

Original Research Article

Association Between Amblyopia and Fundus Ischemic Changes

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Abstract

This study was done in Al- Diwaniah city in Iraq, extended from January 2015-April 2017 and involved 80 patients, among them number of females was higher than males (51 and 29 respectively) and their age range between 45-70 years. Data for the study was collected from the patients attending ophthalmological department in the hospital, out patients and private clinic either for regular checking or sent by their physician to be examined for the presence of ophthalmologic complications, (62) patients among them have combined hypertension and diabetes, (4) patients having only diabetes mellitus, (13) have DM, hypertension and hyperlipidemia and only one have just hypertension, this selected group all have amblyopia unilateral or bilateral; their visual acuities varied from mild to severe and their amblyopia caused by wide ranges of causes mainly refractive error, fundoscopic examination was done to see the association between amblyopia and fundal ischemic changes; the amblyopic eye have delayed awareness regarding ischemia and this affect fundus findings, this idea can be used in future to protect the eye from ischemia by delaying its response to neurological signals that incite cascade of ischemia by using a neuroprotective agents which act on GABAergic neurotransmitters and affect ischemic cascade .

Key Words: amblyopia, fundus ischemia.

العلاقة بين كسل العين الوظيفي واعتلال الشبكية الناتج من الفاقدة الدموية

الخلاصة

اجريت هذه الدراسة في مدينة الديوانية في العراق خلال الفترة من كانون الثاني ٢٠١٥ لغاية نيسان ٢٠١٧، تضمنت (٨٠) مريضاً، منهم (٥١) اناث و(٢٩) ذكور، اعمارهم تراوحت بين ٤٥ - ٧٠ سنة. بيانات هذه الدراسة تم جمعها من المرضى المراجعين في مستشفى الديوانية التعليمي (قسم طب وجراحة العيون) والعيادة الخاصة اما لأعراض المتابعة الدورية او تم ارسالهم من قبل الاطباء في الاختصاصات الاخرى للكشف عن وجود تداعيات الامراض المختلفة على العين وكان تقسيم المرضى كالاتي: داء السكري مع ضغط الدم (٦٢ مريض) وداء السكري فقط (٤ مرضى)، (١٣ مريض) الامراض اعلاه مع زيادة في نسبة دهون الدم و مريض واحد يعاني من ارتفاع ضغط الدم فقط جميع هؤلاء المرضى (المشمولون بالدراسة) يعانون من كسل العين الوظيفي اما في عين واحدة او في كلتا العينين، حدة البصر لديهم تتراوح بين البسيطة الى المتقدمة واسباب الكسل الوظيفي لديهم مختلفة اغلبها اخطاء انكسارية، اجري لهم فحص الحجرة الخلفية للعين ولوحظ انها متأثرة بمضاعفات الامراض اعلاه بنسبة اقل مقارنة بالعين التي لا تعاني من كسل وظيفي وذلك كون العين الكسولة وظيفياً ترتبط بصورة ضعيفة بالدماغ من الناحية الفسلجية.

الكلمات المفتاحية: كسل العين الوظيفي، الفاقدة الدموية.

Introduction

Amblyopia: is a decrease in best corrected visual acuity even with the use of glasses or contact lens, name lazy is inaccurate as the brain is to be blamed [2]. Amblyopia is a functional disorder with no pathology in the eye or visual pathway

but poor visual experience at early childhood abort normal cortical-ocular communication which then lead to this visual problem. It can be classified into: 1) strabismic 2) anisometropic 3) stimulus deprivation 4) bilateral ametropic and 5) meridional amblyopia [1].

There are two aspects of amblyopia; one is reduction of visual acuity of fovea and the other is disturbance of binocular vision, neurophysiologists and clinicians have provided compelling evidence to support their respective cases they thought that lack of adequate control and full communication with brain made considering amblyopia as a resolution term of primary cortical deficit is relatively the most common idea present to the working scene [5]; this is why amblyopic eyes received delayed awareness regarding ischemia as "the brain focus more with better eye".

Neurologic aspects of amblyopia:

1) foveal "sustained" neurons in the retina which provide the basis for the fine spatial discrimination and visual acuity, require well focused stimuli in order to respond effectively. 2) Neural connections require appropriate stimulation during sensitive period of development, for this foveal visual acuity appears to be permanently reduced when foveal sustained neurons don't receive adequate stimulation [9], above physiological criteria support that abnormal visual input at early growth period lead to lack of adequate central neurologic control in the amblyopic eye.

Anatomy: Nerve supply to the eye involve: 1. Optic nerve 2. oculomotor nerve 3. trochlear nerve 4. Abducent nerve 5. Ophthalmic nerves (lacrimal, frontal and nasociliary) 6. Ciliary ganglion: postsynaptic parasympathetic nerve cell bodies [5].

Blood supply to the eye involve: internal carotid artery chiefly via ophthalmic artery and its branches (central retinal artery, supraorbital artery, supratrochlear artery, lacrimal artery, dorsal nasal artery and long and short posterior Ciliary artery [3, 6], this anatomical description for the nerve and blood supply of the eye reveal that blood supply to the eye markedly less than nerve supply which also more differentiated and classified making the eye dependent on nerve supply for well-being and function just like any other organ with little bit more [4].

Ischemia: is inadequate blood supply to a local area due to blockage of blood vessels leading to that area and the most common causes of ischemia are; acute arterial thrombus formation and chronic narrowing

(stenosis) of supplying artery at this time partial pressure of oxygen decrease leading to reduction of mitochondrial respiration and if state of hypoxia is prolonged cellular death will insure, cascade of ischemia summarized by increase calcium influx which when reach to a specific level leading to the release of neurotransmitters "glutamate" which lead to further excitation end with cell death and apoptosis [6, 7] so the modulation of GABAergic transmission and regulation in the brain by the use of neuroprotective factor [8], if introduce to be used in ophthalmology may contribute to the beneficial effects of some neuroprotective agents in future to delay or modulate ischemic cascade.

Materials and Methods:

The study agreed by ethic committee of the hospital, this prospective cohort study design aim to reveal that amblyopic eye doesn't response to ischemic insults as the functionally normal eye due to its delayed awareness for patho-physiological changes occurring in the body; the study conducted in Al-Diwania city in Iraq from January 2015-April 2017, (80) patients involved in the study (51) females and (29) males their age between 40-70 years have systemic diseases like hypertension, diabetes mellitus and hyperlipidemia, all of them complained from amblyopia whether unilateral or bilateral presented to ophthalmology unit to be examined for the presence of fundus ischemic changes.

work up:

1. Adequate inquire about history of ocular trauma, family history regarding any inherited ocular diseases, social history concerning about cultural and economic level and if there is poor vision in early childhood or any previous ophthalmologic insult
2. A careful ophthalmological examination; visual acuity, visual field, anterior and posterior segment examination (fundoscopy).

Statistical analysis: data were analyzed using SPSS version 23. Categorical variables were expressed as number and percent. Chi-square test was used to study association between ischemia and amblyopia. P value was considered significant at ≤ 0.05 .

Results:

Criteria of studied group are explained in the following tables:

Among studied group incidence of bilateral amblyopia is less than unilateral with no difference in etiology for both types.

Table (1): Classification of studied group according to incidence of amblyopia.

Characteristics	Value
Unilateral amblyopia	59 patients(59 eyes)
Bilateral amblyopia	21patients(42 eyes)
Total no. of amblyopic eyes	101
Total no. of patients	80

Table (2): Classification of studied group according to presence of ischemic changes.

Ischemic changes	amblyopic eyes	%	Non-amblyopic eyes	%	P
Present	33(101)	32.7%	48(59)	81.4%	<0.001 HS
Absent	68 (101)	67.3%	11(59)	18.6%	
Total	101		59		

#: percent, P: p value, HS: highly significant.

Incidence of ischemia more with functionally normal eye while amblyopic eyes either not or only mildly affected with ischemic changes. Fundoscopic findings in non-amblyopic eye are more severe and advanced as compare to amblyopic one which may seems to be not affected in some cases or mildly involved;

only in conditions of mild amblyopia the ischemic changes sometimes found to be severe, and these presentations are for both unilateral or bilateral amblyopia and whatever the cause, as shown table 3 a & b.

Table (3): Classification according to signs of ischemia: **a)** for amblyopic eyes.

Signs of ischemia	No. of eyes	%
Null	68	67.3%
Back ground diabetic retinopathy	26	25.7%
Mild macular edema	4	3.96%
Proliferative diabetic retinopathy	2	1.98%
Vitreous heamohrrage	1	0.99%
Total	101	

b) for non-amblyopic eye:

Signs of ischemia	No. of eyes	%
Null	11	18.46%
Macular edema (diffuse, exudative)	18	30.5%
Back ground diabetic retinopathy	7	11.9%
Pre proliferative DR	9	15.3%
Proliferative DR	7	11.9%
Vitreous hemorrhage	2	3.4%
Advanced diabetic eye disease (TRD, glaucoma)	1	1.7%
Venous occlusion (central or branch)	4	6.77%
Total	59	

The most common clinical condition lead to ischemic changes in the fundus is DM and this goes with statistical data offered in ophthalmology sources as this disease mainly hit small size blood vessels which predominant in the retina, DM per it's on can lead to thrombotic changes to occur in the vascular components, other complications

such as hemorrhage, fluid and lipid accumulation, as shown in table 4.

The most common cause of amblyopia is refractive error and the least common one is congenital glaucoma which also associated with more dense amblyopia; visual acuity degree varies from mild to severe.

Table (4): Classification according to systemic disease the patients had.

Disease	No. of patients	%
Diabetes millets (DM)	4	5%
Hypertension + Diabetes millets	62	77.5%
Hyperlipidemia + hypertension + DM	13	16.25%
Hypertension	1	1.25%
Total	80	

Table (5): Classification according to the cause and density of amblyopia.

No. of patients	Cause of amblyopia	Density of amblyopia (visual acuity)
60	Refractive error	6\9 - fingers counting
4	Trauma or infection in early childhood	6\36 - hand movement
3	Congenital cataract	6\24 - hand movement
1	Congenital glaucoma	Fingers Counting – light perception
12	Strabismus	6\12 - fingers counting
Total	80	

Discussion:

The aim of the study is to explain how being amblyopic eye is associated with delayed awareness of neurological and physiological insults accruing in the body comparing with non-amblyopic eye and this can be consider a hint for using neuroprotective agents in future to delay or to decrease the complications of ischemia ;description as follow :during very early childhood adequate neural connection require good visual perception and the amblyopic eye had poor visual acuity [9] so this lead to its insufficient communication with higher brain center [5], the other fact is neurological supply to the eye is larger and more variant in comparison to its blood supply as nerve supply from more than five different nerves with their branches in addition to the sympathetic and para sympathetic supply these as compared to blood supply which is mainly by ophthalmic artery with its branches [4]; criteria support the idea behind delayed awareness of amblyopic eye for ischemia; the whole factors go with insufficient neurological connections that result from inappropriate visual stimulation at early childhood regardless the cause of amblyopia, ischemic cascade which trigger by hypoxia and then improper membrane ion transport (ATPase mechanism) leading to high level Ca^{+2} end with release of excitatory neurotransmitter amino acid "glutamate", then release of free radicals and cell death (apoptosis) [7] any break in this cycle can lead to transient or prolonged protection from ischemia and its blinding complications as many drugs used like afobazole [8] which an anxiolytic agent used to prevent cerebral ischemia (acts on gabanergic receptors), Ca^{+2} channels blocker which used to treat cardiac ischemia and so other drugs. In ophthalmology we trend to treat ischemia with laser (argon or diode) or by using anti-vascular endothelial growth factors like ranibisumab and advanced ischemia may need surgical intervention [10]. These ways are considered as treatment, not as preventive measures and also had no effect on ischemic cycle which can be resumed at any time if the clinical conditions of the patient become worse, in addition to the complications that accompany any modality of treatment which may lead to tissue

damage. From the results obtained we can judge that only in few situations of mild amblyopia the ischemic changes were equivocal to that occurred in non-amblyopic eyes as far as the mild amblyopia still had central brain control which provide it with in formations about body physiologic changes but the conditions is not the same for dense ambloypia which simulated to be isolated from the body systems, what occur in amblyopia resemble to that occurred in pathologic myopia and hereditary fundus dystrophy which are also usually not affected with ischemic changes due to advanced neurodegenerative changes and then decrease complications of ischemia.

Conclusion:

The amblyopic eye had inadequate neurological control because of abnormal visual experience in early childhood this "functional" disability making amblyopic eye respond weakly to body signals regarding any pathophysiological changes occurred inside human body, this idea can open the door for selective neuroprotective agents in future to be used as modulator for abolishing retinal response to ischemia and then prevent its complications which may be blinding in some cases specially in patients with poorly controlled or prolonged systemic diseases.

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