Obesity, Insulin Resistance, Hypertension and Sleep in the Child

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Abstract: Sleep loss produces various insults on human health. The current mini-review introduces recent evidence on the relationship among sleep loss, obesity, insulin resistance, hypertension, and sleep apnea with paying special attention to children. Ten relationships were explained; 1. Sleep loss induces obesity. 2. Obesity induces sleep apnea. 3. Obesity induces insulin resistance. 4. Obesity induces hypertension. 5. Sleep loss induces insulin resistance. 6. Sleep loss induces hypertension. 7. Sleep apnea with obesity induces insulin resistance. 8. Sleep apnea with obesity induces hypertension. 9. Sleep apnea without obesity induces insulin resistance. 10. Sleep apnea without obesity induces hypertension. To secure child health, the need for paying attention to sleep was emphasized.

Keywords: Review, metabolic syndrome, sleep apnea, diabetes, cardiovascular disease.

INTRODUCTION

Sleep is an essential physiological activity for humans. However, recently, sleep has been paid little attention, resulting in the increased of sleep deprived people [1]. Sleep loss directly impacts health, including increasing the risk of accidental and automobile crash injuries, as well as potentially resulting in long-term deleterious effects on the cardiovascular, immune, and various metabolic systems [2]. These facts have recently been recognized especially in adults, but the similar facts have also been pointed out in children [3]. The current mini-review introduced recently published evidence on the relationship among sleep loss, obesity, insulin resistance, hypertension, and sleep apnea with paying special attention to children (Figure **1**).

METHODS

To review recent findings on relationships between child sleep including sleep apnea and obesity, insulin resistance, and hypertension, author searched evidence by means of Pubmed as well as recent abstracts on medical meetings on sleep.

RESULTS

Finally, 44 references cited [1-44] here was considered to be worth discussing on ten relationships between child sleep and obesity, insulin resistance, and hypertension; 1. sleep loss and obesity, 2. obesity and sleep apnea, 3. Obesity and insulin resistance, 4. Obesity and hypertension, 5. Sleep loss and insulin resistance, 6. Sleep loss and hypertension, 7. Sleep apnea and insulin resistance, 8. Sleep apnea and hypertension, 9. Sleep apnea without obesity and insulin resistance, 10. Sleep apnea without obesity induces hypertension. Author also found it important to discuss on the relationship between child sleep and metabolic syndrome. In the following section, the above mentioned 11 issues are discussed.

DISCUSSION

1. Sleep Loss and Obesity (Line 1 in Figure 1)

According to the review published in 2008 [4], there have been prospective studies that have observed an association between sleep duration and weight gain, including four studies in children [5-8] and five in adults [9-13]. All but one [9] of these prospective studies found a significant association between shorter sleep duration at baseline and greater weight gain during the period of follow-up. Short sleep duration has also been shown to significantly increase the subsequent risk of obesity in young children [14].

2. Obesity and Sleep Apnea (Line 2 in Figure 1)

The overall prevalence of obstructive sleep apnea (OSA) in the general population is 2% to 4% [15], and in obese adult individuals the prevalence of OSA is 30% [16]. Obesity among adults is the largest risk factor for OSA [17]. This is also true for children [18].

3. Obesity and Insulin Resistance (Line 3 in Figure 1)

According to the review by Kim & Caprio [19], the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2002 examined the prevalence of insulin resistance, defined as the homeostasis model assessment method (HOMA-IR) greater than 4.39 (upper 2.5 percentile) or greater than 2 SD above mean HOMA-IR, and determined that obesity was a major determinant of insulin resistance independent of age, gender, or ethnicity [20].

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4. Obesity and Hypertension (Line 4 in Figure 1)

Hypertension seems to be the most common obesity-related health problem, although the true mechanisms of obesity-related hypertension remain to be determined [21]. According to the review by Sorof & Danieles [22], obese children are at approximately a 3-fold higher risk for hypertension than nonobese children. Recently, overweight/obese children compared with normal-weight children was reported among Greek children ((9.2 +/- 1.8 years old) to have higher blood pressure [23].

5. Sleep Loss and Insulin Resistance (Line 5 in Figure 1)

According to the review in 2010 [2], sleep restriction results in metabolic and endocrine alterations, including decreased glucose tolerance, decreased insulin sensitivity, increased evening concentrations of cortisol, increased levels of ghrelin, decreased levels of leptin and increased hunger and appetite. However, the same review stated that there has been no laboratory study so far that has examined the impact of experimental recurrent sleep restriction on hormones and metabolism in children.

6. Sleep Loss and Hypertension (Line 6 in Figure 1)

Recent epidemiological studies have revealed relationships between sleep deprivation and hypertension, probably due to increased sympathetic tone [24]. For children, however, Mratikainen *et al.,* [25] reported that neither quantity nor quality of sleep was related to 24-hour ambulatory blood pressure or cardiovascular reactivity after accounting for major covariates (sex, age, height, body mass index, and parental education).

Tonai *et al.,* investigated the life style and blood pressure of 685 children who were the first to third grade of elementary schools in 1985. They followed the same children at 1988 and 1991. They picked up 43 short sleepers, who showed short sleep duration than the average at every three-time investigations, and 113 long sleepers, who had long sleep duration than the average at every three checks, and compared their blood pressure. They found that the average both systolic and diastolic blood pressures showed significantly higher values in the 43 short sleepers than in the 113 long sleepers in 1991 [26]. Short sleep duration may have effect on blood pressure in children.

7. Sleep Apnea and Insulin Resistance (Line 7 in Figure 1)

According to Lindberg *et al*., sleep disordered breathing is independently related to the development of insulin resistance and thereby the risk of manifest diabetes mellitus [27]. Children with OSA have found increased fasting insulin [28], and in obese pubertal children, OSA was associated with worse insulin resistance [29].

8. Sleep Apnea and Hypertension (Line 8 in Figure 1)

Compared with participants without OSA, the presence of OSA was associated with increased adjusted risk of incident hypertension in adults [30].

Marcus *et al.,* [31] were first to systematically study blood pressure in children with obstructive sleep apnea syndrome, and found that child patients with obstructive sleep apnea syndrome exhibited significantly higher diastolic blood pressure during both wakefulness and sleep. Kohyama *et al.,* [32] concluded that blood pressure in pediatric patients with sleep disordered breathing is positively correlated with the degree of sleep disordered breathing. Both Marcus *et al.,* [31] and Kohyama *et al.,* [32] stated that multiple linear regression showed that blood pressure could be predicted also by body mass index. Recently, Horne *et al.,* reported that sleep disordered breathing, regardless of the severity, was associated with increased blood pressure during sleep and wake compared with nonsnoring control children [33].

9. Sleep Apnea without Obesity and Insulin Resistance (Line 9 in Figure 1)

As cited before, sleep disordered breathing is reported to be independently related to the development of insulin resistanc [27]. Yang *et al.,* described that accumulating evidence implicates that adult OSA may be associated with insulin resistance, glucose intolerance, and metabolic syndrome, but independent of obesity [34]. Clarenbach *et al.,* [35] also stated that the present evidence from experimental studies in animals and humans indicate that intermittent hypoxia and concomitant oxidative stress may have a negative impact on glucose metabolism, predisposing to insulin resistance. However, they [35] also concluded in their abstract that further carefully conducted clinical studies are needed to clarify the effects of OSA on insulin resistance.

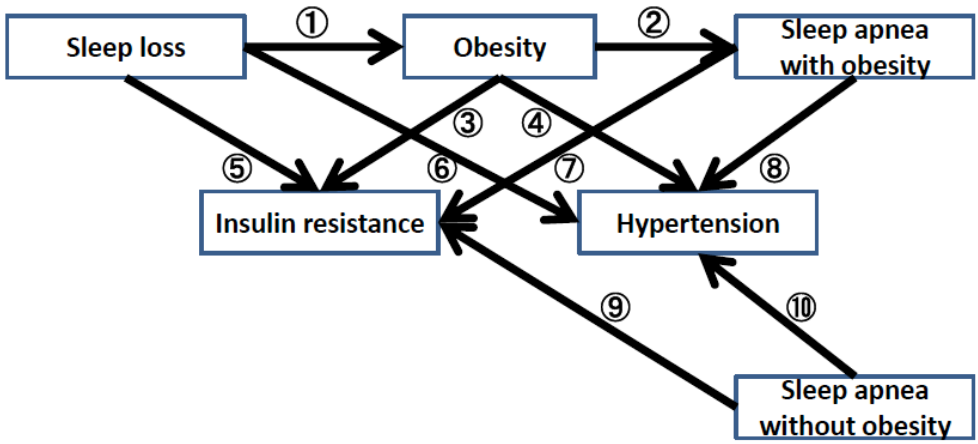

Figure 1: The relationship among sleep loss, obesity, insulin resistance, hypertension, and sleep apnea.
1. Sleep loss may induce obesity.
2. Obesity may induce sleep apnea.
3. Obesity may induce insulin resistance.
4. Obesity may induce hypertension.
5. Sleep loss may induce insulin resistance.
6. Sleep loss may induce hypertension.
7. Sleep apnea with obesity may induce insulin resistance.
8. Sleep apnea with obesity may induce hypertension.
9. Sleep apnea without obesity induces insulin resistance.
10. Sleep apnea without obesity may induce hypertension.

Kohyama *et al.,* reported a disturbance of glucose metabolism in child non-obese OSA patients [36, 37]. They [38] also investigated the relationship between OSA and insulin resistance. Insulin resistance was estimated by the fasting serum insulin levels, the insulin resistance index based on HOMA-IR, and the quantitative insulin sensitivity check index (QUICKI). A total of 85 children aged 25–168 months (average 72.8) who had been referred for polysomnography in order to evaluate OSA were included in the study. Available serum samples were obtained from 64 children. These 64 children were divided into mild and severe groups based on the degree of desaturation. Among 50 non-obese children (39 mild, 11 severe) and 14 obese children (10 mild, 4 severe), children in the severe group had significantly higher average levels of fasting serum insulin and HOMA-IR than in the mild group. Obese children were defined as those with a body mass index of more than 95th percentile for age and sex. However, among 41 normal-weighted children (those whose body mass index was in the 90th percentile or less and also the 10th percentile or more for each age and sex) (33 mild, 8 severe), insulin resistance showed no significant differences between the groups, although multiple regression analysis showed that body mass index was not a significant predictor variable for both the fasting serum glucose levels HOMA-IR, or QUICKI. Based on these results, an association between OSA and insulin resistance in non-obese children could be suggested. However, Gozal *et al.,* reported that OSA does not appear to induce insulin resistance in nonobese pediatric patients but seems to play a significant role in obese patients [39].

10. Sleep Apnea without Obesity and Hypertension (Line 10 in Figure 1)

OSA was independently associated with hypertension in nonobese adult patients [40]. In children, multiple linear regression revealed a significant association between oxygen desaturation index and apnea-hypopnea index with daytime and nocturnal blood pressure, respectively, independent of obesity [41]. OSA was associated with elevated daytime and nocturnal blood pressure, and is an independent predictor of nocturnal hypertension. This has important clinical implications as childhood elevated BP predicts future cardiovascular risks. Future studies should examine the effect of therapy for OSA on changes in BP [42].

11. Sleep and Metabolic Syndrome in Children

As described above, recent evidence suggests that sleep disturbances have strong association with weight gain, insulin resistance, hypertension [43], although

evidence was not obvious for lines 5, 6, and 9 in children. Insulin resistance and hypertension composed of the significant aspect of metabolic syndrome. The metabolic syndrome is a clinical condition composed of anthropometric, physiologic, and biochemical abnormalities predisposing affected individuals to the development of type 2 diabetes and cardiovascular disease, and the principal metabolic abnormality is considered to be insulin resistance [43]. Recently accumulating epidemiological and genetic evidence indicates that disruption of circadian rhythms can be directly linked to many pathological conditions, including sleep disorders, depression, metabolic syndrome and cancer [44]. The relation between sleep and metabolic syndrome should be paid more attention from various areas. Although metabolic syndrome has begun to pay attention in the pediatric area, recent review [43] on the pediatric metabolic syndrome had no description on sleep.

CONCLUSION

Sleep loss, obesity, insulin resistance, hypertension, and sleep apnea have close mutual relationships. Among these, sleep has been paid little attention. We should pay more attention to sleep to secure child health. Finally it should also be noted that delayed bedtimes result in sleep loss [45]. Future studies investigating the details of relationships between sleep and the various physiologic issues described are needed.

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