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Evaluation the Level of Total Fucose and Some Enzymes in The Blood of Patients With Neurological Diseases

Omar M. Hameed [a] , Luay A. Al-Helaly[b]*

[a] *AlNoor University College, Bartella, Iraq*

[b] *Chemistry department, College of science, University of Mosul, Mosul, Iraq*

Abstract

The research included studying of total fucose (TF) and some enzymes in patients with neurological diseases such as Alzheimer's, Epilepsy and Migraine, that may interfere with the level of these enzymes (Fucose dehydrogenase (FDH), Glutathione S-transferase (GST) and Monoamine oxidase-A (MAO-A) that were measured in the male patient group in Mosul city, total samples are (144), male patients (97) and control group (47).

The results showed a significant decrease in TF compared with control group and increase activity of enzymes (fucose dehydrogenase, glutathione S-transferase and monoamine oxidase) in all patients with neurological diseases (Alzheimer's, Epilepsy and Migraine) compared with control group . The study showed the need for TF to perform the body biological functions for neurological diseases, especially with Alzheimer's disease, epilepsy and migraine, respectively. In addition it can use TF as the biochemical marker and an indicator of neurological diseases, especially Alzheimer disease.

*Key words***:** Alzheimer's disease; Epilepsy; Migraine; Total fucose; Fucose dehydrogenase.

Introduction

L - fucose is one of the sugars that the body needs for the ideal communication function from one cell to another, and the (L) shape is the common form of fucose, while the (D) form is the industrial counterpart of fucose and the chemical formula for it is ($C_6H_{12}O_5$) and it is also called 6- Deoxy-L-galactose [1]. When taken orally, it is easily absorbed and has metabolic processes through which it can bind with glycoproteins and glycolipids at different sites in the cell. The cell, as well as the unabsorbed fucose in the intestine, is metabolized by the intestinal bacteria [2]. It has been observed that fucose has a role in treating some diseases such as cancer and some immune diseases [3]. It was found that there are concentrations of fucose at the synapses the neurotransmitter between the nerves, which means that the deficiency of fucose can affect the transmission of nerve signals, as well as it was observed that it is found in the human renal tubules, which indicates need for these sugars for kidney function, it also participates in maintaining skin hydration in the outer layer of it [4]. On the other hand, it has been observed to have a role in immune function [3] as well as an important role in inflammatory diseases and has the ability to suppress allergic skin reactions such as contact dermatitis [5]. In addition, fucose has been used in the treatment of breast cancer through its ability to break down the DNA inside all cancer cells in the treatment [6].

L-fucose dehydrogenase (EC 1.1.1.122) is one of the main enzymes responsible for catabolism of fucose, and it belongs to the group of redox enzymes, as it participates in the transformation of L-fucose into L-fucono-1,5-lactone, in the presence of $NADP^+$, thus producing the coenzyme type NADPH in its reduced form.

The production of NADPH is important in the metabolic pathways (Such as building lipids, including cholesterol) and also has an important role in defense against the toxicity of reactive oxygen species (ROS) by returning glutathione to its reduced form, and have function on thiordoxin and glutathione systems, which are important systems for their role in physiological functions and important antioxidants inside the body [7], as well as interfering

*Corresponding author e-mail: luayhelaly@uomosul.edu.iq.
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with the reactions of removing oxidative compounds with the enzyme glutathione peroxidase and glutathione S-transferase(GST) in addition to that, there are many important functions of GST in humans, including detoxification, stimulation and catalyst for metabolic functions, and its relationship as drug resistance and inhibitory to chronic diseases and cancer [8]. As the GST plays a critical role in alleviating oxidative stress (OS) in all forms of life, the measure of enzyme activity has been widely used as a bio indicator for the detection of oxidative stress, as the central nervous system is very sensitive to the OS process due to low levels or capacities consumption oxygen in high quantities, especially in nerve cells, which makes it more effect to form OS [9] and that this increases the compounds resulting from harmful and toxic oxidative processes, which makes GST enzyme in high quantities and its level rises and that the different levels of this enzyme and its changing functions were studied in several diseases such as Alzheimer's, epilepsy and stroke [10].

The mono amine oxidase-A (MAO-A) has an important adrenaline system and associated with psychological aspect and it also has regulating heart function, as the high level of MAO-A may lead to malfunctions and, damage to nerves and neurotransmitters, and impairment of perceptual awareness [11].

This study aims to estimate of TF, fucose dehydrogenase, glutathione S-transferase, and monoamine oxidase-A for three neurological diseases (Alzheimer's disease, epilepsy and migraine) in Mosul city, and investigate the best biochemical marker for these specific diseases.

Materials and Method

Sample collection:

Serum samples were collected from male patients suffering for Alzheimer's disease, epilepsy and migraine from the Ibn Sina Teaching Hospital in Mosul city, as well as from external laboratories in various locations within the city of Mosul under the supervision of doctors specializing in neurological diseases, for the period between the beginning of July until the end of November for the year 2019, and after recording the required information (age, sex, smoking, alcohol, disease duration, treatment used, are there other diseases), including 97 samples for patients, who were distributed as follows: (23) samples from patients Alzheimer's, (41) samples from epilepsy patients and (33) samples from migraine patients, and (47) samples of healthy people as a control group with ages between 20-72 years.

Venous blood volume (5-6 ml) to obtain serum by placing the blood sample in a dry, clean and tight-fitting plastic tube, and then placed in the water bath at a temperature of (37°C) for ten minutes. After that, I was placed in a centrifuge for 15 minutes at a speed (3000 xg), then the blood serum (Which should be not haemolysis) was withdrawn by a micropipette and divided into three parts in small, dry, clean plastic tubes and kept at a temperature of (-20°C) until it was used to measure the selected biochemical parameters in the study [12].

Measurement methods used for TF and the enzymes selected in the study:

TF was measured by direct interaction of sulfuric acid with blood serum, as the carbohydrates for serum interact with the thiol group (-SH) of sulfuric and the reactants bind with the cysteine and form a colour product, then absorption is measured using a spectrophotometer at wavelengths 396 and 430 nm [13].

Fucose dehydrogenase enzyme was estimated by method used by researchers Horiuchi *et al*. [14], as this method relies on L-fucose oxidation by the L-fucose dehydrogenase (FDH) with $NADP^+$, Which transformed the product into L-fucono-1,5-lactone also produced the coenzyme NADPH in its reduced form, as the amount of NADPH is equivalent of fucose used, and then the absorbance intensity is measured of the solution obtained using a spectrophotometer at a wavelength of 340 nm.

The activity of the glutathione S-transferase (GST) was estimated according to the method used by researchers Habig *et al*. [15], as the GST stimulates the binding of compounds containing electrophilic groups, especially aromatic rings such as compound 1- Chloro-2,4-dinitrobenzene with a thiol group (-SH) for GSH and thus neutralize the electrophilic sites to produce the compound dinitrophenyl thioether and the chlorine ion, and then the absorbance measured using a spectrophotometer at a wavelength of 340 nm.

The researchers' method Buffoni and Blaschko was depended to estimate the activity of the MAO-A enzyme, which depends on the principle of the reaction that works on oxidizing and removing the amine group from the substrate a type of benzylamine, and converting it to benzaldehyde, and then the absorbance is measured at 251 nm [16].

The SPSS-25 statistical program to estimate the mean and standard deviation (SD), and the t-test was chosen to compare two variables and find the difference between the values that appeared through probability and which it occurs at $P \leq 0.05$) a significant difference, and at ($P > 0.05$) a non-significant difference.

Results and discussion

1. Total Fucose:

The results shown in Tables (1), (2) and (3) indicated a significantly low in TF in the blood serum of Alzheimer's, epilepsy and migraine patients compared with the control group at probability level (0.022), (0.046) and (0.005) respectively. The reason may be defect that may occur in catabolism of fucose in patients, as fucose is a sugars associated with proteins or lipids used in the transmission and neurotransmission between different cells, including neurons, and that this imbalance catabolism fucose and affected patients with neurological diseases, may be present in other diseases for example cancer and kidney disease, and also affects immunity [4]. It was found that this decrease in TF levels is identical to a previous study of other diseases in patients suffering from a disorder or over-activity of the thyroid gland[17].

Table 1: Levels of TF and enzymes for Alzheimer's patients compared with the control group.

Measured Parameters	Control group		Alzheimer's patients		(P) value
	Mean	SD	mean	SD	
Age (years)	64.8	3.38	69.1	2.22	0.52
TF (mg / 100mL)	11.01	1.48	5.9	0.91	0.022*
Fucose dehydrogenase (U / L	5.79	0.97	12.27	1.17	0.034*
Glutathione S-transferase (U/ L)	9.34	0.98	15.91	1.82	0.047*
Monoamine oxidase-A (U / L)	54.98	3.99	98.41	4.95	0.037*

* Significant difference at P≤0.05.

Table 2: Levels of TF and enzymes for epilepsy patients and compared with the control group.

Measured Parameters	Control group		Epilepsy patients		(P) value
	Mean	SD	mean	SD	
Age (years)	29.5	5.33	28.1	6.9	0.383
TF (mg / 100mL)	11.55	2.18	6.8	1.1	0.046*
Fucose dehydrogenase (U / L	6.70	0.83	13.91	1.26	0.032*
Glutathione S-transferase (U/ L)	8.34	1.18	11.77	1.35	0.043*
Monoamine oxidase-A (U / L)	47.98	6.99	42.67	7.69	0.643

* Significant difference at P≤0.05

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Table 3: Levels of TF and enzymes for migraine patients and compared with the control group.

Measured Parameters	Control group		Migraine patients		(P) value
	Mean	SD	mean	SD	
Age (years)	29.5	5.33	35.6	6.43	0.577
TF (mg / 100mL)	11.55	2.18	6.68	1.45	0.005*
Fucose dehydrogenase (U / L	6.70	0.83	4.051	1.94	0.029*
Glutathione S-transferase (U/ L)	8.34	1.18	16.97	3.40	0.038*
Monoamine oxidase-A (U / L)	47.98	6.99	132.8	26.16	0.013*

* Significant difference at P≤0.05.

Fucose can in treatment can increase immunity and reduce the incidence of different infections, especially for cancer patients [18]. Hence, TF associated with proteins called fucose-containing glycoproteins, which patients need to increase cell growth in cancerous as oral cancer [18]. No present any studies on fucose with neurological diseases, especially the diseases identified in our current study.

Decreased in the TF may be attributed to its participation as antioxidants to reduce the oxidative compounds. The fucose work to remove oxidation resulting from various diseases [19], Among them, diseases are in our current study, as we will notice later. Fucose has the remove many oxidation compounds, especially those that contain free radicals, as it prevents lipid peroxidation process in blood cells, liver cells and spleen cells, and the fucose is of the type associated with sulfates which polymer is called fucoidan has removing oxidative compounds more than fucose alone as it participates to reduce the oxidant compounds resulting in different metabolic reactions [19-21]. Beside of, fucose,

with sulfate group, participates in many different physiological activities, it has a role as an anti-coagulant and protecting against infections and against viruses, so the fucose may decrease for neurological diseases as consumption for defense and immunological purposes [21].

2. Fucose dehydrogenase (FDH):

The results shown in Tables (1), (2) and (3) indicated that a significant high in FDH of patients for Alzheimer's, epilepsy and migraine compared with the control group at a probability level of (0.034) and (0.032) and (0.029) respectively. Previous study of other diseases in which it was observed high activity in this enzyme in diabetes patients [22], and in cancerous diseases (Breast cancer and oral cancer) [23].

When increase FDH increase NADPH, which is an important enzyme accompaniment for its entry into many different reductive reactions such as lipid-building reactions, including cholesterol, from which many steroid hormones are produced. NADPH coenzyme facilities have role in returning glutathione to its reduced form, and their have role in the functioning of the thiordoxin system and the glutathione system, which are two important systems for physiological and antioxidants inside the body [24], the FDH consumes fucose in high quantities, we have the results of our study that there is a decrease in TF.

TF consumes approximately 20% of all inhaled oxygen as a result of the tremendous demand that it needs in the different metabolism in neurons, since most neurons need ATP[25], and that these mitochondria producing energy it works on the produce many oxidant compounds from H_2O_2 and other oxidant compounds, and therefore it needs antioxidants in high quantities, including the coenzyme (NADPH), which is needed by many antioxidant enzymes, so the FDH produces it in high quantities [26].

Oxidant compounds production in Alzheimer's patients by beta-amyloid (Aβ) involves glial cells that become active and deposition of amyloid plaques. In addition, increased levels of Aβ can accelerate ROS and reactive nitrogen species (RNS) production through direct association with mitochondrial membranes, altering mitochondrial dynamics and function, ultimately leading to abnormal energy metabolism and reduce synaptic function [27]. Of various types, it reducing of harmful compounds in Alzheimer's patients and in preserving mitochondria from destruction.

3. Glutathione S-transferase (GST).

The results shown in Tables (1), (2) and (3) indicated that a significant high in GST in Alzheimer's, epilepsy and migraine patients compared with healthy and at a probability level of (0.047), (0.043) and (0.038), respectively. Previous study that indicated an increase in GST for neurological diseases patients [28].

The GST may be attributed to the increase in oxidation, leading to production of harmful and toxic compounds and increase in GST enzyme to remove these compounds [10].

Besides, the enzyme has removing toxic compounds that enter human or harmful compounds resulting from various oxidative processes, and removing harmful compounds produce from toxic metals such as lead and chromium, which showed to have high and significant levels in all infected patients in neurological diseases [29], which stimulates the GST enzyme for its participation in the removal of toxic compounds by detoxification phase II reactions, and decrease in GSH for patients with neurological diseases [30].

3. Monoamine Oxidase-A (MAO-A):

The results shown in Tables (1), (2) and (3) indicated that significantly high in MAO-A in patients Alzheimer's and migraine compared with the control group at probability levels (0.037) and (0.013) respectively, this is identical to a previous study [31], but a significant decrease in epilepsy patients.

MAO-A type of treatment that is taken for migraine patients as it works to stimulated the MAO-A as a previous study showed that the treatment used is L-5-hydroxytryptophan in migraine patients increases the MAO-A [31], which is used in these patients. The MAO-A enzyme has regulating many neuropsychiatric disorders, as the high activity of the enzyme may defect in the nervous system, damage to nerves and neurotransmitters, and a defect in the perceptual awareness [11]. MAO-A increase in many diseases, for example, hydrocephalus disease in children [32].

In addition, working to reduce of MAO-A, because its harmful effects in various neurological and cancerous diseases [33]. As these inhibitors reduce the oxidant compound (Hydrogen peroxide) and then reduces of oxidation compounds that may be produce the OS [34] as there are many studies aiming to decrease the action of MAO-A by inhibiting its activity as this leads to improved the neurotransmitters and decrease the neurotoxins and improving the functions of mitochondria [35]. MAO-A inhibitors act as antidepressants and anti-anxiety agents, the monoamine oxidase inhibitors are main classes of drugs prescribed for treating depression [36].

Which is done after oxidation of the dopamine, and then hydrogen peroxide is produced

from different oxidant for example hydroxyl radicals (·OH) by Fenton reaction, which subsequently works to lipid peroxidation process, breakdown of the DNA and then cell death. Showed increased in MAO-A in brain tissue, cerebrospinal fluid and in platelets for Alzheimer's patients [37].

MAO-A stimulates remove of amine and oxidation group of monoamine neurotransmitters and neurotransmitters such as dopamine, noradrenaline, serotonin and phenylethylamine, and some other exogenous amines of biologically important [38] the biology role of MAO enzyme defect in this enzyme is effect of a number psychological and neurological disorders, for example schizophrenia, depression, migraine and in people who have used narcotics [39].

Conclusions:

It is concluded from the study must be taken into consideration that consuming quantities of fucose to a reduction of the neurological diseases selected in the study, and the fact use fucose as the biochemical marker for neurological diseases, especially Alzheimer's disease.

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