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FREE RADICAL ACTIVITY IN PATIENTS WITH TYPE II DIABETES

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ABSTRACT

Background: In people with type 1 diabetes mellitus, free radical activity is a major contributor to vascular problems. However, there is a dearth of information on vascular consequences in type 2 diabetes mellitus.

Objectives: This research evaluated the free radical activity of individuals with type 2 diabetes who had hypertension to those who did not.Supplies and Procedures: Fifty type 2 diabetes outpatients had their blood levels of the lipid peroxidation product MDA (malondialdehyde), the free radical scavenger SOD (superoxide dismutase), and NO (nitric oxide) measured. The diabetic outpatients without hypertension were considered the controls.

Result: Among 50 patients thus studied 18 were hypertensive. The concentration (median (range)) ofboth SOD (20.31(5.33–26.64) vs. 16.65(6.66–22.64) U/dl; $p< 0.05$) and NO (19.54 (11.40–37.07) vs.20.40 (15.69–35.65) U/dl; $p< 0.05$) were reduced in the hypertensive group. Similarly, concentration (median (range) of MDA (354(231–718) vs. 390(256–666)lmoles/dl; $p< 0.01$ were increased in thehypertensive group..

Conclusion: In comparison to healthy controls, we concluded that our study shows a considerable increase in free radical activity in Type II diabetes patients.

Keywords: Superoxide dismutase, Nitric oxide, Malondialdehyde, Type 2 diabetes mellitus and Hypertension.

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INTRODUCTION

The emergence of diabetic vascular problems in individuals with type 1 diabetes has been linked to free radical activity. It has a significant impact on diabetes mellitus-related microvascular and macrovascular complications. There are, however, little data on vascular consequences in type 2 diabetes mellitus. When a person has diabetes, cardiovascular diseases (CVD) are the leading cause of death. This high incidence of CVD is caused by a number of variables, including hypertension. Compared to individuals without diabetes, inpatients with the condition have twice as many cases of hypertension. Additionally, hypertension may be the cause of up to 75% of CVD in those with diabetes, prompting suggestions for more aggressive therapy for those with this disease's hypertension[1].

Increased production of free radicals and subsequent oxidative stress are thought to have a role, at least in part, in the long-term consequences of diabetes. We have tried to summarize the experimental data in this area and highlight the potential significance of oxidative stress in the emergence of diabetic vascular problems in this work.

Any chemical entity with unpaired electrons is considered a free radical. An atom or molecule's chemical reactivity is increased by unpaired electrons. The hydroxyl radical (.0H), super oxide anion (02), transition metals like iron (Fe), copper (Cu), nitric oxide (NO), and peroxynitrite (OONO), and other common examples of free radicals [2]. Free radicals and reactive nonradi-cal species derived from radicals exist in biological cells and tissuesat very low concentrations [3,4]. Halliwell and Gutteridge [3] have identified compounds as antioxidants if they can effectively compete with other oxidizable substrates at very low concentrations, therefore delaying or preventing these substrates from oxidizing. The enzymes SOD, glutathione peroxidase (GPx), and catalase are included in this definition, along with nonenzymatic substances that scavenge reactive oxygen species, such as tocopherol (vitamin E), b-carotene, ascorbic acid (vitamin C), and glutathione.

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MATERIALS AND METHODS

STUDY DESIGN: Cross-sectional study

STUDY DURATION: 1 Year

STUDY POPULATION: The study population for investigating "Free Radical Activity in Patients with Type II Diabetes" will consist of individuals diagnosed with Type II diabetes, selected from a variety of settings such as outpatient diabetes clinics, community health centers, or hospitals. The primary cohort will include adults aged 18 and above who have been clinically diagnosed with Type II diabetes, with stratification based on factors such as duration of diabetes, disease severity, and treatment regimen to capture a comprehensive picture of how free radical activity varies with different stages and management of the disease. To ensure robust and meaningful comparisons, a control group of age-matched, healthy individuals without diabetes will also be included. This control group will help delineate the specific impact of Type II diabetes on free radical activity. Additional subgroups within the diabetic population may be examined based on lifestyle factors, such as smoking or physical activity levels, to assess how these variables influence oxidative stress. By including diverse patient profiles and a healthy control group, the study aims to provide a detailed understanding of free radical activity in relation to Type II diabetes, offering insights that could inform both treatment strategies and preventive measures.

SAMPLE SIZE: 50

Inclusion Criteria

1. **Diagnosis of Type II Diabetes:**
    - Confirmed diagnosis of Type II diabetes mellitus by a healthcare provider, typically with elevated fasting blood glucose levels or HbA1c levels.
2. **Age Range:**
    - Specific age range depending on the study's focus (e.g., adults aged 40-70).
3. **Informed Consent:**
    - Ability and willingness to provide informed consent to participate in the study.
4. **Stable Health Status:**

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- Stable glycemic control (e.g., HbA1c within a certain range) or stable medication regimen, depending on the study's focus on chronic or acute free radical activity.

5. **No Major Complications:**
    - Absence of severe diabetes-related complications that might confound the results (e.g., severe diabetic neuropathy, advanced retinopathy).
6. **Non-smokers or Controlled Smoking Status:**
    - If smoking status is a variable, inclusion criteria might specify non-smokers or controlled smoking status.
7. **Body Mass Index (BMI):**
    - Sometimes, studies might focus on specific BMI ranges if obesity is a factor in the study.

Exclusion Criteria

1. **Type I Diabetes:**
    - Exclude patients with Type I diabetes, as the pathophysiology differs significantly from Type II diabetes.
2. **Significant Acute Illness or Infections:**
    - Exclude individuals with acute illnesses or infections that could influence free radical activity and confound results.
3. **Severe Cardiovascular or Renal Disease:**
    - Exclude individuals with severe cardiovascular or renal conditions that might affect oxidative stress levels and complicate the interpretation of results.
4. **Pregnancy or Lactation:**
    - Exclude pregnant or lactating women due to potential changes in metabolism and oxidative stress during these periods.
5. **Severe Mental Health Disorders:**

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- Exclude individuals with severe mental health conditions that might interfere with their ability to participate in the study or affect biological markers.

6. **Use of Antioxidant Supplements:**
   - Exclude individuals who are taking high-dose antioxidant supplements, as these could alter free radical activity and interfere with the study's outcomes.
7. **Recent Major Surgery:**
   - Exclude individuals who have undergone major surgery recently, as this could influence oxidative stress levels.
8. **Drug or Alcohol Abuse:**
   - Exclude individuals with a history of substance abuse, which can impact oxidative stress and overall health.

RESULT

Parameters	Controls	Hypertensives
Number	32	18
Sex (M/F)	24/7	15/4
Age (In years)	54 (35–65)	51 (40–71)
Wt. (kg)	54 (40–70)	52 (40–71)
Duration of diabetes (years)	4 (0A–14)	3 (0–20)
Fasting plasma glucose (mg/dl)	175 ± 67	223± 84 p< 0.001
Glycosylated Haemoglobin (%)	9.6 ± 1.7	11 ± 2.8 p< 0.001
Mean arterial pressure (mmHg)	97 ± 2	116 ± 6 p< 0.05
MDA (moles/dl)	354 (231–718) p< 0.01, SD ± 55.85	390 (256–666), SD ± 63.34
SOD UB/dl	20.31 (5.33–26.64) SD ± 4.64	16.65 (6.66–22.64) SD ± 4.08 p< 0.05
NO (U/dl)	19.54 (11.40–37.07) SD + 4.34	20.40 (15.69–35.65) SD ± 4.79 p< 0.05

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DISCUSSION

Elevated levels of free radicals produced from oxygen have been linked to the development of vascular problems in individuals with diabetes. By deactivating the eNOS, superoxide anion appears to prevent endothelium-derived nitric oxide-mediated relaxation. The Maillard reaction, a non-enzymatic glycosylation process, inhibits the enzyme superoxide dismutase and increases superoxide generation in a hyperglycemic condition [5]. It has been demonstrated that glycation alters the enzyme's C-terminal end, decreasing its affinity for binding heparin. Therefore, diabetes may decrease the cell surface-attached SOD's defense against extracellular radicals, making endothelium cells more vulnerable to superoxide anion damage.Exogenous SOD supplementation either returns the diabetic aorta to normal or reveals even more acetylcholine-induced relaxation. Therefore, to maintain a healthy contractile response in diabetes settings, normal levels of antioxidant enzymes may be insufficient or may be functionally compromised.[6]

Almost at a diffusion-limited pace, nitric oxide and superoxide anion combine easily to generate oxo-ynitrite (OONO). In physiological settings, the production of OONO and O2 scavengers is negligible.Significant amounts of OONO may be formed under pathologic situations, such as when O2 concentrations are elevated or when O2 scavengers are depleted. Peroxynitrite directly induces oxidation, peroxidation, and nitration of molecules that are vital to biology (such as DNA, lipids, and proteins). In several experimental settings, it is more cytotoxic than NO. [7]

The tyrosine titration is a significant illustration of a reaction brought on by OONO. Endothelial cells' cycloskeletal motions are inhibited by tyrosine nitration, which also modifies the kinetics of cytoskeletal protein formation and disassembly and inhibits tyrosine hydroxylase[7].

Nitric oxide affects lipids in several ways, especially when it comes to the oxidation of low-density lipoproteins (LDLs) in the pathophysiology of atherosclerotic lesions. By preventing

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radical chain propagation and reactions via radical reactivity with lipid peroxyl and alkoxyl groups, NO reduces lipid peroxidation. Because NO is a ligand for iron (and other transition metals), it restricts the production of hydroxyl radicals and iron-dependent electron transfer processes by modifying the peroxidant effects of iron. In macrophage and endothelial cell systems, NO suppresses both OONO- and all-mediated lipoproteinoxidation. On the other hand, low density lipoproteins may oxidize to potentially atherogenic species when NO is driven to generate OONO. OONO is more harmful than NO in a range of experimental conditions, and whether physiologically relevant OONO concentrations will arise in tissues depends on the balance of O2, OONO, and scavenging mechanisms. Therefore, by producing relaxant compounds like NO and constrictor molecules like superoxide, the endothelium appears to influence vascular functions. Future treatments will almost definitely center on superoxide since it may be important in the link between metabolic disorders like diabetes mellitus and cardiovascular illnesses. [7]

CONCLUSION

In comparison to healthy controls, we concluded that our study shows a considerable increase in free radical activity in Type II diabetes patients. Diabetes-related problems such nephropathy, neuropathy, and cardiovascular disease are partly caused by the increased oxidative stress that is seen in these individuals. Our results imply that the development of Type II diabetes and its related problems may be significantly influenced by the elevated production of free radicals.

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