



Effect of Omega-3 on Intraocular Pressure

Authors

Uloneme G. C^{1*}, Ozims S. J.², Eberendu, I. F.³, Akukwu, D.¹, Akogu, A. O.³

¹Department of Anatomy & Neurobiology, Imo State University, Owerri, Nigeria

²Department of Optometry, Imo State University Owerri, Nigeria

³Department of Public Health, Imo State University Owerri, Nigeria

Corresponding Author

Uloneme G. C

Department of Anatomy & Neurobiology, Imo State University, Owerri, Nigeria

Email: ulokaima3@gmail.com

ABSTRACT

The study investigated the effect of Omega-3 preparation (countering Omega-3 fatty acids) on the oculo-visual health of rabbits, with emphasis on the intraocular pressure. The experimental animals were separated into two groups of 'A' (which was control) and 'B' with group 'A' being subdivided into R₁, R₂, R₃ and group 'B' subdivided into R₄, R₅ and R₆. The twelve rabbits that constituted groups 'A' and 'B', respectively were fed liberally and medically tended to in the course of the experimentation. Group 'A' rabbits (control) received no Omega-3 capsules, but were placed on placebo while the group 'B' rabbits were treated with Omega-3 capsules, each rabbit receiving 1500mg of the preparation daily (500mg in the morning, afternoon and evening respectively) for five days. The intraocular pressure of the animals was monitored and measured once a day before the oral administration of the Omega-3 preparation, and likewise the control group on placebo. It was observed that while the intraocular pressure of the control group animals (Group A) remained fairly constant, being confined between 15.73mmHg and 15.23mmHg from day 1 to day 5, the intraocular pressure of the group 'B' animals treated with the omega-3 capsules widely vacillated from 17.00mmHg on day 1, to 9.17mmHg on day 5, giving a 46% decrease in intraocular pressure on the last day of experimentation (day5).

KEYWORDS: Omega-3, Fatty Acid, Intraocular Pressure, Rabbit, Glaucoma

INTRODUCTION

Over the years, the roles of different nutrients in the prevention of certain diseases and sustenance of good and quality health have been elucidated. While the role of nutrition in coronary heart disease seems to have been centre stage, the effects of nutrient deficiencies on other organs are also critical. A diet rich in vitamins and trace minerals is essential for example, good vision.

Vitamin A and pro-vitamin A, for example also, play essential roles in the proper functioning of the eye and the prevention of diseases like age-related glaucoma, cataract, retinopathy, degeneration and even glaucoma. Recent studies are also highlighting the roles and importance of nutrients like zinc, selenium, vitamin E and omega-3 in the sustenance and maintenance of the eye integrity. It is worth knowing that every cell

in our body is composed of the fat we consume, and this calls for the reason why we should get the right type of fat in a balanced proportion to maintain an optimal health.

The polyunsaturated fatty acids (PUFAs) are the fatty acids mainly used for body building, and they are called essential because they are necessary for our day to day living, but cannot be synthesized in the body¹. We therefore need a regular supply of these essential fatty acids in our diet, as they form the frame work of the human cell membranes². Omega-3 and Omega-6 are the two families of the polyunsaturated essential fatty acids. Omega-3 fatty acids (also called ω -3 fatty acids or n-3 fatty acid include alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and docosapentaenoic acid (DPA). These Omega-3 acid components can be found in nuts, canola oil, green vegetables, fish, eggs, milk, and in animals fed partly on linseed (Boute)³. Researchers have also discovered that very little of alpha-linolenic acid found in plants are converted to the major omega-3 (eicosapentaenoic acid and docosahexaenoic acid).

However, the three types of Omega-3 fatty acids involved in human physiology are alpha-linolenic acid (ALA), found mainly in plant oils, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), both commonly found in marine oils). Marine algae and phytoplankton are primary sources of omega-3 fatty acids, and common sources of plant oils containing the omega-3 ALA fatty acid include walnut, edible seeds, clary sage seed oil, algal oil, flaxseed oil, sacha inchi oil, Echium oil, and hemp oil, while sources of animal omega-3 EPA and DHA fatty acids include fish oils, egg oil, squid oils, and krill oil^{4,5}.

Generally, omega-3 fatty acids are considered to be very important for normal metabolism⁶ although scientist have asserted that the ability to make the longer-chain omega-3 fatty acids from ALA may be impaired in aging^{7,8}.

In as much as evidence does not support a beneficial role for omega-3 fatty acid

supplementation in preventing cardiovascular disease (including myocardial infarction and sudden cardiac death or stroke⁹, omega-3 fatty acid supplementation greater than one gramme daily for at least a year may be protective against cardiac death, sudden death, myocardial infarction¹⁰, and also needed for the development of the brain and normal functioning of some ocular tissues such as the retina. Patients with retinitis pigmentosa have therefore in some occasions been reported to have a low blood level of DHA¹¹, while evidence also suggests that omega-3 fatty acids modestly lower blood pressure (intraocular pressure inclusive) in people with hypertension and in people with normal blood pressure¹², other evidence suggests that people with certain circulatory problems, such as varicose veins, may benefit from the consumption of EPA and DHA, which may stimulate blood circulation and increase the breakdown of fibrin, a protein involved in blood clotting and scar formation^{13,14}.

The polyunsaturated fatty acids (PUFAs) form part of the structure of cell membranes which constitute barriers with highly selective permeability. These membranes which are involved in energy transformation processes regulate information flow between cells and contain receptors sensitive to external stimuli¹⁵.

Again, the outer membrane of the human cell which acts as a gateway allowing raw materials in, and the processed materials out, requires a constant turnover of polyunsaturated fatty acids to remain functional. Omega-3 has been found to be an essential part of the replenishment as shortage of omega-3 has been shown to reduce the ability of the cells (ocular cells inclusive) to efficiently perform their function, leading to nutrient starvation and some ocular disorders.

The conversion of ALA to EPA, and further to DHA in humans has been reported to be limited, but varies with individuals¹⁶. Goyens et al, however, argue that it is the absolute amount of ALA, rather than the ratio of omega-3 and omega-6 fatty acids, that controls the conversion efficiency¹⁷.

The usefulness of the omega-3 fatty acids has been so stressed that the Canadian Food Inspection Agency has recognized the importance of DHA omega-3 and makes the following claim for DHA: "DHA, an omega-3 fatty acid, supports the normal physical development of the brain, eyes, and nerves primarily in children¹⁸. The declaration was so made because feeding of infants with formula devoid of omega-3 fatty acids resulted in lack of deposition of DHA in their visual and neural tissues with adverse effects in vision and nervous systems¹⁹, and according to Connor, the signs of omega-3 deficiency in infancy are subtle, as it may result in impaired vision, abnormalities on the electroretinogram, hyperactivity and some other ocular disturbances relating to the intraocular pressure which the eye needs to maintain for proper functioning²⁰. The level of the intraocular pressure (IOP) was used in the past to define and diagnose glaucoma. But in recent times it has been observed that many individuals with glaucomatous optic nerve damage lack elevation of the intraocular pressure, and so, intraocular pressure is now seen as one of the many risk factors for the development of optic nerve damage. Its measurement involves the use of two basic techniques, - contact tonometry (through indentation or applanation on the cornea) and non-contact tonometry (which flattens the cornea through air puff).

However, transpalpebral tonometry which is a recent development has been introduced, and it measures the intraocular pressure (IOP) through the eyelid. The intraocular pressure in most individuals ranges between 10mmHg to 20.5 mmHg, with an average of approximately 16mmHg²¹. However, the New American Committee on Standardization of tonometers of 1954 declared IOP of 22mmHg to 23mmHg as pathological; and 20mmHg to 21mmHg as suspicious and may be a precursor to the development of glaucoma²².

It is believed that the components inflating the eyeball to its shape are the vitreous humor which has a fixed volume and the aqueous humour which has a variable volume, and whose volume

determines the intraocular pressure of the eye. A sustained increased intraocular pressure (glaucoma) can be a devastating disease often leading to visual impairment and blindness. Its management is most times, directed to lowering the existing intraocular pressure and this can be accompanied either pharmacologically or by increasing aqueous outflow. The miotic agents generally bring about lowered intraocular pressure, and also reduce uveoscleral outflow facility as well as produce a simultaneous increase in trabecular outflow, the net effect being a decrease in the intraocular pressure. The mydiatric agents, on the other hand, usually produce an increase in intraocular pressure, especially in eyes with shallow anterior chambers and narrow anterior chamber angles. A recent study conducted by Nguyen et al on the effect of dietary omega-3 fatty acid intake with age and on intraocular pressure showed that the animals raised on omega-3 fatty acid had a 13% decrease in intraocular pressure at forty weeks of age. When the intraocular pressure was again determined relative to forty five weeks of age, same animals showed a 23% decrease in intraocular pressure. This lower intraocular pressure of the animals administered omega-3 fatty acid rich diet was said to be associated with a significant increase in outflow facility, and a decrease in ocular rigidity²³. Interestingly, the omega-3 fatty acid fed animals also showed a 3.3 times increase in ciliary body docosahexaenoic acid (DHA), with an insignificant change in arachidonic acid (AA), which has a significant implication for intraocular pressure regulation. Nguyen et al was of the view that the increased aqueous facility in the animals could be due to either higher levels of DHA metabolites, leading to the lowering of the intraocular pressure, or the shift towards anti-inflammatory omega-3 products and against pro-inflammatory omega-6 eicosanoids action in concert to reduce any intraocular pressure elevating inflammatory tendency. In agreement with this report, Ren et al²³ observed that open angle glaucoma patients have reduced blood level of docosahexaenoic acid (DHA) and

eicosapentaenoic acid (EPA). Being a major structural lipid of retinal photoreceptors in the outer segment membranes, its biophysical and biochemical properties may affect photoreceptor membrane functions by altering permeability, fluidity, thickness and lipid phase properties, meaning that tissue DHA status affects retinal cell-signaling mechanisms involved in phototransaction. EPA, a substrate for DHA, is considered to be the parent fatty acid for a family of eicosanoids that have the potential to affect arachidonic acid (AA), which are derived eicosanoids implicated in abnormal retinal neurovascularization, vascular permeability, and there has been a consistent evidence to suggest that omega-3 long-chain polyunsaturated fatty acids (LCPUFAs) may act in a protective role against ischaemia, inflammatory and age-related pathology of the vascular and neural retina²⁴.

It is based on the afore stated result oriented works and observations that this work is fashioned to study the effect of omega-3 on the oculo-visual health of rabbits, especially the intraocular pressure (IOP).

MATERIALS AND METHOD

The locally bred rabbits weighing between 1.2 to 1.7 kg used for this study procured from a rabbitary in Owerri, Imo State were subjected to examination by a veterinary doctor who ascertained their health status and body fitness for the experiment. The three month old rabbits were fed ad libitum and were properly tended to during the experimentation that took place in the animal house of the Anatomy and Neurobiology Department of Imo State University, Owerri. Prior to the research investigation proper, each of the rabbits was examined with a pentorch to rule out presence of any disease, especially within the external parts of the eye. A test of direct papillary reflex was also done with the use of pentorch to ascertain the effectiveness of the visual pathway. Again, since ophthalmoscopy could not be carried out on the animals, a shadow test using a pentorch directed at an angle of 90⁰ to the line of sight was done to check the nature of the anterior chamber

(whether deep or shallow). These investigations were all done to rule out any abnormality on the pupil and or the anterior chamber which could affect the intraocular pressure of the eye. The rabbits were then separated into two groups identified as 'A' and 'B' respectively. The animals in group is 'A' served as the control, while the group 'B' animals were subjected to treatment with omega-3 capsules. The group 'A' rabbits were again divided into subgroups captioned R₁, R₂, and R₃, even as those in group 'B' were also shared into R₄, R₅, and R₆, sub-groups. Each of the group 'B' rabbits was made to consume 1500mg of omega-3 fatty acid (3 capsules of omega-3) daily, with a capsule administered by 8.00am, 1.00pm and 6.00pm respectively all through oral intubation. The intraocular pressure of the rabbits were then measured once daily at every twenty four hours interval before administering the drug throughout the experimentation period.

The Schiotz indentation tonometer was then used to determine the intraocular pressure of the rabbits after anaesthetizing them with primax (0.5% proparacaine hydrochloride) solution for about 1.5 minutes prior to indentation. Same procedure was also carried out on the control group animals that received only distilled water for five days. There was a three-time repetition of the intraocular pressure measurement in each case, and the mean was recorded to reduce error.

RESULTS**Table 1:** Values of the intraocular pressure (IOP) of control group

	R₁ (IOP) (mmHg)	R₂(100) (mmHg)	R₃ (IOP) (mmHg)
Initial IOP (mmHg)	18.50	15.60	13.10
Day 1	18.50	15.60	14.30
Day 2	17.00	15.60	14.30
Day 3	18.50	14.30	14.30
Day 4	18.50	15.60	14.30
Day 5	17.00	15.60	13.10

Table 2: Values of the Intraocular Pressure (IOP) of the Rabbits Treated with Omega-3 Capsules

	R₄ (IOP) (mmHg)	R₅(IOP) (mmHg)	R₆ (IOP) (mmHg)
Initial IOP (mmHg)	18.50	17.00	15.60
Day 1	18.50	17.00	15.60
Day 2	14.30	14.30	13.10
Day 3	13.10	12.00	10.90
Day 4	10.90	10.00	7.50
Day 5	10.00	10.00	7.50

Table 3: Comparing the IOP Mean Values for Control and Treated Rabbits

	CONTROL (IOP) (mmHg)	TREATED (IOP) (mmHg)
Initial IOP (mmHg)	15.70	17.00
Day 1	16.13	17.00
Day 2	15.63	13.90
Day 3	15.70	12.00
Day 4	16.13	9.47
Day 5	15.23	9.17

DISCUSSION

Essentially, this study focused on the effect of omega-3 on the intraocular pressure of rabbits, and therefore, was able to unravel the association between dietary Omega-3 and glaucoma (increased intraocular pressure). The results showed that the intraocular pressure in the control group (group A) remained relatively constant within the entire period of experimentation (see table 3) when juxtaposed with that of the group treated with omega-3 capsules. The experimental animals (group 'B'), however, showed a significant decrease in intraocular pressure starting from day 2 to day 4, with 46% reduction

in intraocular pressure on day 5 (table 3), the intraocular pressure having depreciated from 17.00mmHg in day1 to 13.90mmHg in day 2, and descending to 12.00mmHg on day 3, and then inclining to 9.47mmHg and 9.17mmHg on day 4 and day5, respectively. There is, therefore, evidence that omega-3 is of great benefit in lowering or correcting increased intraocular pressure that could cause vision loss. A further scientific explanation to this assertion was provided by Kulkarni et al, who reported that omega-3 produces metabolites that increase aqueous outflow, the eicosanoids and the docosanoids in particular, which are known to

modulate fluid dynamics and the inflammatory response²⁵. The results of this study is also in strong agreement with the reports of Ren et al²³, that there was a decreased omega-3 fatty acid levels in glaucoma patients compared with their health siblings, and have concluded that a lower level of omega-3 consumption was associated with increased glaucoma prevalence.

CONCLUSION

From the results of this study, it could be concluded that omega-3, containing omega-3 fatty acids causes a reduction in the intraocular pressure (IOP) of rabbits, which is probably due to increased aqueous outflow facility and a shift towards anti-inflammation. This same result can be expected in the human eye since rabbits and human have similar oculo-visual physiological constitution.

REFERENCES

1. Van West, Dirk, Maes, Michael (2003). "Polyunsaturated Fatty acids in Depression". *Acta Neuropsychiatrica* 15(1):15-21.
2. "Related Terms". Omega-3 Fatty Acids, Fish Oil, Alpha-Linolenic Acid. Mayo Clinic Retrieved June 20, 2012.
3. Azcona, J. O., Schana, Schana, M. J., Garcia, P. T., Gallinger, C., R. Ayerza, and Coates, W. (2008). "Omega-3 enriched broiler meat. The influence of dietary alpha-linolenic omega-3 fatty acid sources on growth, performance and meat fatty acid composition". *Canadian Journal of Animal Science* 88(2): 257-269.
4. Rizos EC, Ntzani EE, Bika E, Kostapanos MS, Elisaf MS (September 2012) "Association Between Omega-3 Fatty Acid Supplementation and Risk of Major Cardiovascular Disease Events. A Systemic Review and Meta-analysis" *JAMA* 308(10): 1024-1033.
5. Maclean CH, Newberry SJ, Mojica WA, Khanna P, Issa AM, Suttorp MJ, Lim YW, Traina SB, Huton L, Garland R, Mortonsc (2006-01-25), "Effects of Omega-3 Fatty Acids on cancer risk: a systematic review". *JAMA: the journal of the American Medical Association* 295(4): 403-15.
6. Omega-3 Fatty Acids and Health: Fact Sheet for Health, Office of Dietary Supplements 2005 Retrieved 12 April 2014.
7. Freemantle E, Vandal M, Tremblay-Mercier J, Tremblays, Blachere JC, Begin ME, Brenna JT, Windust A, Cunnane SC (2006). "Omega-3 Fatty Acids, energy substrates, and brain function during aging". *Prostaglandins, Leukotrienes and Essential Fatty acids* 75 (3): 213-220.
8. Gao F, Taha AY, Ma K, Chana L. Kiesewetter D, Rapport SI (2012). "Aging Decreases rate of docosahexaenoic acid synthesis secretion from circulating unesterified & linolenic acid by rat liver". *AGE* 35(3): 597-508.
9. Kwaksm, Myung SK, Lee YJ, Seo HG (2012-04-09). Efficiency of Omega-3 Fatty Acid Supplements (Eicosapentaenoic Acid and Docosahexaenoic Acid) in the Secondary Prevention of Cardiovascular Disease: A Meta – analysis of Randomized, Double-blind, Placebo-controlled Trials". *Archives of Internal Medicine* 172(9): 686-94.
10. Casula M, Soranna D, Catapano AL, Corrao G, (August 2013). "Long-Term effect of high dose omega-3 fatty acid supplementation for secondary prevention of cardiovascular outcomes: A meta-analysis of randomized, placebo-controlled trials (corrected) Atherosclerosis. *Supplements* 14(2):243-51.
11. Miller PE, Van Elswyk M, Alexander DD (July 2014). "Long-Chain Omega-3 Fatty Acids eicosapentaenoic acid and docosahexaenoic acid and blood pressure a meta-analysis of randomized controlled

- trials". American Journal of Hypertension 27(7): 885-96.
12. Moris MC, Sacks F, Rosner B (1993). "Does fish oil lower blood pressure? A meta-analysis of controlled trials". Circulation 88(2): 523-533.
 13. Mori TA, Bao DQ, Burke V, Puddey IB, Beilin LJ (1993). "Docosahexaenoic acid but not eicosapentaenoic acid lowers ambulatory blood pressure and heart rate in humans" Hypertension 34(2): 253-260.
 14. Omega State University Micronutrient Information Centre: Essential Fatty Acids Metabolism and Bioavailability <http://ipioregonstate.edu/infocentre/otehrn uts/omega3fa/#metabolism>.
 15. Goyens PL, Spilker ME, Zock PL, Katan MB, Mensink RP (1 July 2006) "Conversion of Alpha-linolenic acid in humans is influenced by the absolute amounts of alpha-linolenic acid and linolenic acid in the diet and not by their ratio". American Journal of Clinical Nutrition 84(1): 44-53 PMID 16825680.
 16. Canadian Food Inspection Agency Acceptable nutrient function claims Accessed 30 April 2015
 17. Connor, W. E. (2000): Omega-3 Deficiency and Common Diseases; American Journal of Clinical Nutrition, Vol.71, 171-175.
 18. Khurana, A.K (1998). Anatomy and physiology of the eye.CBS Publishers India.P.470.
 19. Irving, B.M (1970). Clinical refraction.3rd edition professional press roots fair field publication. New York P.487.
 20. Nguyen BD, Aboh KL, Potempa K, Kobor MS, Archambault J, Greenblatt J, Lagault P, Omichinski JG. Complex containing the TFIIIF subunit RAP74 and the RNA polymerase II Carboxy-terminal domain phosphatase FCPI. Proc.Natl Acad sci USA 100 (10):5688-93.
 21. Ren, H, Magulike, N., Ghebremeskel, K., Crawford, M. (2006): Primary Open-angle glaucoma patients have reduced levels of blood docosahexaenoic acid and eicosapentaenoic acids. Institute of E. Publication, Vol.74: 157-163.
 22. www.sciencedirect.com/science/omega-3
 23. Kulkarni, P. S., Srinivasan, B. D. (1989). Cyclooxygenase and Lipoxygenase Pathways in anterior uvea and conjunctiva: Investigative Ophthalmology and visual science; Vol. 3/2:39-52.