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INTRODUCTION AND AIM OF WORK

Visual impairment among the elderly is a major health problem, the normal function of eye tissues decreases and there is an increased incidence of ocular pathology with age (***Loh and Ogle, 2004)***.

There is strong evidence that the retina degenerates with age, the mechanism behind this phenomenon is a very interesting area for scientific and medical study. Current data support the link between retinal degeneration and increased oxidative stress ***(Militante and Lombardini, 2004).***

Taurineor 2-aminoethanesulfonic acid, is a derivative of cysteine (an amino acid containing a sulfhydryl group). It is widely distributed in animal tissues ***(Carey, 2006).*** Mammalian taurine synthesis occurs in the pancreas via the cysteine sulfinic acid pathway ***(Brosnan and Brosnan, 2006).***In addition, Taurine occurs naturally in food, especially in seafood and meat. Nowadays, Taurine is regularly used as an ingredient in energy

drinks***(Wójcik, Koenig, Zeleniuch-Jacquotte, Costa and Chen, 2010).***

Taurine has been shown to be tissue protective in many models of oxidant-induced injury ***(Yu, Chen, Wei, Qianyong, Jihuan and Mantian, 2007)***, it is essential for cardiovascular function, development and function of skeletal muscle, and health or integrity of the retina and the central nervous system ***(Huxtable, 1992).***Taurine supplementation is possibly beneficial for the prevention of atherosclerosis and coronary heart disease***(Zhang, Bi, Fang, Kuwamori and Kagamimori, 2004)***. Moreover, in a study on diabetic rats, there was evidence that taurine may exert a beneficial effect in preventing diabetic nephropathy***(Verzola, Bertolotto, Villaggio, Ottonello, Dallegri, Frumento, Berruti and Gandolfo, 2002).***

Taurine is an essential component for the maintenance of retinal structure and function in the rat ***(Ishikawa, Shiono, Ishiguro and Tamai, 1996)***. Possible functions for taurine in the retina include protection of the photoreceptors, regulation of Ca^{2+} transport and regulation of signal transduction ***(Lombardini, 1991)***.

Taurine is present at high levels in the retina of many vertebrates. In the rat retina, taurine comprises more than 50% of the total amino acids, specifically in the photoreceptor layer, which is the light-sensitive cell layer of the retina. Taurine has been considered an essential component in the development and maintenance of retinal form and function. In experimental models, taurine deficiency has been demonstrated to result in visual dysfunction and cellular damage to the retina ***(Militante and Lombardini, 2002).***

Age-related deficiency in retinal levels of taurine may contribute to the retinal degeneration associated with age ***(Militante and Lombardini, 2004).*** So, it became the aim of the present work to study the alterations in the retinal structure with age, and to investigate the possible role of taurine in the treatment of senile retinal changes.

REVIEW OF LITERATURE

Normal Anatomy and Histology of the Retina

1. Anatomical structure of the eye

The eye is an organ specialized for the detection and analysis of light. It is a fluid chamber enclosed by three layers of tissue. The outermost layer consists of cornea, limbus and sclera, the middle layer; the uveal tract, includes the iris, ciliary body and choroid, and the innermost eyeball layer is the retina that works as a computer that receives inputs from 100 million photodetectors. This portion of the nervous system processes the light information and transmits it to the brain via the optic nerve which exits the eyeball from its posterior pole. The retina detects light and sends it to the brain, but not as a simple point-by-point representation of the image. In the retina, complex processes are carried out before sending the information to superior centers ***(Khurana, 2009).***

2. Embryology of the retina

The retina is derived from an evagination of the anterior cephalic vesicle (prosencephalon), the optic vesicle, which comes

into contact with the surface ectoderm. In adult, the ectoderm gives rise to a thin membrane called the pigment epithelium while the optical or functioning part of the retina is derived from the optic vesicle ***(Thomas, 2012).***

3. Functional histology of the retina

Visual perception is a sensory process initiated at the retina, and completed in the cerebral cortex. Two main functions are currently performed by the retina: 1) the initial conversion of light energy into electric signals, phototransduction, which is carried out by photoreceptors; 2) a series of physiological processes performed by retinal interneurons in order to encode the different attributes of the visual stimuli in electrical signals. The basic system of retinal information processing consists on a direct pathway of visual information that flows from photoreceptors to bipolar cells to ganglion cells. The ganglion cells fire action potentials in response to light, and these impulses propagate down the optic nerve to the projection nuclei in the brain. This direct pathway is influenced by two transverse fluxes of modulatory signals coming from horizontal in outer plexiform layer and amacrine cells in inner plexiform layer. Horizontal cells receive input from the photoreceptors and project their processes laterally to influence surrounding bipolar cells. Amacrine cells receive

input from bipolar cells and project their processes laterally to influence surrounding bipolar and ganglion cells. Both, horizontal and amacrine cells usually make electrical and chemical synapses with neighbor cells of the same type ***(Germain, Pérez-Rico and Vicente, 2010).***

4. Retinal structure: layers and cells

Vertebrate retina is one of histological complex tissue which consists of multiple layers, formed by different types of nerve cells of different morphology and is specialized for processing of visual information.It is known to contain approximately 55 separate neuronal types ***(Masland, 2001).***

They are organized in four layers; i. the photoreceptor layer, containing photoreceptor outer and inner segments, ii. the outer nuclear layer, containing the photoreceptor nuclei, iii. the inner nuclear layer, containing diverse kinds of information processing neurons and iv. the ganglion cell layer (GCL), containing ganglion and displaced amacrine cells ***(Nag and Wadhwa, 2012).***

These neurons make synaptic connections in two separate layers, the outer plexiform layer (OPL), where photoreceptor, horizontal and bipolar cells are interconnected, and the inner plexiform layer (IPL), where the processes of amacrine and bipolar cells make synapses with ganglion cell dendrites ***(Nag and Wadhwa, 2012).***

The mammalian retina, like that of other vertebrates, is constructed of 10 different layers ***(Csillag, 2005),*** they are arranged as follows:

Layer (1):The pigmented epithelial layer (RPE): This is a single layer of closely packed cells, which are hexagonal in shape. Their base is opposed to the Bruch's membrane and participates in its formation while the apical part is thrown into long cytoplasmic processes engulfing the outer segments of rods and cones. These pigment cells are connected by tight junctions ***(Csillag, 2005).*** The retinal pigmented epithelium performs a number of important physiological functions, including transport of nutrients to photoreceptors, phagocytosis of shed photoreceptor outer segment discs and regeneration of the visual cycle photopigment ***(Holtkamp, Kijlstra, Peek and de Vos, 2001; andStrauss, 2005).***

The pigmented epithelial layer is separated from the choroid by Bruch's membrane. The latter is responsible for supplying nutrients to photoreceptors via the RPE basal infoldings and the apical processes ***(Nag and Whadhwa, 2012).***

Layer (2): The photoreceptor layer: It contains the rods and cones. Rods are long and slender, whereas cones have a more bulky shape. Both rods and cones consist of inner and outer segments. The inner segment is rich in glycogen and has a remarkable accumulation of mitochondria which is related to the production of energy necessary for the visual process and protein synthesis. The rest of the outer segment is packed with stacks of flattened double lamellae (discs), which are generated by invagination of the plasma membrane ***(Csillag, 2005).***

Layer (3): The outer limiting membrane: It is the expanded outer extremity of a neuroglial cell known as Muller cell. It consists of a series of zonulae adherents, which are formed between photoreceptor outer fibers and Muller cell processes, and occasionally between two adjacent Muller cell processes ***(Omri, Omri, Savoldelli, Jonet, Thillaye-Goldenberg, Thuret, Gain, Jeanny, Crisanti and Behar-Cohen, 2010).***

Layer (4): The outer nuclear layer: This zone is composed of the cell bodies of the rods and cones and it is about the same thickness in central and peripheral retina. However in the periphery, the rod cell bodies outnumber the cone cell bodies while the reverse is true for central retina ***(Snodderly,Weinhaus and Choi, 1992***). Cones are adapted to photopic conditions, permitting the perception of color. Conversely, rods are sensitive to dim monochromatic light, allowing night vision ***(Bonnel, Mohand-Said and Sahel, 2003).***

Layer (5): The outer plexiform layer: It is the synaptic connections between the rod and cone segments (axons) and the dendrites of bipolar ganglion cells. It is well visible by silver staining and appeared as a homogenous pink zone in Hx&E preparations. The photoreceptor synaptic terminals are aligned in one to two rows in the outer plexiform layer. The terminals possess synaptic ribbons, vesicles and mitochondria. They form synapses with bipolar and horizontal cells in triads, in which a bipolar cell dendrite is sandwiched between two horizontal cell processes in the invaginated terminals ***(Stone, Van Driel, Valter, Rees and Provis, 2008).***

Layer (6): The inner nuclear layer: This zone comprises fewer rows than the nuclei of the rods and cones. It consists of three classes of neurons (horizontal, bipolar and amacrine cells) and one class of macroglial cells; Muller cells ***(Nag and Wadhwa, 2012).***

Layer (7): The inner plexiform layer: Amacrine cell processes synapse with bipolar cell axon terminals and dendrites of ganglion cells ***(Nag and Wadhwa, 2012)***.

Layer (8): The ganglion cell layer: It is a discontinuous layer of large neurons. Muller cell processes, microglia and astrocytes are present also in this layer and surround the blood vessels present therein ***(Nag and Wadhwa, 2012).***

Layer (9): The optic nerve fiber layer: It consists of the non-myelinated axons of the ganglion cell. The axons form bundles, course towards the optic disc and leave the eyeballs to form the optic nerve ***(Nag and Wadhwa, 2012).***

Layer (10): The inner limiting membrane: This is formed by joining of the adjacent Muller cell end feet, and to some extent by astrocyte processes. It is involved in fluid transfer between the retina and vitreous ***(Savige, Liu, DeBuc, Handa, Hageman, Wang, Parkin, Vote, Fassett, Sarks and Colville, 2010).***

Moreover, it was proclaimed that mammalian retina shows almost same characteristics in all species. Both human and rat retina consist of the same ten histological layers ***(Hofstetter, Suckow and Hickman, 2005).*** Similarities in the physiology and cell biology of retina in humans and rats make rats a valuable model to study. Also, they are small enough to allow for the use of statistically sample sizes ***(Bonilha, 2008).***

Blood supply of the retina:

The outer retinal layers, including the photoreceptors, are avascular and, like the peripheral avascular retinal area, receive their metabolic energy from the choroid (***Pournaras, Rungger-Brandle, Riva, Hardarson and Stefansson, 2008***). On the other hand, the inner retinal layers are supplied by the central retinal artery, which enters the optic disc through the lamina cribrosa,

where it branches into four principal intra-retinal arteries. Whilst termed retinal arteries, even the central retinal artery is only of a caliber of an arteriole and if accurate terminology is used, only retinal arterioles exist, not arteries ***(Kur, Newman and Chan-Ling, 2012).***

The venous system of the retina has a similar arrangement to the arterial supply. The central retinal venule is leaving the eye through the optic disc to drain venous blood into the cavernous sinus ***(Kur, et al., 2012).***