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Central Nervous System Agents in Medicinal Chemistry, **2019**, *19*, **1-8**

CASE REPORT

The Role of Melanin to Dissociate Oxygen from Water to Treat Retinopathy of Prematurity

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ARTICLE HISTORY

Received: April 03, 2019
Revised: June 14, 2019
Accepted: June 17, 2019

DOI:
10.2174/1871524919666190702164206

Abstract: ***Background*:** Retinopathy of prematurity (ROP) is a potentially blinding disorder that commonly afflicts premature infants who are born prior to 31weeks of gestation or with a body weight less than 1250 grams (about 2.75 pounds). Another risk factor is excessive oxygen in incubators, which can lead to blindness. A compounding factor is that survival rates for premature infants are rising with concomitantly more cases of ROP.

We have reported an unsuspected intrinsic property of melanin to dissociate water. This capability can be considered an alternative treatment option for adult and neonatal diseases. It is known that exogenous surfactant administration suppresses bronchopulmonary dysplasia and consequent death, randomized, controlled trials with various respiratory interventions did not show any significant reductions in morbidity and mortality rates.

During a descriptive study about the three leading causes of blindness in the world, the ability of melanin to transform light energy into chemical energy through the dissociation of water molecule was unraveled. Initially, during 2 or 3 years; we tried to link together our findings with the widely accepted metabolic pathways already described in molecular pathway databases, which have been developed to collect and organize the current knowledge on metabolism scattered across a multitude of scientific evidence.

***Observations*:** The current report demonstrates the main problems that afflict premature babies with an emphasis on the growth of abnormal vessels in the retina, the explanation for which is unknown until date. We also reported a case of a baby who suffered digestive and respiratory problems with a brain haemorrhage that was successfully treated by laser photocoagulation. We hypothesise that most likely this effect was due to the melanin level and melanin itself produces oxygen *via* dissociating with water molecules.

***Conclusion*:** We postulate that the intrinsic effect of melanin may easily convert visible and invisible light into chemical energy *via* a water dissociation reaction similar to the one in plant's chlorophyll, and markedly elevated with diagnosis and treatment of the complications related to premature babies.

Keywords: Energy, hydrogen, melanin, oxygen and prematurity, retinal detachment.

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1871-5249/19 $58.00+.00

1. INTRODUCTION

Historically, most births -premature or full term- have taken place at home or otherwise under conditions that increase susceptibility to sudden death and other maladies. Mortality and morbidity rates in premature infants swiftly climb with a lack of medical care [1].

Medical care for premature infants has achieved gratifying reductions in mortality and morbidity. A notable example is recognition that control of body temperature enhances survival. This finding led to the invention of the infant incubator, an idea derived from the chicken egg hatchery [2]. By 1835, the Russian von Ruehl developed the first incubator for infants. Concomitantly, Dr. Stephane Tarnier's from the Paris Maternity Hospital worked on isolates that could keep premature infants in warmer conditions. The infants that were kept in the incubators at 4°C warmer than the regular body temperature had a better chance of survival compared to the control infants. Nevertheless, it took many years before being these practices became a part of regular medical care of premature infants. For example, until the mid-1960s, premature infants were deemed normal when they had body temperatures lower than typical full-term infants [3]. This finding is startling in that concepts for the treatment of premature infants had been studied since the 1800s [4, 5].

Warm conditions were essential. But the common use of incubators was not achieved until the 1940s. This apparently slow adoption was affected by the attention given to birthing itself: Most infants were delivered at home, sometimes with the help of a midwife but often with little or no medical support. Physicians, mainly obstetricians, also were not of one accord regarding the value of incubation. As but one example, at Southmead Hospital in Bristol, obstetricians were not using incubators routinely. But their dissent minimized after premature quadruplets born in 1948 were treated successfully using incubators.

In addition, sufficient nourishment required human milk: "The breast is the best." However, there is a potential downside in that higher protein intake may give rise to fluid retention, azotemia, and metabolic acidosis. Using whey alternatives for preterm infants in 1980s fixed this dilemma [6, 7]. The remaining prime challenges include; parenteral nutrition in infants with disabilities to obtain sufficient amounts of both calcium and phosphorus, and the probable progress to nutrition-induced cholestasis [8, 9].

Many clinical improvements have enabled physicians the means to rescue lower birth weight infants. Of course, there are significant threats to these infants' survival: difficulties in breathing, necrotizing enterocolitis [10], intraventricular haemorrhage [11], and infections. These factors have been major objectives of ongoing and experimental and clinical research.

Until the mid-1950s, the provision of supplemental oxygen was the main support for respiration. The logic is simple and still applies: give oxygen to a human who is having trouble breathing. Unfortunately, the common sense notion that "if a little is good, then more is better" proved false. An oversupply of oxygen leads to retrolental fibroplasia, currently termed retinopathy of prematurity (ROP) [12].

Early incubators were designed to prevent the passage of more than 40 percent oxygen unless baffles were closed on the rear of the incubator [13]. The studies of Barcroft J, *et al* revealed that fetal animals needed less circulating pO_2 than human newborn babies. Moreover, fetal humans exhibited half SpO_2% compared to adults. This finding is difficult to account for considering that the body's metabolism is based only on glucose as the energy source [14]. Today, the risk of ROP with unrestricted oxygen has given rise to the practice that requires a prescription for 100 percent oxygen to be administered.

Cerebral palsy (CP) is another condition that was believed would benefit from additional oxygen. It was presumed that the prevalence CP would decline with the careful fetal evaluation. Nearly 15 percent of cases were attributed to the intrapartum asphyxia, which proved to be false [15]. Intrapartum asphyxia resulted from the imperfect uteroplacental blood flow associated with hypertensive disorders or sudden hypoxemia as a result of the prolapsed umbilical cord or acute placental abruption. Preventative procedures have been explored to reduce the consequences associated with extended asphyxia [16] as well as efforts to diminish brain metabolism *via* mild systemic hypothermia or local brain hypothermia for a short time [17].

Additionally, the respirator-lung may give rise to accumulated agents: barotrauma (pressure), intrinsic oxygen toxicity, and the predisposition period of immature lungs for both. Unusual lung cystic changes and marked hyperinflation could lead to corepulmonale and death. Premature chronic lung disease treated with surfactants exhibited radiographic characters associated with prolonged oxygen dependence [18].

The harmful effects of oxygen toxicity are well known. Even nasopharyngeal tissue damage has been observed where oxygen is simply passing. Moreover, trial results of early therapy with continuous positive airway pressure versus surfactant administration in infants gave a nonsignificant divergence toward either suffering from bronchopulmonary dysplasia (BPD) or sudden death. The lower versus the upper range of oxygen saturation was correlated with the lower risk for severe retinopathy but with higher mortality [19, 20]. Though oxygen supplementation seems to be vital for saving preterm infants, many studies have revealed its connection to a higher risk for ROP [20], BPD [21], periventricular leukomalacia [22], and CP [23].

Many multi-center studies have been carried out where treatment with a non-invasive CPAP immediately after birth was compared to the surfactant administration and early intubation. Despite these attempts, the rate of death or BPD or other forms of morbidities at about 36 weeks of postmenstrual age were not reduced at all [24].

Therefore, unanswered questions remain about the use of supplementary oxygen and contradictory findings. The exact dosage of oxygen that premature patients require remains

elusive even after more than 70 years of use Perhaps it is time to re-evaluate its use, taking into consideration established and well known factors.

2. NECROTIZING ENTEROCOLITIS (NEC)

NEC is a devastating disease that develops in many premature infants. Mortality rates tend to be high, but early detection along with heroic medical and surgical management may overcome it. Although breastfeeding ensures some protection, NEC still affects 7-10% of infants who weigh less than 1500 g, which is associated with increased morbidity and longer hospital stays [25].

3. RETINOPATHY OF PREMATURITY (ROP)

Retinal adhesion mechanisms in mammals are complex and multifactorial. Many aspects are unknown [for the detail and references see 42]. The detailed mechanisms of the retinal adhesion are incompletely understood due to a variety of chemical, physical, and physiological forces impinging upon retinal tissue: retinal pigment epithelium, nearby tissues as sclera and vitreous, the subretinal space, and the highly complex interphotoreceptor matrix that fills subretinal space. Moreover, the adhesion of the retina to the choroid, rather than anatomical, is an active dynamic process, as the retina detaches a few minutes after life ceases [42].

The adhesion mechanisms described in the current database, report intraocular pressure and oncotic pressure of the choroid seem to push the retina towards the choroid, the delicate anatomical relationships between the rod and cone photoreceptors, the retinal pigment epithelium, the existence of a complex material called interphotoreceptor matrix, as well as other metabolic and structural factors. We still cannot explain fully the remarkable features observed in the adhesion mechanisms between the photoreceptor and retinal pigment epithelium layer.

Retinopathy of prematurity, formerly known as retrolental fibroplasia, occurs when the retina could be detached or scarred by fibrous tissue with permanent damage to eyesight. The misuse of oxygen was implicated by William A. Silverman [12]. Admittedly, oxygen may not be the only factor because ROP is a complicated disorder that requires more investigation. It is hard to diagnose due to the difficulties of ophthalmoscopic examination in newborns and the necessity for retinal blood vessels to reach a certain level of maturity. Typically, examinations should start at the age of six weeks after delivery.

Severe forms of ROP were thought to lead irrevocably to blindness. However, in 1988 there was a hopeful report of ROP recovery by using cryotherapy. This treatment was based on ROP blinding complications associated with the retinal neovascularization development [26]. Posteriorly, the close objectives were to remove a proliferation of blood vessels by laser therapy with or without cryotherapy. This therapy does not provide normal vision, but is considered as a successful treatment method [2].

Retinal hypoxia is thought to be the main cause of opacity surrounding the retinal NV in pathogenesis. Other factors including hypoglycaemia, high levels of pro-angiogenic factors such as vascular endothelial growth factor (VEGF), and elevated free radical levels as well as minor oxygenation response (vasospasm) [27]. Two hypotheses commonly are presented to explicate the role of hypoxia in the development of the retinal NV. Hypoxia at the borders of the vascular and non-vascular retina take place based on the retinal demands. This is critical with lower levels of hypoxia needed for the NV development. Surprisingly, both hypotheses do not have any supporting experimental or clinical proof [27, 28].

Theoretically, oxygen could reach the retina by both the retinal and choroidal vasculature. It is used by retinal tissues in accordance with metabolic demands. Disturbances in oxygen delivery or its metabolism lead to retinal disorders such as diabetic retinopathy, ROP, vascular occlusion, and age-related macular degeneration [29].

4. MELANIN AS AN UNSUSPECTED BIO-ENERGETIC MOLECULE

Melanin is a dark pigment that is present in hair, skin, and the eyes. It has been considered a sunscreen that protects us from the dangerous effects of UV rays. Its extraordinary stability has been an obstacle to a deeper understanding of its biological functions. Additionally, melanin is almost impossible to study in laboratory conditions (Fig. **1**).

We note that melanin has an intrinsic ability of melanin to convert visible and invisible light into chemical energy *via* dissociation of water molecules. This ability is similar to that of chlorophyll in plants. It contributes to the morphological features of blood vessels of the optic nerve and the relationship with major causes of blindness such as glaucoma, diabetes, and macular degeneration [30, 31].

The optic nerve in humans is about 1200 μm; therefore, the detailed study requires us to enlarge the image using digital and optical tools. At higher magnifications, we found melanin near the optic nerve. Our previous study based on almost 6000 patients found melanin to be present in every patient regardless of the diagnosis [31, 32].

However, our major variables were morphological characteristics exhibited with blood vessels of the optic nerve. This is where we noticed a second important detail: the blood vessels seemed to respond to the presence of melanin [30-32]. We reported that the unexpected intrinsic property of melanin to absorb light energy and transform it into chemically based free energy can explain normal adhesion of the sensory retina to the pigment epithelium. Furthermore, we offered the finding that melanin may be able to provide a new treatment avenue against devastating neurodegenerative and other non-treatable properties.

The effect of melanin is so important that we proposed an axiom: a greater level of melanin results in fewer blood vessels and vice versa. To explain the apparent anti-angiogenic effect of melanin, we searched for any peptide factors. But melanin is not an amorphous substance such as a membrane

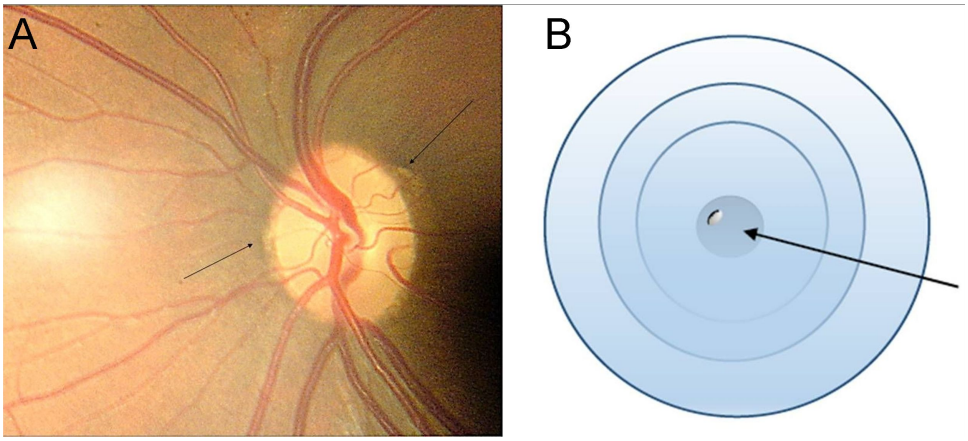

Fig. (1). A. The arrows indicate the discrete but it always presence of the melanin in the surroundings of the optic nerve (arrows). **B.** Growing spheres of energy that come from melanin (arrow).

receptor, nor does it have enzymatic machinery associated with it. Also, its effect is highly consistent, more than that seen through peptide factors because biological variability does not play a big role. We also detected high levels of oxygen in greater pigmented tissues compared to less pigmented tissues. The differences ranged from 10 to 35% which was significant despite other substantive differences [33]. The best anti-angiogenic factor is high levels of oxygen. The apparent solution was the anti-angiogenic effect of melanin. What remained to be explained was the source of oxygen.

We tried to find molecules in eye tissues that were capable of donating oxygen consistently and continuously, day and night. We examined several possible candidates but dismissed them all because there is a high amount of oxygen required to be produce a palpable change sooner or later, and these molecules were not inducing the major changes consistent with the continuous donation of oxygen. The best candidate that we found was the vitreous humour, which is more than 95 percent water. Thus, water from the vitreous humour seemed the best candidate, but water does not give oxygen freely: it has to be dissociated.

We studied several mechanisms, some more intricate than others; but we did not get a satisfactory explanation until February 2002. We found that melanin has the intrinsic property of dissociating water molecules, which is a way that it dissipates the enormous amount of electromagnetic radiation that it is capable of absorbing. Within a few month's, we deciphered how to dissociate water and re-shape it. The following equation explains the mechanism: $\mathbf{2H_2O \rightarrow 2H_2 + O_2 \rightarrow 2H_2O + 4e^-}$

It can be interpreted that, for every two molecules of water that is re-formed, four high-energy electrons are released. The expensive part of the energy side of the process is dissociation, which requires temperatures up to 2000°C in the laboratory. The re-forming of the molecule is exergonic by what occurs spontaneously. Reviewing physical and chemical properties of the gaseous elements that make up the molecule of water, we realized that the primary reaction product is the molecular hydrogen (H_2), which is an energy carrier nature uses throughout the universe. Therefore, our body cannot be different. Also, according to the scientific literature, oxygen is toxic at any concentration; hence, plants expel it into the atmosphere [34].

What if our organism has more sources of energy than we expected? Our body can gain light energy through melanin. Glucose is the perfect building block that our body has used from the beginning of time to synthesize almost 99 percent of the biomolecules that are required for bodily function. Gathering energy by using light to separate water molecules is adaptive [35].

5. MELANIN LIBERATES ENERGY IN SYMMETRICAL FORM, IN ALL DIRECTIONS

Melanin releases energy similarly to spheres that grow energy, which distribution follows the laws of the simple diffusion**.** A sphere contains higher concentrations of diatomic hydrogen and molecular oxygen, but the next greater concentration is in re-formed water and electrons of high energy. The discovery that our body can convert light into chemical energy *via* dissociation of water, much like chlorophyll in plants, shifts the dogma of glucose as an energy source [31].

Glucose is the ideal building block. Its carbon atoms and chains are the backbone of the 99 percent of biomolecules. Our body can extend, break up, rotate, and combine other elements; but is not able to provide the energy needed for its metabolism. Therefore, our body is able to dissociating molecules of water thanks to melanin [36]. The chemical reaction involving melanin is surprisingly accurate. Administering supplemental oxygen results in an unbalanced equation, leading the body to form water that is manifested by edema [37].

6. PRETERM BIRTH, AN IMBALANCE IN THE GENERATION AND DISTRIBUTION OF ENERGY FROM MELANIN

Critically ill premature infants are susceptible to neurosensory deficiency in childhood [38]. The risks for neurodevelopmental impairment and its severity increase with the gestational age reduction. Biochemical processes in

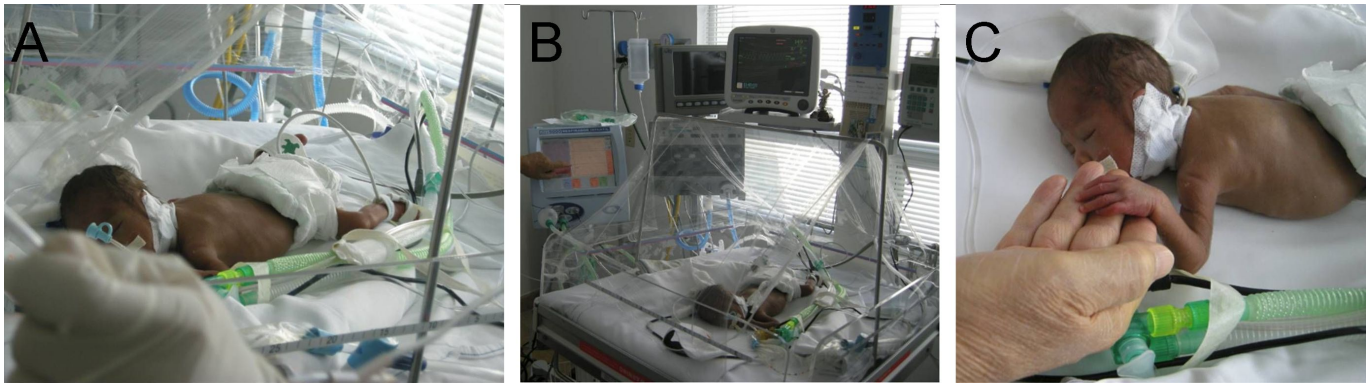

Fig. (2). A. General view of the patient after a few days of having been hospitalized. The treatment (QIAPI 1) to intensify the dissociation of the water by the melanin was started within few days, to the dose of three drops per oz., six times a day. **B.** The general aspect of the technological armamentarium and the methodology those were available for the care of the patient. **C.** It was not possible to obtain details of the treatment administered to the patient for reasons other than medical practice. We can only say that QIAPI 1 medication was donated by us for the treatment of the patient.

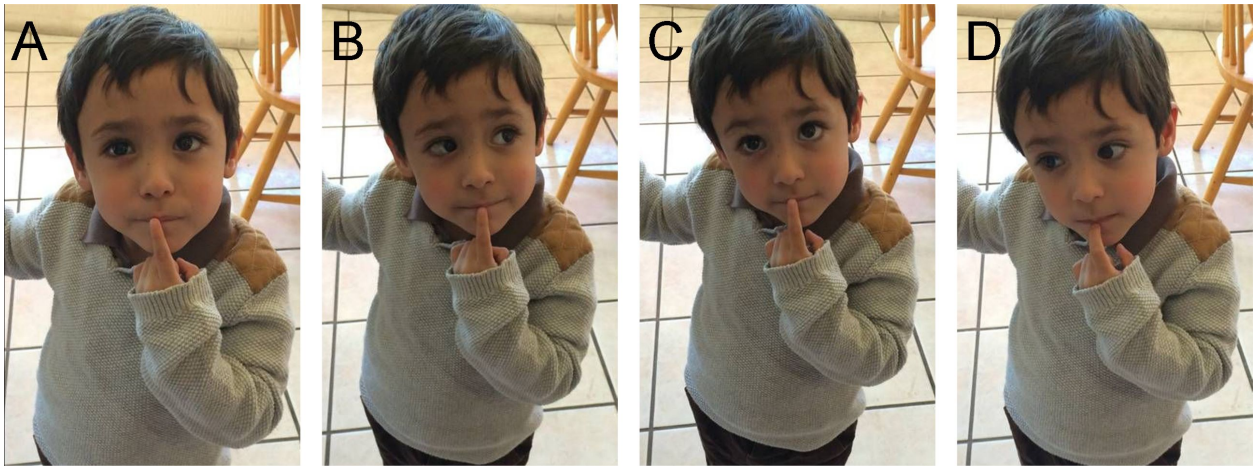

Fig. (3). A. At the approximate age of 28 months, were taken these photographs that show generally normal development. The appearance of the eyes is completely normal. To tell of the parents not has he minimum data of visual or auditory deficiency. The alignment and appearance of both eyes are unremarkable. **B.** The ocular motility following objects is within normal parameters. **C.** The parallelism of the visual axis is conserved in all directions. **D.** The vision is preserved and the displacement of the eyeballs not presents limitations in any direction.

humans are surprisingly accurate and well balanced. Yet, numerous factors could lead to an unbalanced state such as contaminated water, polluted air, pesticides, herbicides, fertilizers, metals, plastics, stress, anaesthetic agents, *etc*. Therefore, premature birth can explain the imbalance in the generation and distribution of energy coming from the melanin that forms the basis of the energy system of the cell.

Based on our observations, we are confident that ROP is an imbalance between the dissociation and reformation abilities of the water molecule, which is accentuated by administering supplemental oxygen to premature infants. The explanation is as follows: the chemical reaction of the dissociation and the re-forming of water by melanin depend on the physical factors and reaction products just like any chemical reaction. If the concentration of any of the components is high, then the reaction tends to go toward the opposite direction. For example, if the concentration of oxygen is high (*e.g*., by supplementary oxygen), the cell or the body tends to form water. But that process consumes hydrogen and its valuable load of energy.

What is the effect on body tissues? Energy levels affect cell stress. In our experience, when the generation and distribution of energy decrease sharply, tissues form edema and create the potential for the formation of haemorrhage. If the decline is chronic, fibrosis occurs and, subsequently, uncontrolled mitosis. Progressive fibrosis always is accompanied by the abnormal growth of the blood vessels, which is the main characteristic of ROP and other proliferative retinopathies. Since 2006, we have treated ROP and other the proliferative retinopathies through pharmacological methods that have restored the energy balance with permanent positive results.

7. CURRENT FINDINGS

Report of a case: A premature male baby weighing less than 1,000 g (2.2 lbs) was delivered at about 24-28 weeks after gestation. The boy suffered digestive and respiratory problems as well as brain haemorrhage (Figs. **2** and **3**).

Experimental measurements of ischemic retina oxygen partial pressure support the hypothesis that tissue hypoxia

triggers neovascularisation. Therefore, laser photocoagulation should be done over the ischemic retinal areas to remove the hypoxia in the inner retina. The existing oxygen in the retina does not come from the lungs because melanin produces it *via* dissociating with water molecules. The low oxygen levels indicated a deficiency in water dissociation and raised the question of whether levels of molecular hydrogen or di-atomic oxygen levels were typical or not. While the application of laser photocoagulation eliminates hypoxia, it introduces a confounding factor and can be interpreted wrongly. Intense light stimulates transiently the transformation of light into the chemical energy using water dissociation within melanin. The increase of oxygen levels leads to the beneficial changes in tissues by inducing high levels of chemical energy that correspond to higher tissue levels of molecular hydrogen (H_2). Therefore, the increase of water dissociation increases the tissue oxygen levels and subsequently the molecular hydrogen levels. In fact, the therapeutic benefit of the laser is due to the levels of chemical energy in the tissues that are restored to their appropriate levels, but the effect is diminished.

The development of oxygenation theories relies primarily on animal research. There are few studies involving human subjects that investigate retinal oxygenation levels. These are problematic because we lack reliable, non-invasive methods [39]. Thus, the early assumption that the retinal disrupted oxygen in severely premature neonates is the main reason for the development of ROP should be modified. Therapies based on oxygen as the main factor have been fruitless.

The rates of ROP and eye surgery were higher in a high oxygen-saturation group than in the lower one. The rates of unilateral or bilateral blindness and other vision impairment did not show any significant difference between groups at 18 to 22 months of corrected age. Furthermore, the more severe ROP happens at high proportions with lower weight white infants than black infants 7.4% versus 3.2 %, respectively, for an unknown reason. However, authors speculated that differences in retinal pigmentation may provide an solid explanation against the free radical-mediated phototoxic injury in the black infants [40].

Oxygen saturation may serve as an indirect indicator of the dissociation rate of water. Therefore, theories that attempt to elucidate the oxygen metabolic pathway were unnecessarily complicated and failed to reach a useful conclusion. The discovery of melanin's critical role in the water dissociating reaction breaks the paradigm because the resulting molecular hydrogen is a significant product of the dissociation and brings the energy that tissues require to perform their normal physiological functions [31]. Oxygen by itself, however, is toxic at any concentration. It is possible to resuscitate infants with or without supplemental oxygen. Oxygen administration leads to the dissociation equation imbalance that disposes the body to begin to form water *versus* the valuable hydrogen, creating further energy imbalance in tissues [41].

CONCLUSION

The presented case is a salient sample of the efficiency of melanin as a significant source of energy. The case study involved an infant near the end of prematurity classification (24-28 weeks) but extremely low birth weight. The infant progressed successfully and did not develop retinopathy of prematurity.

AUTHORS' CONTRIBUTIONS

Arturo Solís Herrera, María del Carmen Arias Esparza, Paola Eugenia Solís Arias, Ghulam M. Ashraf, Gjumrakch Aliev, designed experiments, María del Carmen Arias Esparza and Paola Eugenia Solís Arias performed experiments. Arturo Solís Herrera, Ghulam M. Ashraf, Osama F. Mosa, Vladimir P. Fisenko, Alexander V. Sokolov, Elena V. Bovina, Vladimir N. Chubarev, Vadim V. Tarasov, Siva G. Somasundaram, Cecil E. Kirkland and Gjumrakch Aliev interpreted results and wrote the paper. All authors reviewed the manuscript and approved it before submission.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocol was approved by the US Ethical Committee of Primary Health Care in Human Photosynthesis® Research Centre, Aguascalientes 20000, México.

HUMAN AND ANIMAL RIGHTS

No animals were used for studies that are base of this research. All the humans used were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013 (http://ethics.iit.edu/ecodes/node/3931).

CONSENT FOR PUBLICATION

The parents of the case included in this study received written informed consent.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

FUNDING

This work supported by Human Photosynthesis® Research Center, Aguascalientes 20000, México, and Russian Academic Excellence project "5-100" for the Sechenov University, Moscow, Russia. This research was also supported in part by RSF project #14-23-00160P and the scientific projects of IPAC (topics 48.8. and 48.9). Authors' also very grateful for the animal facilities were provided by Center for preclinical trials of IPAC RAS.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

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