Graphpad prism software).

RESULTS

Protective or degenerative effects of hyper caloric diet on biochemical as well as respiratory parameters in diet induced obesity in male & female Swiss albino mice. The obtained results demonstrated in Table-3 & Table-4 which revealed that administration of hyper caloric diet in male and female mice

Table 3: Effects of Hypercaloric diet on some serum and lung tissue biochemical parameters & Respiratory parameters in male swiss albino mice at the end of experimental period (64 days).

Experimental group / Parameters	Control	Asthma	Obesity	Obese asthma
TG (mg/dl)	125.8 ± 5.28	131.9 ± 3.84*	207.0 ± 6.56*	211.5 ± 5.70*
TC (mg/dl)	181.4 ± 4.02	185.5 ± 3.95*	218.1 ± 2.94*	234.6 ± 3.03*
SGOT (U/dl)	59.7 ± 2.18	60.5 ± 1.94*	69.6 ± 3.31*	79.4 ± 2.61*
SGPT (U/dl)	24.2 ± 1.16	24.5 ± 1.46	30.7 ± 1.21	29.8 ± 2.01
SOD (U/g.tissue)	26.5 ± 1.40	19.1 ± 1.24*	15.4 ± 1.07*	12.5± 0.71*
*significantly alter when compared to control group (P<0.05)				
Experimental group / Parameters	**Control**	**Asthma**	**Obesity**	**Obese asthma**
Tidal Volume	0.14 ± 0.01	0.09 ± 0.00*	0.10 ± 0.00*	0.07 ± 0.00*
Respiratory rate	26.5 ± 0.66	32.5 ± 0.51	30.0 ± 0.33	33.0 ± 0.33
Airflow rate	0.510 ± 0.03	0.263 ± 0.01*	0.339 ± 0.01*	0.202 ± 0.01*

(Data represented with mean ± SEM)

Table 4: Effects of Hypercaloric diet on some serum and lung tissue biochemical parameters & Respiratory parameters in female swiss albino mice at the end of experimental period (64 days)

Experimental group / Parameters	Control	Asthma	Obesity	Obese asthma
TG (mg/dl)	140.7 ± 6.09	142.4 ± 3.62*	213.3 ± 6.14*	222.7 ± 4.56*
TC (mg/dl)	170.4 ± 2.28	182.9 ± 2.89*	204.9 ± 4.25*	236.9 ± 2.96*
SGOT (U/dl)	59.2 ± 1.29	59.9 ± 0.74*	65.4 ± 1.21*	71.4 ± 2.57*
SGPT (U/dl)	26.1 ± 0.62	27.7 ± 0.84	31.0 ± 0.48	32.0 ± 1.04
SOD (U/g.tissue)	25.1 ± 0.52	15.5 ± 0.66*	15.8 ± 0.42*	14.2 ± 0.21*
*significantly alter when compared to control group (P<0.05)				
Experimental group / Parameters	**Control**	**Asthma**	**Obesity**	**Obese asthma**
Tidal Volume	0.13 ± 0.01	0.08 ± 0.00*	0.09 ± 0.00*	0.05 ± 0.00
Respiratory rate	26.5 ± 0.31	32.2 ± 0.44	32.5 ± 0.70	35.0 ± 0.33
Airflow rate	0.491 ± 0.03	0.233 ± 0.01*	0.278 ± 0.01*	0.143 ± 0.01*

(Data represented with mean ± SEM)

significantly increased Total cholesterol, Triglycerides, SGOT & anti-oxidant parameter Superoxide dismutase & no change in SGPT when compared with the normal control group. The same has been observed in respiratory parameters. Respiratory parameter like Tidal Volume & Airflow rate significantly decreased while Respiratory rate significantly increased when compared with the normal control group.

DISCUSSION

The global burden of asthma is high with provenance increasing dramatically in recent decades. Change in dietary habits as well as physical activity contributes to the development of asthma. Evidence suggests that features of a westernized diet such as low antioxidant intake and high saturated fat intake, contribute to an elevated inflammatory state due to activation of the innate immune response. The present study is carried out to check the gender specific issue related hypercaloric diet as well as standardization of diet. Hyper caloric diet feeding allows the characterization of obesity development in vivo experimental model that is pathophysiologically very similar to the obese human[13]. In the present study, the mice of both genders fed with hyper caloric diet for 8 weeks showed obesity, which was associated with significantly increased body weight with the development of dyslipidemia. After 8 weeks asthma was induced by Ovalbumin exposure for 8 consecutive days. At the end of study the body weights, serum total cholesterol (TC), triglycerides, SGPT, SGOT levels as well as respiratory parameters were measured. SOD level was measured as anti-oxidant parameter.

In this study, we observed that Total cholesterol and triglycerides was found to be significantly increased when compared to control while in the case of serum SGOT level fluctuate and found significantly increased when compared to control group. Serum SGPT not affected as such. Interestingly, respiratory parameters like airflow rate and tidal volume was significantly decreased when compared to control group which indicates the breathing pattern changes, indicative of asthmatic state.

The ability of circulating adipokines, which augmented due to hypercaloric feeding, modify lung health is plausible as the development of systemic pro-inflammatory mediators in asthma pathophysiology. This is the first study, to our knowledge to examine the effects of hyper caloric diet, which alters the respiratory pattern and add one segment that obesity may alter the state of asthma or makes existing asthma more severe.[14]

In conclusion, this study has demonstrated that obesity may aggravate asthma or makes existing asthma more severe. Furthermore result also reveals that both genders were prone to obesity with hyper caloric diet & the correlation between reduction in body fat mass and increase physical activity reinforces to improve clinical outcomes in obese asthma state.

ACKNOWLEDGEMENTS

The authors wish to thank Faculty of Pharmacy, Dharmsinh Desai University, Nadiad & K. B. Institute of Pharmaceutical Education & Research, Gandhinagar for their valuable assistance with sample collection, analysis as well as statistical analysis.

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