The role of topical taurine (Bestoxol) drops in improving vision in patients with diabetic retinopathy".

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Abstract

Diabetic retinopathy is not only the major cause of blindness in people with diabetes, but also in working-age adults in the Western world. There are 2 types of diabetic retinopathy: macular edema and degeneration, caused by leaky vessels in the retina; and non-proliferative leading to proliferative retinopathy, caused by the formation of new vessels in ischemic retinal vessels [(1)]. Taurine is believed to play a role in treating a number of conditions, including congestive heart failure, high blood pressure, diabetes, and retinal damage[(2)]. Dietary taurine supplements used to improve the retinal functions, while topical taurine drops (Bestoxol) role in the management of diabetic retinopathy is not well established [(2)]. The aim of this study was to assess the role of topical taurine (Bestoxol) drops in improving vision in patient with diabetic retinopathy. Cross section, randomly selected study involved (100) patients with diabetic retinopathy with different stages, the ophthalmological examination was done including visual acuity assessment pre and post topical BESTOXOL drops usage for one month. The statistical analysis was done with SPSS version 11. The results of study showed that high percentage (64%) of the selected sample mentioned an improvement in the quality of vision on one month usage of topical Bestoxol and most of them describe this improvement as an increasing field of vision. Visual acuity assessment determined that 41% of patients have an improvement in the vision at least one line of Snellens chart, and 23% of patients have different levels of retinal improvement. This study concluded that topical BESTOXOL, which is topical taurine, is a useful drug to be used in diabetic retinopathy patients.

دور القطرات الموضوعية توريين في تحسين الرؤية البصرية لدى مرضى السكري المصابيين بأعتلال اعصاب البصري

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الملخص

عنوان البحث: دور قطرات (BESTOXOL) في تحسين الابصار لدى مرضى اعتلال شبكية العين الناتج عن داء السكري. هدف الدراسة: معرفة دور علاج (BESTOXOL) في تحسين الابصار لدى مرضى اعتلال شبكية العين الناتج عن داء السكري. النتائج: اظهرت النتائج ان نسبة 64% من العينة اكدوا تحسن الابصار لديهم عند استخدام هذه القطرات لمدة شهر بمعدل مرتين يوميا ، كما ان الدراسة اظهرت تحسن الابصار ل 41% من العينة و بمعدل سطر ابصار اضافي حسب Snellens chart. كما ان 23% من المرضى قد شهدوا تحسنا في وضع شبكية العين وبدرجات مختلفة.

Introduction

Diabetes mellitus (DM) long-term complications are progressive and almost resulting by chronic exposure to high blood levels of glucose resulting from defects in insulin metabolism and dysfunction in carbohydrate, lipid and protein metabolism [3]. Retinopathy is characterized by increased vascular permeability, by vascular closure mediated by the formation of new blood vessels -neovascularization, on the retina and posterior surface of the vitreous [4].

Diabetic retinopathy

Diabetic retinopathy is a disease resulting from diabetic chronic hyperglycemia characterized by micro vascular complications in the retina, where neuronal elements responsible for vision are located. It is the main cause of adult blindness in developed countries[5]. The major risk factors for diabetic retinopathy are known to be predominantly the hyperglycemia and the increased duration of diabetes. Other risk factors include hypertension, hyperlipidemia, pregnancy, and micro albuminuria[5]. The initial disease is characterized by increased vascular permeability due to a breakdown in the blood-retinal barrier (BRB), which causes macular edema, with a progressive vascular occlusion and retinal neovascularization [5]. The clinical profile of this condition is chronologically subdivided in two stages, nonproliferative (NPDR) and the proliferative diabetic retinopathy (PDR) [6]. In diabetes, the retina exhibit increased Oxidative stress(OS), since the eye is constantly subjected to light irradiation, atmospheric oxygen, environmental chemicals, and physical abrasion. The retina has also a natural high content of poly unsaturated fatty acid (PUFA) and possess the highest oxygen uptake and glucose oxidation relative to any other tissue, which makes it more susceptible to OS than other organs or structures [7]. Antioxidant defenses are further depleted by other mechanisms, but it is initiated by high glucose levels [7]. In retinopathy, OS has been widely involved in decreased retinal blood flow, increased vascular permeability, disruption of blood retinal barrier and the appearance of cellular capillaries from the apoptotic loss of retinal capillary cells [8]. Oxidative stress creates a vicious cycle of damage to macromolecules by amplifying the production of more ROS and also activates other metabolic pathways that are detrimental to the development of diabetic retinopathy [8]. Treatment with antioxidants is associated with partial restoration of diminished pericytes in retinal vessels in diabetic rats [8]. Well-established antioxidants derived from the diet are vitamins C, E, A, and carotenoids, which have been studied intensively. Vegetables and fruits have in their natural composition other substances besides these antioxidant vitamins which guarantees health benefits associated with its consumption [9]. Antioxidants may act at different levels, inhibiting the formation of ROS or scavenge free radicals, or increase the antioxidants defense enzyme capabilities [9]. Administration of antioxidants to diabetic rats is able to prevent the development of retinopathy and also retinal metabolic abnormalities postulated to be involved in the development of retinopathy [9]. The potential benefit of vitamin E, has been shown in diabetic retinopathy by its free radical scavenger activity outside the cell through nonenzymatic mechanisms [10].Studies in humans suggested that antioxidant therapy with vitamin E and taurine might normalize diabetic retinal hemodynamics[10]. Taurine is a non-essential amino acid produced by the

body through the synthesis of two other amino acids, methionine and cysteine. It is an important component of bile acids, which are used to absorb fats and fat-soluble vitamins. It also regulates heartbeat; maintains the stability of cell membranes; transports calcium in and out of cells; and regulates the activity of brain cells. It is also a potent antioxidant [10]. Normally our bodies manufacture taurine rather than obtain it from natural diet. It is produced by a combination of cysteine, methionine and vitamin C, but low amounts of these substances can in turn lead to taurine deficiency [11]. The many possible functions of taurine are :

(a) neurotransmitter (or neuromodulator) in the CNS.

(b) stabilizer of biological membranes in many tissues.

(c) protector of rod outer segments (ROSS) from exposure to toxic levels of light and chemicals.

(d) modulator of calcium binding and fluxes.

(e) Inhibitor of protein phosphorylation[12].

In recent years taurine function in the retina has centered around 3 possibilities:

(1) Protection of the photoreceptor-based on the shielding effects of taurine on ROSS exposed to light and chemicals.

(2) Regulation of Ca2+ transport-based on the modulatory effects of taurine on Ca2+ fluxes.

(3) Regulation of signal transduction-based on the inhibitory effects of taurine on protein phosphorylation[12].

Taurine is an important antioxidant in the body, and especially high amounts are found in the retina of the eye. Deficiencies of taurine are known to cause retinal lesions and visual deterioration, which can be reversed with dietary taurine [13]. In diabetes, the high extracellular levels of glucose disturb the cellular osmoregulation and sorbitol is formed intracellularly due to the intracellular polyol pathway, which is suspected to be one of the key processes in the development of diabetic late complications and associated cellular dysfunctions. Intracellular accumulation of sorbitol is most likely to cause depletion of other intracellular compounds including osmolytes such as myo-inositol and taurine [14]. When considering the clinical complications in diabetes, several links can be established between altered taurine metabolism and the development of cellular dysfunctions in diabetes which cause the clinical complications observed in diabetes, e.g. retinopathy, neuropathy, nephropathy, cardiomyopathy, platelet aggregation, endothelial dysfunction and atherosclerosis [14]. In a 1975 study, a diet deficient in taurine was associated with retinal degeneration in cats [11]. One of the negative consequences of our "sugar laden" modern diets is the harmful effects of excess fructose. In animals, high fructose diets are known to cause a diabetes-like syndrome and dramatically lower antioxidant levels and glucose tolerance. Supplements of taurine have been shown to effectively counter this in laboratory animals [14]. Taurine works by increasing the action of insulin, improving glucose tolerance and enhancing antioxidant levels which are important functions to balance the negative effects of high sugar diets [14]. The aim of this study was to assess the role of topical taurine (Bestoxol) drops in improving vision in patient with diabetic retinopathy.

Patients and Methods

In this study we estimated one hundred (100) of patients with diabetic retinopathy, in different stages, who admitted to ophthalmology department - in Tikrit Teaching Hospital- for

checking, for diabetic complications, for the period [June 2010- February 2011]. We assess the level of vision with visual acuity and refraction before we prescribe the drug (BESTOXOL). Also, retinal fundoscopy was done for each patient to determine the stage and severity of retinopathy. Then we prescribe the drug and inform the patients to use it three times daily for one month, and after this period (one month), we do another assessment including the previous variables.

Topical taurine (Bestoxol)

-A drug manufactured by world medicine pharmaceutical company .

-composition: each ml contains taurine 0.04g.

-therapeutic indications include eye degenerative disorders, cataract, and open angle glaucoma[14].

Also the patients asked about the change in the quality of vision whether is it same , better or worsen. Regarding the statistical analysis of this study, SPSS version 11 was done to analyses and interpret the data and P value <0.005 considered statistically significant.

Results

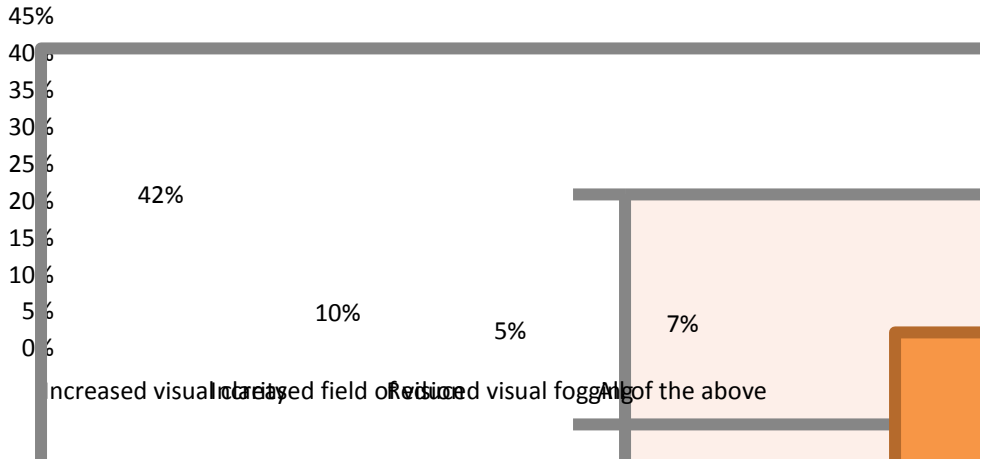
The results showed that 64% of the estimated patients with diabetic retinopathy mention that they have an improvement in the quality of vision on topical BESTOXOL drops, while 36% of those patients didn't feel improvement, (Table1). Regarding the fields of visual improvement , 42% of those patients who mentioned improvement in the quality of vision describe this improvement as an increase visual clarity, 10% as an increase in the field of vision, 5% as reduced visual fogging, and 7% mentioned all the above benefits .(Figure1). The assessment of visual acuity determined that 27% of the selected sample showed an improvement in the vision about 1 line Snellens chart, 9% about two lines improvement, and only 5% have an improvement more than 2 lines (that's mean 41% of the sample gain some degree of visual benefits with topical BESTOXOL) , while 59% with no change in the level of visual acuity .(Figure2). Regarding the fundoscopical changes following topical BESTOXOL, 15% of patients have an improvement in macular oedema, 7% reduced retinal exudate. 1% regression of neovascularization, and 77% no retinal changes. (Table2) .

Table (1):- patients response (regarding visual quality) to topical Bestoxol.

Visual quality	No.	%
Improve	64	64
Not improve	36	36
Total	100	100

Table (2):- fundoscopical findings following one month topical BESTOXOL.

Findings	No.	%
Reduce macular oedema	15	15
Reduce retinal exudates	7	7
Reduce neovascularization	1	1
No change	77	77
Total	100	100



Figure(1): the fields of visual quality improvement.

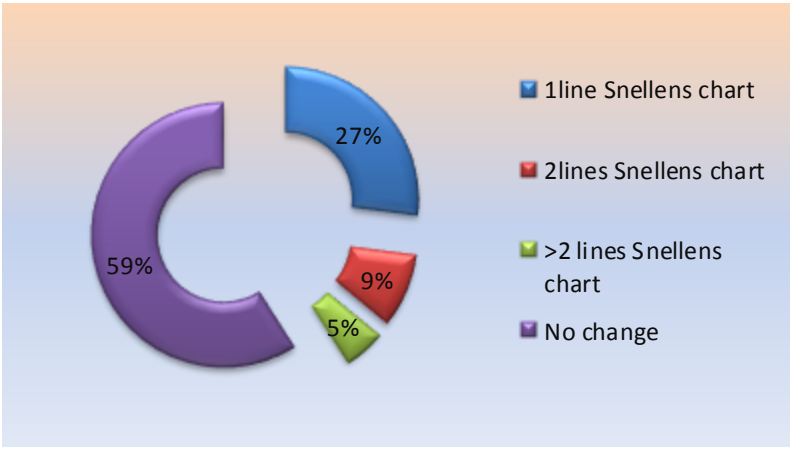


Figure (2): the effects of topical taurine (BESTOXOL) on the level of visual acuity.

Discussion

Retinal photoreceptors sustain one of the highest rates of oxidative metabolism of any tissue in the body and, together with the continuous recycling of their outer segment proportions, require an uninterrupted and rapid supply of blood-borne metabolites.1,2 Nutritional support is provided primarily by the choroidal circulation. The transport pathway between the choroidal capillaries and the outer retina comprises two serially connected compartments, the a cellular Bruch's membrane and the monolayer of retinal pigment epithelial (RPE) cells, the site of the outer blood–retinal barrier[10]. The role of oral taurine in maintaining retinal functions have been discussed by many researches, while the benefits of topical taurine drops (BESTOXOL) in diabetic retinopathy in human eye were not fully discussed previously[12], so that in this study we try to concentrate on these benefits. High percentage (64%) of estimated sample mentioned that they get benefits from topical BESTOXOL after one month of daily 2-3 times

dropping. The main field of improvement of vision was related to visual quality (42%)10% as an increase in the field of vision, 5% as reduced visual fogging, and 7% mentioned all the above benefits, and these changes were significant (p value=<0.005). Significant percentage of the selected patients (41%) developed an improvement in the visual acuity with variable degree of improvement according Snellens chart , and these changes were statistically significant (p value =<0.005). Regarding the fundoscopical changes following topical BESTOXOL usage 23% of patients showed different changes in the retinal picture of diabetic retinopathy, which is statistically significant(p value=<0.005).

Conclusion

The using of topical BESTOXOL is a useful drug in improving vision in patients with diabetic retinopathy, by improving visual acuity and variable degree of improvement of diabetic retinopathy.

Recommendations

The present study recommended to use topical BESTOXOL in patients with diabetic retinopathy, mainly those with early stages to get maximum benefits.

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