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مقدمه من

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Study of relation between serum IGF-1 level and dementia in Diabetic patients and non Diabetics.

Thesis

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Introduction

Dementia is the loss of mental functions -- such as thinking, memory, and reasoning -- that is severe enough to interfere with a person's daily functioning. Dementia is not a disease itself, but rather a group of symptoms that are caused by various diseases or conditions ***(Engelberg, 2004).***

Vascular dementia and Alzheimer's disease are the most common forms of dementia in old people. Dementia is an enormous and frightening problem, which can only become worse as the average length of human life increases ***(Watanabe et al., 2005).***

Dementia develops when the parts of the brain that are involved with learning, memory, decision-making, and language are affected by one or more of a variety of infections or diseases.Although dementia has always been somewhat common, it has become even more common among the elderly in recent history. It is not clear if this increased frequency of dementia reflects a greater awareness of the symptoms, or if people simply are living longer and thus are more likely to develop dementia in their older age ***(Yamamoto et al., 2005).***

Diabetes is one of the most common metabolic disorders, and its prevalence increases with age. Pathological complications of diabetes affect several organs including the brain, ***(Rita P et al., 2002)***. In addition to somatic and autonomic peripheral diabetic neuropathy, stroke and acute metabolic catastrophes; progressive end-organ damage to the brain is now recognized as a long-term complication of diabetes. This cerebral damage is manifested in impaired cognitive performance and subtle structural cerebral abnormalities. In addition, the risk of dementia is increased. ***(Cukierman T et al., 2005)***

Both type 1 and type 2 diabetes mellitus are associated with cognitive performance impairments. ***(Awad N et al., 2004)***. In type 1 diabetes mellitus this is reflected in a mild to moderate slowing of mental speed and a diminished mental flexibility. In type 2 diabetes cognitive changes mainly affect learning and memory, mental flexibility and mental speed. ***(Allen KV et al., 2004)***

Insulin-like growth factor 1 (IGF-1) is a polypeptide protein hormone similar in molecular structure to insulin. It plays an important role in childhood growth and continues to have anabolic effects in adults ***(*Velcheti, *2006).* Also has an important role** in nervous system homeostasis, including metabolic, neurotrophic, neuromodulatory and neuroendocrine actions ***(Engelberg, 2004).***

IGF-1 is actively transported across the blood brain barrier and possibly produced locally in the brain ***(Schulingkamp et al., 2000).*** It plays a role in brain development and is present in the brain throughout life, where it maintains appropriate neuronal functions and stimulates neuritic growth ***(Engelberg, 2004).***

IGF-1 deficiency may be involved in cognitive deficits seen with aging, especially in neurodegenerative diseases such as Alzheimer's disease ***(Dik et al., 2003).*** It exerts neurotrophic activities in the hippocampus, which is involved in learning and memory. A decrease in IGF-1 may result in the development of neurofibrillary tangles, one of the hallmarks of Alzheimer's disease ***(Gasparini & Xu, 2003).***

Aim of Work

To study the relationship between serum levels of IGF-1 and incidence of dementia in older people.

Subjects and Methods:

- A cross-sectional case-control study will be conducted on 40 subjects, including 30 cases with dementia and 10 non-demented individuals. Participants age 60 years or more attending the inpatient and the outpatient clinic of geriatric department.

Group I "cases"; 30 individuals with a clinical diagnosis of dementia based on clinical history, examination and MMSE test score, with cut off point of 27.
Classified as:

Group I a: 15 demented diabetic patients
Group I b: 15 demented non diabetic patients

Group II "controls"; 10 healthy volunteers' age and sex matched.

- *All participants will be subjected to :*
  a. Full clinical history.

b. Neurological examination and cognitive function assessment
c. Serum (IGF-1) (by ELISA).
d. Fasting and 2h post prandial blood sugar.
e. Liver function tests (serum albumin, SGOT, SGPT).
f. Kidney function tests (serum creatinine).

Exclusion criteria:

1. Alcoholic patients.
2. History of any endocrine disorders except (DM)
3. Chronic liver disease.
4. Kidney dysfunction.

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Mohamed abozeid

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LIST OF ABBREVIATIONS

A1C	Glycosylated hemoglobin
ACE	Angiotensin converting enzyme
AD	Alzheimer's disease
ACS	Acute coronary syndrome
ACTH	Adrenal corticotropic hormone
AGT	Abnormal glucose tolerance
ALS	Acid-labile subunit
AMI	Acute myocardial infarction
APP	Amyloid precursor protien
BCS	British Cardiac Society
BDS	Blessed Dementia scale
BUN	Blood urea nitrogen
CABG	Coronary artery bypass graft
CBD	Corticobasal degeneration
CDR	Clinical dementia rating
CHD	Coronary Heart Disease
CHF	Congestive heart failure
Ck	Creatine kinase

List of abbreviations

CPK	Creatinine Phosphokinase
Cr	Creatinine
CVD	Cardiovascular disease
CHMP2B	Charged multivesicular body protein 2B
CJD	Jakob-creutzfeldt disease
DLP	Dementia with Lewy bodies
DM	Diabetes Mellitus
ECG	Electrocardiogram
FBG	Fasting blood glucose
FSH	Follicle stimulating hormone
FTD	Fronto-temporal dementia
GH	Growth hormone
GHR gene	Growth hormone releasing gene
GHRH	Growth hormone releasing hormone
HTN	Hypertension
ICD-10	International classification of diseases (10^{th} revision)
IGF	Insulin-like growth factor
IGFBP	Insulin-like growth factor binding protein

IGFBP-R	Insulin-like growth factor binding protein receptor
IGF-IR	Insulin-like growth factor-I receptor
IHD	Ischemic heart disease
INR	International normalized ratio
IR	Insulin receptor
IRS	Insulin receptor substrate
ISAR-REACT	Intracoronary stenting and antithrombotic regimen - rapid early action for coronary treatment
MCI	Mild cognitive impairment
MI	Myocardial infarction
MMSE	Mini mental state examination
MW	Molecular weight
NGT	Normal glucose tolerance
NHS	National Health Service
NICTH	Non-Islet cell tumor hypoglycemia
OGTT	Oral glucose tolerance test
PD	Parkinson's disease
PPPG	Post prandial plasma glucose
PI3K	Phosphoinositol 3-kinase

List of abbreviations

po	Oral administration
QALY	Quality adjusted life year
RCT	Randomised controlled trial
REACT	Rescue angioplasty following failed thrombolysis
rh IGF-I	Recombinant human insulin-like growth factor-I
SC	Subcutaneous administration
SD	Standard deviation
SD	Semantic dementia
SERM	Selective estrogen-reuptake modulator
SMK	Smoking
TGF-β	Transforming growth factor- β
VaD	Vascular dementia
WHO	World Health Organisation

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