LITERATURE REVIEW

Relevance of the obstructive sleep apnea syndrome on the metabolic disorders

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ABSTRACT

Breathing is a critical function for survival and has an intimate connection with the other systems that allow the survival of the organism. More recently, a strict relationship between respiration and metabolic control has emerged. It is not really difficult to conceive that the breathing pattern may influence all the metabolic functions that rely on the oxygen delivery. At present, we have enough data to accept the existence of an interaction between obstructive sleep apnea syndrome (OSAS) and metabolic disorders recently described, but understanding the mechanism is a much more complicated matter.

KEYWORDS: OSAS, metabolic syndrome, sleep-disordered breathing

INTRODUCTION

Breathing is a critical function for survival and has an intimate connection with the other systems that allow the survival of the organism. This point has been largely undervalued in the past. Usually, the ENT disorders reducing the oxygen delivery were intended as a local mechanical / surgical problem and no care to the systemic effects was given.

More recently, a strict relationship between respiration and metabolic control has emerged. It is not really difficult to conceive that the breathing pattern may influence all the metabolic functions that rely on the oxygen delivery. On the same wavelength we can understand how the organism may respond to the reduced oxygen delivery, adapting the metabolic rate to this new condition. This viewpoint leads to some points: (a) usually, the most critical time when the oxygen deficit is at its nadir is during night-time, event we define as OSA (Obstructive Sleep Apnea) that seriously disrupts the sleep pattern; (b) any obstruction of the upper respiratory pathways may impact on the metabolic function directly, reducing the oxygen delivery or indirectly disrupting the sleep pattern (SDB= Sleep-Disordered Breathing), or both mechanisms may be additive; (c) the ENT disturbances interfering with the normal oxygen delivery must be regarded as systemic and not local / organ diseases.

OSAS AND METABOLIC DISORDERS

Our knowledge of this topic is still in its infancy because of the difficulty to demonstrate the interconnection of more biological systems (Systems Biology) and the consequences of the malfunction of one on the other. Furthermore, the available literature does not easily distinguish the role of the reduced oxygen delivery – altered sleep pattern from that of sleep fragmentation. Almost all the available studies use the presence of OSAS as a marker of the breathing disorder, but we do not know which is the possible role of minor disturbances that reduce the oxygen delivery to a lesser extent; differently stated, we are not aware of the existence of a dose effect response versus a threshold effect.

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Some studies could demonstrate a role for the OSAS (obstructive sleep apnea syndrome) using the polysomnographic recording and the Oral Glucose Tolerance Test (OGTT)[1]. The work of Punjabi[2] in 118 non-diabetic subjects who underwent a test of insulin sensitivity, FSIGT (Frequently Sampled Intravenous Glucose Tolerance)[3] could prove that OSAS reduces the insulin sensitivity by 27%, 37% and 48% according to the seriousness of the oxygen reduction, defined as modest, moderate or serious. However, in this paper, the criteria to define these categories are not clear, neither do we know if the definition was based on the number of OSA episodes or on the level of Oxygen deprivation they caused. Also, another study of 150 males proved that an increase of the Apnea-Hypopnea Index is associated with an increased risk for Impaired Glucose Tolerance (IGT) and to develop Insulin resistance. Both these conditions are considered as prodromic to Diabetes and an essential part of what we call "the Metabolic Syndrome". We recently demonstrated in 60 OSAS subjects that the number of nocturnal awakenings was strictly related with the instability of the glucose values upon awakening (Glycemic variability)[4]. This variability is now deemed to be one of the major risk factors for cardiovascular diseases both in the diabetic and the non-diabetic population. There are many more interesting papers on this topic that were accurately evaluated in a recent review[5].

There are also some interesting studies that demonstrate the increase of the inflammatory factors in the subjects with OSAS. Among these, the C-reactive protein and the cytokines, that are responsible for the systemic atherosclerosis and probably have a role in the appearance of neoplasm[6,7]. There are also proofs of an increase of the atherogenic dyslipidemia in subjects with OSAS[8].

The metabolic – OSA connection goes far beyond. We know that bad sleep / OSA may have a negative effect on the body weight. OSAS subjects have great difficulty losing weight, and rather tend to increase it[9]. Among the numerous mechanisms hypothesized to explain this effect, a critical one involves the hormone Leptin. This hormone regulates appetite[10]. OSAS subjects show resistance to this hormone and a concomitant increase in appetite drive[11,12]. Some years ago we could prove the presence of high ineffective levels of leptin in obese type 2 diabetic subjects as markers of insulin resistance[13]. Another interesting connection, not yet sufficiently explored, is the one between OSAS and erectile dysfunction[14].

At present, we have enough data to accept the existence of an interaction between OSAS and metabolic disorders recently described[15], but understanding the mechanism is a much more complicated matter. We have recently proposed a model of this interaction as seen in Figure 1.

CONCLUSIONS

It is now evident that the respiratory system and, consequently, the respiratory distress, have a high degree of correlation with the other systems critical to survival (systems biology). What we have always considered minor disturbances of the respiratory pattern have a much greater impact on the general well being of the body. It is now time to critically review the matter and start thinking of a greater picture.

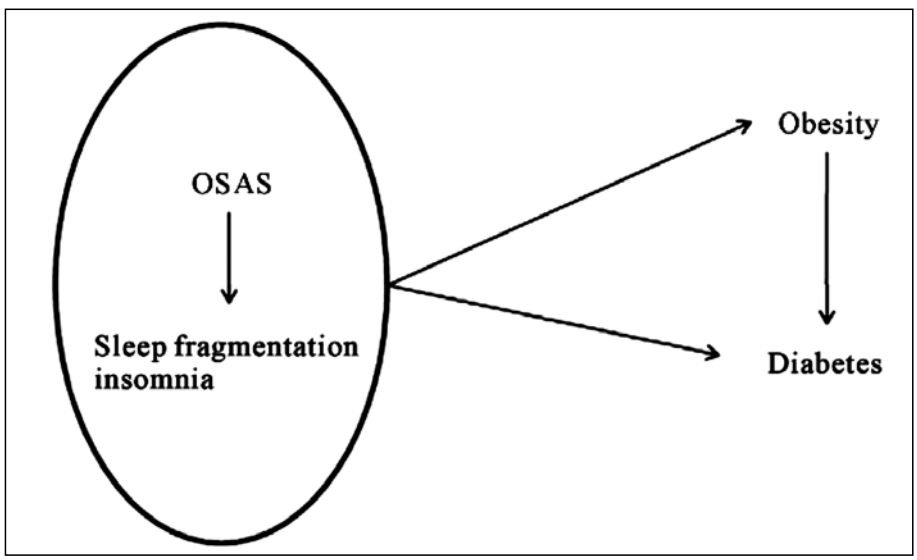

Figure 1 A simplified scheme of the interactions between respiratory distress and metabolic disorders

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