

## **Macular Degeneration, Carbon Dioxide and Hyperventilation.**

### **"Carbon Dioxide May Improve Vision in AMD Patients by Dan Roberts April 2002**

AMD patients are benefitting from a new combination drug therapy being tested at the University of Texas Health Science Center at San Antonio (UTHSC). The therapy involves a combination of medicines which includes carbon dioxide, an element which dilates the blood vessels in the retina for the maintenance of proper blood flow. William E. Sponsel, M.D., associate professor and director of research in the department of ophthalmology at UTHSC, maintains that it is the diminished circulation of these vessels that can cause the photoreceptor cells to deteriorate, leading to macular degeneration and loss of central vision.

With certain combinations of chemicals called "carbonic anhydrase inhibitors" (CAI) given as eye drops, Dr. Sponsel is "tricking" the eye into maintaining its carbon dioxide while supplying important nutrients. As a result, he reports that 60

of 65 patients have shown "dramatically" improved vision, no matter whether their vision loss was a result of AMD or glaucoma. Dr. Sponsel says that the results "bode well for treatment of these disorders in the future."

Of course, I was very interested in this intention of Dr. Sponsel of "tricking the eye into maintaining its carbon dioxide" (the first and best way to achieve this result would appear to be avoiding CO<sub>2</sub> loss by avoiding hyperventilation!); I intensified my search and I found a few more interesting articles. In the website of the UT Health Science Center-San Antonio, where Dr. Sponsel is working, I found this:

#### **"Subjects seeing better after use of CO<sub>2</sub>-enhancing drug(2-22-02)**

Eye redness was the clue that something was happening to Celia Ramirez's vision. Although she wasn't having trouble driving or doing other tasks, her children urged her to have a checkup. It turned out she was in the early stages of age-related macular degeneration

(AMD), a disease that attacks a person's central field of vision..... her central vision continued to deteriorate. Her specialist is William E. Sponsel, M.D., associate professor and director of research in the department of ophthalmology at The University of Texas Health Science Center at San Antonio (UTHSC). Dr. Sponsel's research led him to prescribe treatment with new combinations of medications.

"These last two medicines he's had me on, they have really worked," Mrs. Ramirez said. "We've done a lot of praying. This is somewhat of a miracle." The miracle involves carbon dioxide, which is crucial for vision. The healthy eye produces enough carbon dioxide to dilate blood vessels around the retina and maintain proper blood flow. The ailing eye does not produce enough. This holds important implications for the treatment of patients with blinding eye diseases such as AMD and glaucoma, which are marked by diminished circulation of blood in the back of the eye. Eye pressure also is a conventional barometer of eye health. About 60 of 65 patients have seen their vision improve while receiving treatment at UTHSC's teaching hospital, University Hospital..... *The miracle agents are called "carbonic anhydrase inhibitors" (CAI's). Given as eyedrops, CAI's reach the back of the eye rapidly and slow the clearance of carbon dioxide while increasing the supply of nutrients. They help dilate blood vessels within and behind the retina, which is the structure that receives, processes and transmits visual images relayed from the brain.*

Dr. Sponsel pursued this line of research in an intriguing way — *after discovering that adults who hyperventilated and rapidly blew off their body's carbon dioxide showed decreased vision, eye pressure and circulation in the back of the eye.* He was treating subjects one week with a CAI called dorzolamide and the next week with placebo eyedrops. During hyperventilation, the subjects on dorzolamide maintained good light sensitivity in their central field of vision, while the same subjects during placebo treatment showed central visual loss....."

In the following article there is a more recent study that confirms the favourable effect of carbonic anhydrase inhibitors on the blood flow in the eye:

**"Acta Ophthalmologica Scandinavica. 82(6):730-737, December 2004.**

**Januleviciene, I. 1; Harris, A. 2; Kagemann, L. 2; Siesky, B. 2; McCranor, L. 2**

Abstract:

Purpose: To evaluate the effects of dorzolamide/timolol fixed combination (D/T) compared to latanoprost on intraocular pressure (IOP) and pulsatile ocular blood flow (POBF) in primary open-angle glaucoma (POAG) patients.

Methods: Thirty patients with POAG were randomized in an open-label, cross-over study. Intraocular pressure reduction was achieved by 4 weeks medical therapy with D/T twice daily or latanoprost 0.005% dosed once in the evening. During a 4-week run-in and a 4-week wash-out period between study arms, patients ceased use of all other glaucoma medications and used timolol maleate 0.5% twice daily. Primary efficacy variables were IOP and POBF.

Results:.....Repeated measures ANOVA detected significant changes in POBF with treatment ( $p = 0.0361$ ). Dorzolamide/timolol fixed combination statistically significantly increased pulse volume by  $0.767 \mu\text{l}$  ( $p = 0.0087$ ), while latanoprost therapy had no significant effect ( $p = 0.2407$ ).

Conclusions: Both drugs had similar effects in terms of IOP reduction. Dorzolamide/timolol significantly increased pulse volume while latanoprost had no effect....."

And here an Italian study on the benefits of Carbonic anhydrase inhibitors also for other problems, through their "*physiological function related to respiration and transport of CO<sub>2</sub>/HCO<sub>3</sub>*:"

**"Carbonic anhydrase inhibitors and their therapeutic potential. Claudiu T Supuran, Andrea Scozzafava**

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Carbonic anhydrases (CAs, EC 4.2.1.1) are wide-spread zinc enzymes, present in archaeo- and eubacteria, algae, green plants and animals. Within these organisms CAs are encoded by three distinct, evolutionarily unrelated gene families: the  $\alpha$ -CA, the  $\beta$ -CA and the  $\gamma$ -CA families, respectively. These enzymes are very efficient catalysts for the reversible hydration of CO<sub>2</sub> to bicarbonate.....

sulphonamide CA inhibitors (CAIs) are useful as diuretics, or in the treatment and prevention of a variety of diseases such as glaucoma, epilepsy, congestive heart failure, mountain sickness, gastric and duodenal ulcers, neurological disorders and osteoporosis among others, as well as diagnostic tools. Their applications are due to the wide distribution of the different  $\alpha$ -CA isozymes (14 are presently known) in higher vertebrates, where they play important physiological functions related to respiration and transport of CO<sub>2</sub>/HCO<sub>3</sub> between metabolising tissues and the lungs, pH and CO<sub>2</sub> homeostasis, electrolyte secretion in a variety of tissues/organs, and biosynthetic reactions, such as gluconeogenesis and ureagenesis, among others. CA activators have recently been described and their mechanism of action at molecular level elucidated. Such agents might be useful for developing therapies for the CA deficiency syndrome."

And finally, *one more recent study that refers to the "vasoconstriction during acute hyperventilation-induced hypocapnia"*, which can be avoided by Dorzolamide. "Topical dorzolamide increases pericentral visual function in age-related maculopathy: pilot study findings with short-wavelength automated perimetry.

**Acta Ophthalmologica Scandinavica. 83(2):154-160, April 2005. Remky, Andreas 1; Weber, Anke 1; Arend, Oliver 1; Sponsel, William Eric 2**

Abstract:

Purpose: Numerous studies have confirmed the enhancement of ocular circulation by carbonic anhydrase inhibitors (CAIs). Topical CAI treatment with dorzolamide averts the significant pericentral visual function loss accompanying retinal and choroidal vasoconstriction during acute hyperventilation-induced hypocapnia. This study was designed to discern whether dorzolamide might similarly enhance macular function in patients with age-related maculopathy (ARM).....

Conclusions: This study demonstrated a significant increase in short-wavelength sensitivity in ARM with dorzolamide and the lack thereof with placebo. These encouraging pilot study data suggest a potential role for topical CAIs in ARM patients, and establish objective parameters for prospective studies to further evaluate the effects of dorzolamide in ARM. Copyright (C) 2005 Blackwell Publishing Ltd." Even if Dr.Sponsel and the Scandinavian doctors do not *reach the conclusion that one of the first*

*things to do would seem to be to avoid "hyperventilation-hypocapnia" by cessation of hyperventilation, I think it is very positive that the damage done by hyperventilation is once more confirmed, especially in a field as important as that of preventing visual loss."*