RESEARCH ARTICLE

Use of Oral Antidiabetic Drugs (Metformin and Pioglitazone) in Diabetic Patients with Breast Cancer: How Does It Effect on Serum Hif-1 Alpha and 8Ohdg Levels?

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Abstract

Objective: The aim was to investigate indicators related to DNA damage and cancer pathogenesis in Type II diabetes cases with breast cancer. It was planned to evaluate the relationship between these markers with oral antidiabetic drugs. Research Design and Methods: Fourty patients and 10 healthy individuals were included in the study. HIF-1α and 8-OHdG are examined in blood samples taken from these individuals with an ELISA Kit. Statistical analysis of data was performed with 95% confidence using Windows package program SPSS 15.0. Results: HIF-1α parameters were found to be meaningfully higher in the patient group than the controls in both pretreatment and posttreatment periods ($p<0.05$). No significant differences in terms of 8-OHdG between patients and controls. However, posttreatment serum HIF-1α ve 8-OHdG levels was found lower than pretreatment levels in patients receiving metformin, but not with pioglitazone. Conversely, serum 8-OHdG levels decreased significantly in these patients. When patients were evaluated according to the treatment groups (pioglitazone vs. metfformin) no significant differences in terms of serum HIF-1α and 8-OHdG levels between treatment groups. Conclusions: HIF-1α levels decreased significantly in the patient group receiving metformin. However, there was no significant difference in terms of HIF-1α levels in the patients receiving pioglitazone.

Keywords: Breast cancer - diabetes - 8-OhdG - HIF-1α levels

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Introduction

Type 2 diabetes is a well-known endocrine and metabolic disorder which has reached epidemic proportions worldwide and represents a serious public health concern. It is estimated that it will affect approximately 366 million people by 2030 (Rathmann et al., 2004). Although the underlying mechanisms of the pathogenesis of Type 2 diabetes still remain to be determined, oxidative stress has been shown to be responsible, at least in part, for the progression of Type 2 diabetes, and supported by increased oxidative damage to lipids and DNA and impaired antioxidative defence systems in these patients (Bonnefont-Rousselot et al., 2000; Rosen et al., 2001). Numerous evidences have indicated that 8-OHdG not only is a biomarker of generalized, cellular oxidative stress but might also be a risk factor for cancer, atherosclerosis and diabetes. The oxidative hydroxylation of guanine in the 8-position is the most frequent and most mutagenic lesion in nuclear DNA. Oxidative damage to DNA, reflected in the formation of 8-OHdG, is important mutagenesis and carcinogenesis (Wu al., 2004). Many authors have examined the relationship between oxidative stress and several diseases such as cancer, obesity, Type 1 diabetes (Bast et al., 2002; Martinez-Outschoorn et al., 2010; Samuni et al., 2010; Van et al., 2010), Type 2 diabetes (Fridly and LE et al., 2006; Arif et al., 2010).

Diabetes and cancer are two heterogeneous, multifactorial, severe, and chronic diseases. Epidemiological studies clearly indicate that the risk of several types of cancer (including pancreas, liver, breast, colorectal, urinary tract, and female reproductive organs) is increased in diabetic patients. Obesity, hyperglycemia, and increased oxidative stress may also contribute to increased cancer risk in diabetes (Paolo et al., 2009).

Diabetes is frequently associated with hypoxia and is known to impair ischemia-induced neovascularisation and other forms of adaptive cell and tissue responses to low oxygen levels. Hyperglycaemia appers to be the driving force of such deregulation. Recent data indicate that destabilisation of HIF-1 is most likely the event that transduces hyperglycaemia into the loss of the cellular response to hypoxia in most diabetic complications (Bento et al., 2011). HIFs are nuclear transcription factors and function as oxygen-sensitive α subunit and β heterodimers (ARNT). All isoforms of HIFα, HIF1α, HIF2α and HIF3α require the ubiquitously expressed subunit aryl hydrocarbon nuclear translocator (ARNT or HIF1β) as

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