

Plasma Levels of CA125, CEA, AFP and Cortisol in Obesity

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Abstract

Background: In obesity, modulation of metabolic pathways plays critical roles in the pathogenesis of many diseases. The present study therefore tried to link obesity, metabolic stress and tumor by evaluating the levels of tumor markers and cortisol (a stress-induced hormone) in obesity.

Materials: Thirty-three obese (18 males, 15 females, body mass index= 34 ± 3.8 Kg/m²) and 37 apparently non-obese (19 males, 18 females, body mass index= 22 ± 1.4 Kg/m²) individuals (controls) volunteered to participate in this study. All participants were not on drugs (i.e. alcohol, cigarette or steroids) and were healthy adults without apparent medical problems. Every participant had his/her body weight and height taken, and the body mass index (BMI) calculated before inclusion in the study. Plasma levels of carbohydrate antigen 125 (CA125), carcino-embryonic antigen (CEA), alpha fetoprotein (AFP) and cortisol were determined in these subjects using enzyme linked immunosorbent assay methods.

Results: In the obese subjects, plasma values of CA125 and cortisol increased significantly ($p < 0.05$), when compared with controls. But the plasma levels of CEA and AFP did not show significant ($p > 0.05$) changes in the obese when compared with controls

Conclusion: Metabolic changes could account for the increased rate of synthesis of cortisol and CA125 in obesity.

Keywords: Tumor markers; Cortisol; Obesity

Introduction:

Obesity is a consequence of hypertrophy and hyperplasia of the adipocytes, secondary to factors such as genetic susceptibility [1], endocrine disorders, medications, sedentary life-style, psychiatric illness [2] and the obesogens that enhance fat accumulation in tissues [3-5]. Several stimuli have been implicated in promoting the inflammatory profile associated with obesity [6]. Esposito et al. [7] reported that systemic stress induced by obesity is the cause of an abnormal production of adipokines that contributes to the development of the metabolic syndrome. Such dysfunction could enhance the conversion of inactive cortisone to active cortisol through the expression of 11-beta-hydroxysteroid dehydrogenase type-1 [8]. White adipose tissue-derived adipokines cause modulation of several metabolic pathways which results in metabolic syndrome, inflammation, autoimmune conditions and rheumatic diseases in obesity [9,10]. The hypertrophic-hyperplastic adipocytes also exhibit a lower density of insulin receptors and a higher beta-3 adrenergic receptor, which facilitates the diapedesis of monocytes to visceral adipose stroma, initiating a pro-inflammatory cycle [11].

A common product of chronic inflammation in adipose tissue is higher level of tumor necrotic factor-alpha (TNF- α) [12]. Excess TNF- α in turn may activate tumor progression locus 2 expression by a variety of cell types [13,14]. These may include the tumor specific and

tumor associated antigens which are peptides of tumor-cell proteins (antigens) presented by major histocompatibility complex molecules. Increased expression of the activation marker (i.e. CD11b) on circulating monocytes confirms the existence of chronic inflammation in obese patients [15]. Also, loss of electrons in the mitochondria of these adipocytes results in the formation of superoxide radical that has potential to oxidize other molecules and cause gene mutation [16-18].

Tumor associated antigens may be expressed on the membranes of some normal cells but there is over-expression on membranes of tumor cells which leads to shedding and appearance of the abnormal proteins into the blood [19,20]. The physiological roles of tumor markers on the cell membrane remain unclear. But the associations of obesity with cancer risk have been attributed to alterations or distortion of the normal balance between cell proliferation, differentiation, and apoptosis [21,22]. The tumor specific antigens and tumor associated antigens are therefore associated with tumors and malignancies [23]. Since obesity represents a serious risk factor in several metabolic diseases, identifying the status of plasma cortisol, carbohydrate antigen-125 (CA-125), carcino-embryonic antigen (CEA) and alpha fetoprotein (AFP) would further link obesity, metabolic stress and tumors.

Materials and Methods

Materials

Thirty-three obese individuals and another 37 apparently normal, non-obese individuals (controls) participated in the study. The obese and controls had normal blood pressure and were free from metabolic disorders such as diabetes, liver problems or renal diseases at the time of this study. None of them was on medications (e.g. steroid or hormone supplements), had HIV-infection or hepatitis B infection at the time of this study. Smoking and alcohol consumption were ruled out in all participants. All subjects fasted overnight before blood sampling. Anthropometric measurements which included weight and height were performed. Five (5) ml of fasting blood sample was collected from each participant into lithium heparin bottle, centrifuged and the plasma stored at -20°C until ready for analysis.

Method

Determination of plasma cortisol, CA125, CEA and AFP

Cortisol, CA125, CEA and AFP were determined by using commercially prepared enzyme linked immunosorbent assay (ELISA) reagents (cat. numbers 24, 94K032, 1110010 and 1107029 respectively) by InterMedical S.R.I. Villanica (NA) Italy.

Briefly, an aliquot of the plasma (at room temperature) was incubated with enzyme conjugate (corresponding monoclonal antiserum-antibody conjugated with horseradish peroxidase) in the microtiter wells coated with corresponding monoclonal antibody, directed towards a unique antigenic site of either cortisol, CA125, CEA or AFP. After incubation, the unbound conjugate was washed off, the wells drained and the substrate solution added for color development. Sulphoric acid was later added to stop the reaction. The intensity of the color corresponding to the concentration of the analyte was read at 450 nm with a microplate reader.

Statistical Analysis

Data were expressed as Mean \pm SD. Student's (t) test was used for comparison of fibroid patients and controls. Changes were considered significant when p-values were less than 0.05.

Results

Anthropometric values of the obese and controls are demonstrated in Table 1. The body weight and BMI were significantly ($p < 0.05$) higher in the obese when compared with the controls. The systolic and diastolic blood pressures were similar ($p > 0.05$) in the obese and controls. As shown in Table 2, the mean values of CA125 and cortisol increased significantly ($p < 0.05$) in the obese when compared with the controls, while the mean plasma values of CEA and AFP did not show significant ($p > 0.05$) differences in the obese when compared with the controls.

	N	Body mass (Kg)	Height (M)	BMI	Syst. Press (mmHg)	Diast. Press (mmHg)
Control	37	67 \pm 5.3	1.7 \pm 0.06	22 \pm 1.4	124 \pm 4.8	84 \pm 3.6

Obesity	33	85 \pm 7.5	1.6 \pm 0.08	34 \pm 3.8	126 \pm 8.0	79 \pm 3.3
p-value		<0.01*	>0.02	<0.01*	>0.2	>0.05

Table 1: Physical Characteristics and Blood Pressure of the Obese and Controls. *Value is significantly different from controls. BMI=body mass index. Syst. Press.=Systolic pressure. Diast Press=Diastolic pressure.

	N	CEA (ng/ml)	AFP (ng/ml)	CA125 (ng/ml)	Cortisol (ng/ml)
Controls	37	1.54+0.48	1.8+2.91	22.0+4.1	98.3+32.0
Obesity	33	1.83+1.08	1.2+3.1	27.4+5.6	170.7+81.7
p-values		0.33	0.52	0.003*	0.02*

Table 2: Levels of Tumor markers and cortisol in Obesity and controls. *Value is significantly different from controls.

Discussion

Higher level of cortisol observed in this study agrees with several theories suggesting enhanced cortisol production in the obese. Stewart et al. [8] reported enhanced conversion of inactive cortisone to active cortisol through the expression of 11-beta-hydroxysteroid dehydrogenase type 1 in obesity [8]. In another studies, Tyrka et al. [24] and Anagnostis et al. [25] reported that the derangement of hypothalamic-pituitary-adrenal axis activity in obesity enhances excessive cortisol secretion, and plays a critical role in the pathogenesis of metabolic syndrome and obesity-related disorders. Both human and animal models showed that glucocorticoid secretion in obesity is sensitive to adrenocorticotrophic hormone and stress [26]. Significantly higher level of cortisol observed in this study could be stress induced, in response to abnormal production of adipokines in the obese individuals recruited for this study.

Insignificant changes in the plasma levels of CEA and AFP in this study agree with Stone [27] in a study of the relationship between alpha-fetoprotein and albumin during fetal development, where they observed no relationship between AFP and obesity. The present study contradicts the report of Park et al. [28] who observed that hemodilution effect from increased plasma volume caused decreased CEA concentration in their obese patients. Meanwhile, significantly higher level of CEA had been reported in obesity by Lee et al. [29] and Herbert et al. [30]. The present authors would therefore suggest further investigation by interested workers.

Significantly higher level of CA125 observed in this study seems to link obesity and tumors. This agrees with the previous reports that individuals with a BMI of 30 kg/m² or higher have a 23% higher risk of cancer than non-obese individuals [31]. Perfield et al. [32] reported abnormal expression of tumor progression locus 2 associated with metabolic complications in obesity. Several other studies have associated chronic inflammation and high free radical load in obesity to DNA damage and genomic instability, which may facilitate subsequent progression of cancer cells [33]. Erbağci et al. [34] reported that excess adipose tissue in obesity has positive effect on the expression of CA-125. In the study conducted by Hamdy[12], CA 125 is markedly elevated in obesity and correlated with serum TNF- α ,

IL-6, and sIL-2R/CD25 levels. Bast et al. [35] also stressed that elevated levels of CA 125 is consistently detected in conditions like endometriosis, epithelial ovarian cancer, pancreatic, breast, colon and lung cancers. Disruption of the normal balance between cell proliferation, differentiation, and apoptosis in our obese subjects could therefore account for the significant expression of CA125 observed in this study.

In conclusion, obesity is a metabolic disorder that could enhance the synthesis of cortisol and CA125.

Competing Interests

The authors declare that they have no competing interests.

Authors Contributions

MOA, BOS, AMUA and TOK designed the study, MOA and AMUA did the analysis, and all authors prepared and approved the final manuscript.

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