The influence of sleep disturbances on the development of insulin resistance - a literature review

Anna Chmura, Katarzyna Skowrońska, Anna Karaś, Patrycja Baciur, Filip Białas

Anna Chmura, chmura.anna96@gmail.com; Medical Faculty, University of Rzeszow, Pigonia Street 6, 35-310 Rzeszow, Poland

Katarzyna Skowrońska, skowro4@gmail.com ; Medical Faculty, University of Rzeszow, Pigonia Street 6, 35-310 Rzeszow, Poland

Anna Karaś, annamariakaras12@gmail.com ; Medical Faculty, University of Rzeszow, Pigonia Street 6, 35-310 Rzeszow, Poland

Patrycja Baciur, patryciabaciur@gmail.com ; Medical Faculty, University of Rzeszow, Pigonia Street 6, 35-310 Rzeszow, Poland

Filip Białas, cdomix@gmail.com ; Medical Faculty, University of Rzeszow, Pigonia Street 6, 35-310 Rzeszow, Poland

ABSTRACT

Introduction and purpose of the work: Sleep is essential for the proper functioning of the body. Adequate quality and quantity of sleep affects metabolic processes, including glucose metabolism, as well as the sensitivity of tissues to insulin, the reduction of which is called insulin resistance. It leads to an increased production of glucose in order to maintain normal blood glucose levels. Insulin resistance is a modifiable risk factor of, inter alia, type 2 diabetes. The aim of this study is to summarize the current knowledge on the relationship between sleep deprivation and an increased risk of developing insulin resistance.

State of knowledge: Sleep undoubtedly has a strong influence on glucose metabolism and insulin sensitivity. Numerous studies show that even partial sleep deprivation lowers insulin sensitivity. The available literature shows that shift work and a shifted bedtime, combined with an insufficient amount of it, lead to a significant reduction in insulin sensitivity. The positive effect of increasing the time of night rest on the sensitivity of tissues to insulin may be an
element of the prevention of diseases such as obesity or type 2 diabetes. Moreover, disturbances in sleep continuity lead to formation of insulin resistance. An example would be obstructive sleep apnea, the treatment of which affects metabolic processes.

**Summary:** Adequate sleep hygiene is an extremely important part of a healthy lifestyle. More research is needed on the relationship between sleep and the regulation of carbohydrate metabolism, due to the fact that the appropriate sleep-wake rhythm may give hope for improvement in health in people with metabolic disorders and may be an important protective factor for many diseases.

**Key words:** sleep, insulin resistance, sleep deprivation

**INTRODUCTION AND PURPOSE**

Sleep plays a vital role in maintaining homeostasis and affects many metabolic pathways. There are numerous relationships between the sleep-wake rhythm and glucose metabolism and insulin sensitivity. They result from the operation of circadian clocks, both in the central nervous system and in peripheral tissues. [2]

Each person spends about 2/3 of their lifespan active and 1/3 sleeping. [11] Proper sleep allows you to regenerate strength, replenish life energy and it is a state of renewal. Moreover, it is very important for the proper functioning of the nervous system. It enables, among others effective learning and adequate memory forming processes. The duration and time of bedtime change a lot these days. In the modern world, there is a tendency to shorten the length of sleep. [11, 12]

At the same time, the epidemic of civilization diseases is developing, including obesity and diabetes and strongly connected with them - insulin resistance. The main reasons for this are a sedentary lifestyle, low physical activity and an inadequate diet. Insulin resistance (IO) is a state of decreased sensitivity of peripheral tissues to insulin, leading to greater than physiological production of this hormone in order to maintain adequate blood glucose levels. It is a potentially modifiable risk factor for the development of type 2 diabetes, obesity, and cardiovascular diseases.

The aim of this study is to summarize the current knowledge on the relationship between sleep deprivation and an increased risk of developing insulin resistance.

**DESCRIPTION OF THE STATE OF KNOWLEDGE**

Decreased quantity of sleep is associated with impaired glucose tolerance and an increased risk of developing diabetes. The available literature indicates that sleep restriction, however short time period may it cover, significantly affects insulin sensitivity, reducing it even to several dozen percent. [4,6,9,10]

It has been shown that just one night with partial sleep deprivation (reduction of sleep time to 4.5 hours) in young men is enough to reduce insulin sensitivity by as much as 16% compared to full sleep (8.5 hours). Furthermore, the study shows that sleeping at least 7 hours a day can reduce insulin resistance. [10] This proves that slight changes in sleep duration can have a negative effect on short one-night sleep and a positive effect on improvement in insulin sensitivity with optimally long sleep.

Major tissue resistance to insulin appears with prolonged shortening of sleep time. This was observed with the restriction of sleep to 5 hours per night for a period of 1 week. Mentioned
sleep reduction resulted in a 20 +/- 24% decrease in insulin sensitivity after an intravenous glucose load test. [4]

Insulin resistance is a preventable and potentially reversible condition. Melatonin, the main hormone responsible for falling asleep and proper sleep, influences the cellular level of the sensitivity of pancreatic beta cells to glucose. In young, healthy women in an in vitro study, long-term exposure to melatonin increases the sensitivity of these cells to glucose, and short-term exposure reduces it. [7] In healthy subjects who habitually reduce sleep, it has been shown that extending sleep time for a relatively long period of time (6 weeks) may bring metabolic benefits. [8] The general attention of the society in the prevention of diabetes, metabolic syndrome and cardiovascular diseases is focused on increasing physical activity and changes in eating habits. However, little awareness is raised of the role of sleep duration in regulating glucose metabolism. These reports shed new light on the normal duration of sleep in people with metabolic diseases. Nevertheless, more research is needed using the effect of extending sleep time and its effect on improving glucose metabolism in these study groups.

Available literature indicate that not only the amount of sleep, but also the time of sleep, can have a significant impact on health. In industrialized countries, around 20% of working adults work in shifts. Epidemiological studies prove that people who work shifts and therefore sleep during the day, have an increased risk of developing obesity, DMII, and cardiovascular disease. [3] Inverted circadian rhythms may have a more unfavorable effect on insulin function and secretion than sleep loss alone. [9] Comparing two groups with limited sleep, one of which additionally had a delayed time of falling asleep, an almost two-fold decrease in insulin sensitivity was observed in people with a shifted sleep-wake rhythm. [9] These people should remember about regular check-ups for the above diseases.

Moreover, chronic sleep disturbance also may result in the development of insulin resistance. These types of disorders include, among others obstructive sleep apnea (OSA) or obesity-related hypoventilation syndrome (OHS), which are characteristic complications of people with high BMI. It is estimated that approximately 90% of OHS patients have OSA. It should be remembered that obstructive sleep apnea itself (even without the coexistence of obesity) leads to disturbance of the lipid metabolism and insulin resistance. [5] Treatment of respiratory ailments in obese patients has a potentially positive effect on metabolic disorders. Therefore, attention should be paid to the importance of preventing obesity and maintaining proper sleep hygiene in the prevention of civilization diseases.

**CONCLUSIONS:**

Good sleep hygiene is extremely important. It is not only the length of sleep that matters, but also its quality, continuity and time of falling asleep. Abnormal sleep is one of the risk factors for the development of insulin resistance, type 2 diabetes, obesity, and cardiovascular disease. Although the specific role of sleep in the pathogenesis of many diseases is still under investigation, there are numerous reports saying that sleep deficiency and disorders are associated with it. More research is needed on the relationship between sleep and the regulation of carbohydrate metabolism, due to the fact that the appropriate sleep-wake rhythm may give
hope for improvement in health for people with metabolic disorders and may be an important protective factor for many diseases.

LIST OF REFERENCES:

1. Vgontzas, A., Fernandez-Mendoza, J., Miksiewicz, T. et al. Unveiling the longitudinal association between short sleep duration and the incidence of obesity: the Penn State Cohort. Int J Obes 38, 825–832 (2014). https://doi.org/10.1038/ijo.2013.172

2. Stenvers DJ, Scheer FAJL, Schrauwen P, la Fleur SE, Kalsbeek A. Circadian clocks and insulin resistance. Nat Rev Endocrinol. 2019 Feb;15(2):75-89. doi: 10.1038/s41574-018-0122-1. PMID: 30531917.

3. Pizinger T, Kovtun K, RoyChoudhury A, Laferrière B, Shechter A, St-Onge MP. Pilot study of sleep and meal timing effects, independent of sleep duration and food intake, on insulin sensitivity in healthy individuals. Sleep Health. 2018 Feb;4(1):33-39. doi: 10.1016/j.sleh.2017.10.005. Epub 2017 Nov 20. PMID: 29332677; PMCID: PMC5771427.

4. Buxton OM, Pavlova M, Reid EW, Wang W, Simonson DC, Adler GK. Sleep restriction for 1 week reduces insulin sensitivity in healthy men. Diabetes. 2010 Sep;59(9):2126-33. doi: 10.2337/db09-0699. Epub 2010 Jun 28. PMID: 20585000; PMCID: PMC2927933.

5. Khalyfa A, Gozal D, Masa JF, Marin JM, Qiao Z, Corral J, González M, Marti S, Kheirandish-Gozal L, Egea C, Sánchez-Quiroga MÁ, de Terreros FJG, Barca FJ. Sleep-disordered breathing, circulating exosomes, and insulin sensitivity in adipocytes. Int J Obes (Lond). 2018 Jun;42(6):1127-1139. doi: 10.1038/s41366-018-0099-9. Epub 2018 Jun 11. PMID: 29892042; PMCID: PMC6195831.

6. Broussard JL, Ehrmann DA, Van Cauter E, Tasali E, Brady MJ. Impaired insulin signaling in human adipocytes after experimental sleep restriction: a randomized, crossover study. Ann Intern Med. 2012 Oct 16;157(8):549-57. doi: 10.7326/0003-4819-157-8-201210160-00005. PMID: 23070488; PMCID: PMC4435718.

7. Ciaran J. McMullan, Gary C. Curhan, Eva S. Schernhammer, John P. Forman, Association of Nocturnal Melatonin Secretion With Insulin Resistance in Nondiabetic Young Women, American Journal of Epidemiology, Volume 178, Issue 2, 15 July 2013, Pages 231–238, https://doi.org/10.1093/aje/kws470

8. Rachel Leproult, PhD, Gaëtane Deliens, PhD, Médhi Gilson, MS, Philippe Peigneux, PhD, Beneficial Impact of Sleep Extension on Fasting Insulin Sensitivity in Adults with Habitual Sleep Restriction, Sleep, Volume 38, Issue 5, 1 May 2015, Pages 707–715, https://doi.org/10.5665/sleep.4660

9. Rachel Leproult, Ulf Holm bäck, Eve Van Cauter; Circadian Misalignment Augments Markers of Insulin Resistance and Inflammation, Independently of Sleep Loss. Diabetes 1 June 2014; 63 (6): 1860–1869. https://doi.org/10.2337/db13-1546
10. Cedernaes J, Lampola L, Axelsson EK, Liethof L, Hassanzadeh S, Yeganeh A, Broman JE, Schiöth HB, Benedict C. A single night of partial sleep loss impairs fasting insulin sensitivity but does not affect cephalic phase insulin release in young men. J Sleep Res. 2016 Feb;25(1):5-10. doi: 10.1111/jsr.12340. PMID: 26361380.

11. Reutrakul S, Van Cauter E. Sleep influences on obesity, insulin resistance, and risk of type 2 diabetes. Metabolism. 2018 Jul;84:56-66. doi: 10.1016/j.metabol.2018.02.010. Epub 2018 Mar 3. PMID: 29510179.

12. National Sleep Foundation. Sleep in America poll. Available from https://sleepfoundation.org/sleep-polls-data/sleep-in-america-poll/2009-health-and-safety; 2009, Accessed date: 30 June 2017.

13. Cappuccio FP, Taggart FM, Kandala NB, Currie A, Peile E, Stranges S, et al. Metaanalysis of short sleep duration and obesity in children and adults. Sleep 2008;31 (5):619–26.

14. Anothaisintawee T, Reutrakul S, Van Cauter E, Thakkinstian A. Sleep disturbances compared to traditional risk factors for diabetes development: systematic review and meta-analysis. Sleep Med Rev 2015;30:11–24.