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REVIEW ARTICLE

Mouth Breathing: Understanding the Pathophysiology of an oral habit and its consequences

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ABSTRACT

Mouth breathing is a sign associated with Sleep and Breathing related Disorders and Obstructive Sleep Apnea in children. The aim of this paper is to provide a comprehensive overview of the changes in the human physiology when mouth breathing and, how it may affect the oral and general health in humans. The potential reactions produced at the cellular level and, how those reactions may lead to a negative impact in the human health are presented. Mouth breathing affects the O_2/CO_2 exchange at the lungs, which may lead to the production of the Hypoxia Inducible Factor (HIF) in all the cells in the human body, as well as stimulates the production of Erythropoietin in the kidney. Mouth breathing also causes a major loose of CO_2, which increases the production of bicarbonates in the kidney and release of essential minerals through the urine. All those reactions may facilitate the development and progression of chronic diseases in humans. It is recommended to consider mouth breathing as an oral habit that may associate with a cascade of events in the human physiology leading to chronic health problems. The health professionals should consider mouth breathing as a health risk factor and treat it as early as possible.

Introduction

Mouth breathing has been recognized for many years in the dental literature as a deleterious habit. Some studies have demonstrated the negative impact of mouth breathing on the craniofacial structures, as well as on the dental occlusion. [1,2] It has been reported that mouth breathing affects the craniofacial growth and development, producing malocclusions, such as open bite, as well as clockwise mandibular rotations. [3,4] A recent review of the literature found mouth breathing should be considered as a potential cause of growth retardation in children. [5]

The current knowledge also identifies mouth breathing as a common finding in patients with sleep and breathing related disorders. Although there is not strong evidence of mouth breathing association with a lower level of oxygenation in the human body, a clinical study and a couple of animal studies have suggested an association between mouth-breathing with a reduction in SPO_2. Furthermore, the physiology of breathing also indicates that mouth breathing may reduce the exchange of O_2/CO_2 in the lungs, reducing the amount of O_2 brought into the blood stream.

Based in the current knowledge, the author hypothesizes that mouth breathing may cause a generalized hypoxia in the human body, and therefore may trigger a cascade of events at the cellular level in the human body, which could negatively impact the physiology and lead to chronic/degenerative diseases. Therefore, the aim of the current paper is to produce a comprehensive overview of how mouth breathing, an oral habit, may end affecting the general health of human beings.

In that context, it is necessary to understand first, when a patient is considered a mouth breather; second, to comprehend how mouth breathing may lead to reduced levels of oxygen in our body, causing a generalized cellular hypoxia; and third, how a hypoxic state may affect the body's biology at the cellular level, which associates with or facilitates chronic diseases, a public health issue rising over the last decades.

How much breathing through the mouth makes a mouth breather?

It has been reported in the past that mouth breathing solely due to gross nasal obstruction is comparatively rare. [6] A recent study, [7] described three types of mouth breathers: The *Organic* mouth breather, who has some type of mechanical obstruction making nasal breathing more difficult; The *Purely Functional* mouth breather, who generally or partially breaths through the mouth, even there is no mechanical or pathological obstacles for breathing through the nose; And, the *Special Needs* mouth breather, who has a neurological disorder/dysfunction associated with mouth breathing.

There is a culture of thinking in the dental and medical community considering a mouth breather only those patients who are breathing through the mouth most of the time and keeping the mouth open. Many patients may maintain breathing through their nose most of the time during the day. But, during the night when sleeping, they may be breathing through the mouth. A couple of studies have reported that a nasal breather maintains breathing through the nose approximately 94 per cent of the sleeping time. [8,9] A recent study with functional mouth breathers, who continued breathing through the mouth after removing the tonsils and adenoids, reported that children breathing through the mouth less than 20 per cent of the sleeping time did not present any clinical complaint, whereas, children breathing through the mouth 40 per cent of the time or more did present clinical complaints. [9] In that study, the investigators proposed a mouth breather should be considered a patient who breaths through the mouth more than 15 per cent of the time during the sleeping time.

Mouth breathing has been reported as one of the symptoms present in children with obstructive sleep apnea (OSA). [10] It produces a more elongated and narrow upper airway, which may aggravate the collapsibility of the upper airway, so increasing the risk for developing OSA or increasing its severity. [11] In that context, mouth breathing in children may be considered a sign of sleep and breathing related disorders, as well as potential trigger in the domino phenomenon conducting to OSA in adults. [12-15] Together with noisy breathing and snoring, [16] mouth breathing should also be considered one of the initial signs in the pathway to developing OSA at a later age.

Another interesting result from some studies in this field is that the removal of the tonsils and adenoids did not result in a systematically return to nasal breathing when sleeping, [9] and therefore, the prognosis for complete resolution of the symptoms in children with sleep and breathing disorders is very low after the surgery. [17] Those results agreed with another study proposing the removal of the tonsils and adenoids may result in a "temporary cure" of the snoring in children, but the symptoms associated with sleep disorders may relapse in a relatively short term. [18] In that context, it may be suggested the continuation of mouth breathing may play a role in the re-appearance of the symptoms in children with sleep and breathing disorders later on.

There are many symptoms in human beings associated with mouth breathing. Among others, increased levels of anxiety and behavioral problems have been the major ones reported in the literature. [19,20] However, a chronic low level of oxygen on every cell of the human body, which may result from mouth breathing, could become a negative effect. That may conduct to or facilitate chronic/degenerative problems as it will be discussed later. Prior to that, it is important to visualize how mouth breathing may create a general hypoxic state, low level of oxygen, in all the tissues of the human body.

Mouth breathing and low levels of Oxygen

Mouth breathing has been associated with low oxygen saturation in children, [21] and, nocturnal oximetry has been proposed as a valuable tool to screen OSA in children and facilitate treatment decisions when polysomnography is not available. [22] Based on those studies one may infer that mouth breathing may negatively affect oxygen saturation, a constant observed in children with sleep and breathing disorders. [7,23]

To understand how breathing through the mouth may affect the oxygen saturation in the blood, it is important to priory review the physiology of breathing. Here, the author presents a brief summary of the physiology of respiration and the gases exchange in the lungs, as well as how that function plays a critical role on the buffer equilibrium in the blood. For further information, the reader is invited to review the Unit VII in Guyton and Hall Textbook of Medical Physiology, 13th Edition (Elsevier).

The pulmonary function and the respiratory muscles recruitment differentiate when breathing through the nose versus breathing through the mouth. [24] Our body may maintain a low level of oxygen due to mouth breathing. Breathing through the nose moves approximately 1/2 liter of air through the nose and the upper airway, whereas breathing through the mouth may move a higher amount of air through the airway. Considering that, it would be arguable to say mouth breathing would bring more air into the respiratory system, and therefore, more oxygen into our body. However, when breathing through the nose, the diaphragm, a muscle at the base of the lungs, contracts and expands the ribcage outward and downward, so permitting the air to fulfil the whole lungs. [25-27] That is known as diaphragmatic breathing. Conversely, breathing through the mouth is performed more with the chest muscles, which only fulfil the superior two thirds of the lungs. The latter is known as chest or shallow breathing.

Diaphragmatic breathing permits the air to reach the alveoli located at the base of the lungs. Those alveoli are able to distend easier comparing with those located at the superior part of the lungs, the apex. The alveoli at the base of the lungs are capable of more O_2/CO_2 exchange as they maintain a less negative pressure, so they can be fulfilled easier. Besides that, there is a higher amount of blood vessels at the base of the lungs, so facilitating a higher O_2/CO_2 exchange in that area. On the other hand, mouth breathing associates with chest or shallow breathing. Such breathing moves more air to the upper areas of the lungs, with much less air reaching the base of the lungs. The alveoli located at the superior areas of the lungs ventilates less efficiently, and so, smaller volumes of oxygen are exchanged at that region. Also, the superior part of the lungs is surrounded by a lesser amount of blood vessels, which reduced the level of O_2/CO_2 exchange at that area.

Beside to the fact that breathing through the nose moisturizes, warm and clean the air, the anatomical and physiological features described above, leads to state that nasal breathing is a more efficient and healthy way of breathing. [24,27] It produces a higher O_2/CO_2 exchange at the alveoli in the lungs, so reaching a higher oxygen saturation in the blood, which results in more oxygen reaching all the body tissues. On the other hand, mouth breathing produces a lower O_2/CO_2 exchange at the lungs moving less oxygen through the cardiovascular system in the human body. In other words, mouth breathing produces a lower level of oxygen in the blood and the tissues, which can be described as a silent cellular chronic hypoxia.

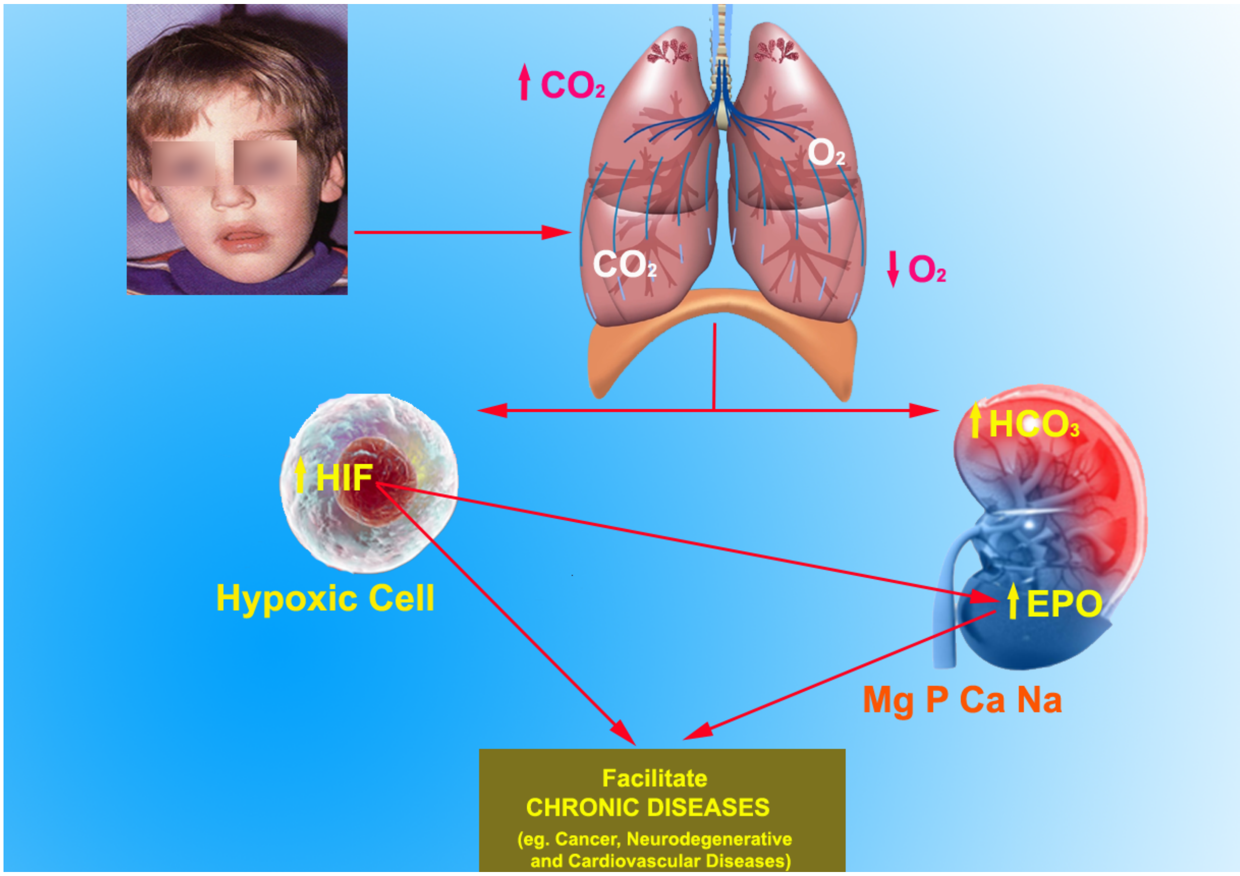

Figure 1. Mouth breathing produces negative effects which may facilitate the progression of chronic diseases. It affects the O2/CO2 exchange at the lungs, which leads to cellular hypoxia at the tissues. A lower level of O2 at the cell stabilizes the Hypoxia Inducible Factor (HIF) in hypoxic cells. Simultaneously, a major loose of CO2 when mouth breathing, increases the production of bicarbonates (HCO3) in the kidney and the release of essential minerals through the urine. HIF stimulates the production of Erythropoietin (EPO) in the kidney. All those reactions may facilitate the development and progression of chronic diseases in humans.

Another important factor that needs to be considered being responsible for producing hypoxia at the tissues of the human body is the higher amount of CO_2 removed from the body when breathing through the mouth. [28] A decreased level of CO_2 in the lungs associates with a decreased level of CO_2 in the blood. That causes a reduction in the amount of carbonic acid (H_2CO_3), which is required to maintain the buffer balance in the blood, which maintain the blood pH moving between a narrow window, 7.35 to 7.45. A reduction in the amount of H_2CO_3 moves the blood pH towards a more alkaline state, increasing the pH of the blood closer to 7.45. [29,30] Such a situation produces a reaction at the kidney, which releases bicarbonates intending to facilitate a decrease in the blood pH, so bringing it close to 7.35. This compensatory mechanism produces two negative effects. First, the kidney has to release minerals such as Magnesium, Sodium, Phosphorus and Calcium to the urine, which are essential for cellular energy (ATP synthesis) and mineralization of the bone tissue. [31] Second, a more alkaline pH in the blood creates a stronger bind between the hemoglobin in the red cells and the O_2 they carry. That causes that the red cell cannot easily release the oxygen from the tissues, nor capturing the CO_2 released by the cells. [30] Therefore, mouth breathing reduces the levels of O_2/CO_2 levels at the lungs and, stimulates blood alkalosis which difficult the release of O_2 to the tissues, thus increasing the potential of the cells in the human body reaching a hypoxic state.

Cellular hypoxia and its consequences

The 2019 Nobel Prize in Physiology or Medicine was awarded to William G Kaelin Jr., Sir Peter J Ratcliffe and Greg L Semenza. Those three scientists explained the biological effect that hypoxia has in all the cells in the human body. Let's see what we have learned from the Nobel winners.

Oxygen is the combustive the mitochondria in the cells uses to convert glucose in adenosine triphosphate (ATP), the energy required by the cells to synthetize its bio-products. In that process the cell releases CO_2 and water. One of the bio-products our cells is constantly producing is the Hypoxia Inducible Factor (HIF). It is a cellular product sensing the level of oxygen at every cell in our body. [32,33] This is another mechanism, together with the carotid body, to sense the level of oxygen in the human body informing the brain how breathing should be regulated.

The HIF is produced in the cells by two sub-products, the Hypoxia Inducible Factor-1 alpha (HIF-1 α) and another transcription factor known as ARNT. When oxygen levels are at a normal level in the cell, known as normoxia, HIF-1 α is destroyed by the proteasome in the cellular cytoplasm. [34] For that HIF-1 α is added with two hydroxyl (OH^-) groups, which permits the Von Hippel-Lindau's disease factor (VHL) to add to HIF-1 α and being degraded. Conversely, in a low level of Oxygen in the cell, known as cellular hypoxia, the hydroxyl groups are not added to HIF-1 α, so that transcription factor is not labeled by VHL to be degraded. In such a situation, HIF-1 α is able to joint to ARNT stabilizing HIF, which is going to stimulate DNA sequences in hypoxia regulated genes. [35]

One of the processes controlled by the hypoxia regulated genes in the cells is the production of Erythropoietin (EPO) in the kidney, which leads to a higher production of red blood cells (erythropoiesis) and new blood vessels. [33] This reaction at the cellular level is intending to facilitate the transport of more oxygen to the tissues. In a physiological state (eg. Muscular fatigue caused by exercise), it becomes a beneficial process as more blood cells would be available to transport oxygen to the muscles and remove the waste products causing the fatigue as lactic acid. Conversely, in a pathological state (eg. cancer or tumor cells), an increase in HIF production in the cells, as well as EPO higher production in the kidney may lead to higher proliferation and more blood vessels formation in tumours. [36]

Negative effects due to cellular hypoxia

Cancer is a chaotic and pathological development capable of proliferate, invade adjacent tissues, generate a blood supply and avoid rejection by the immune system. HIF may have an effect on cellular proliferation, but more importantly, it facilitates angiogenesis, secretion of matrix metalloproteinases and production of immune-suppressive factors, which are key modulators for cancer progression. [37] in that context, the hypoxic state that may be produced by mouth breathing may create a worse scenario for the cancer patient, as cellular hypoxia leads to higher risk of tumors development, stimulating more rapid cell division and aberrant blood vessel formation. [38] Furthermore, a hypoxic state in the cells shifts their metabolism to glycolysis and reduces the biological responses reducing the cell dependence on the oxidative metabolism, so permitting the cancer cells to survive in such a harsh environment. [39] In that context, a silent chronic cellular hypoxia may alter the trajectory of cancer and makes tumors more difficult to treat. Based on that evidence, it can be suggested that mouth breathing may facilitate cancer as it creates a hypoxic environment for the cells, which stabilizes HIF at the cellular level producing all the cellular factors that can mediate cancer and metastasis progression, as well as increase the risk of mortality in the patient. [36]

Another tissue highly affected by a hypoxic state in the human body is the brain. Chronic hypoxia leads to oxidative stress in the neural cells and brain damage. [40] As mentioned above, mouth breathing leads to OSA, [12] which associates with intermittent hypoxia. [41] The later, intermittent hypoxia, stimulates in the brain and the heart a higher level of reactive oxygen species/reactive nitrogen species (known as ROS/RNS). Those substances promote oxidative stress in the neural and cardiac cells, as well as ischemia, which may cause neuronal brain injury at an early age. [41,42]

The respiratory and sleep alterations that associate with sleep and breathing disorders in children, such as mouth breathing, substantially affects the autonomic nervous system, activates the systemic inflammatory pathways and, disrupts the vascular function. [43,44] Children with sleep and breathing disorders maintain a higher baseline blood pressure when sleeping, which may be the first step of a higher blood pressure at day time at adulthood. [45] Based on those reports, it may be suggested that mouth breathing may also be one of the initial steps in a cascade of events that may lead to cardiovascular diseases.

The current knowledge permits to say that mouth breathing leads to breathing disorders, such as obstructive sleep apnea, as well as stimulates a hypoxic state in all the cells of the human body, which may facilitate cancer progression, metastasis, brain deterioration, heart damage and cardiovascular problems later in life.

Conclusions

The current knowledge permits to explain how mouth breathing may initiate a cascade of events which may lead to a low level of oxygen in all tissues of the human body, so facilitating neurological degenerative and cardiovascular diseases, as well as facilitating a faster progression of tumors and cancers in humans. This paper reviewed the current knowledge on the consequences of a low level of oxygen at the cellular level in the human body which may be one of the consequences of mouth breathing.

Treatment is generally denied or delayed for a mouth breather child who show sleep and breathing issues. Mouth breathing and noisy breathing have been identified as some of the signs associated with non-hypoxic sleep and breathing disorders, and so, may trigger the cascade of events presented in this review. Many of those patients may report an apnea-hypopnea index which do not categorize them as an OSA patient rendering to treatment. The current evidence indicates that mouth breathing should be treated when identified, as it is the initial sign of developing OSA and may facilitate the appearance and development of chronic diseases later in life. In that context, mouth breathing should be considered a severe deleterious habit producing negative effects in humans at the mouth as well as in the general health. It is an oral habit which should be treated as early as possible and should be considered a health problem by the dental and medical communities.

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