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Sleep Disturbances and Type 2 Diabetes: Observational Study Data Suggest a Link

Sleep disturbances may be strongly associated with impaired glucose metabolism, insulin resistance, and a risk of type 2 diabetes incidence in older adults, according to the results of a population-based observational study published in this issue of *Diabetes Care* (p. 2050). The study by Strand et al. examined nearly 6,000 U.S. individuals aged ≥ 65 years over a 10-year period (1989–1999) and looked at various subjectively reported sleep disturbances and their associations with risk factors for and risk of incidence of type 2 diabetes. The main outcomes of the study are clear: sleep apnea, snoring, and daytime sleepiness were associated with higher glucose levels, higher insulin secretion, and lower insulin sensitivity. The 10-year risk of developing type 2 diabetes was also positively associated with such sleep disturbances in older adults. The authors suggest that monitoring glucose in older adults with such symptoms may help to identify potentially at-risk individuals to allow earlier interventions. Quite conversely, however, insomnia symptoms were not consistently associated with the same risk factors, suggesting a need to study insomnia and diabetes in older adults as data are not generally consistent in this area. As the authors note, observational studies cannot be used to infer causation; they do point out that while they adjusted outcomes for several confounding factors, they cannot exclude the possibility that others do not exist. Equally, possible mechanisms underlying the observations are largely unknown, although they do suggest, based on previous studies, a possible link that might explain how sleep deprivation leads to insulin resistance and eventually diabetes. Commenting on the further implications of the study, Dr. Strand noted: “The results from our study improve our understanding of how sleep disturbances are related to glucose metabolism, insulin resistance, and risk of developing type 2 diabetes, and seen from a primary prevention perspective, the results are very promising. Sleep apnea and snoring are prevalent and manageable conditions, and increased focus on adverse health effects could be helpful in the prevention of type 2 diabetes. However, to determine whether there is a causal link, we need evidence from randomized controlled trials looking at whether treatment of sleep disturbances in high-risk individuals can prevent or delay the onset of type 2 diabetes.”

Strand et al. Sleep disturbances and glucose metabolism in older adults: the Cardiovascular Health Study. *Diabetes Care* 2015;38:2050–2058

Environmental Factors Drive Type 2 Diabetes and Obesity Rates in Pima and Non-Pima Populations in Mexico

Lifestyle factors rather than genetic predisposition may be more important in determining development of type 2 diabetes and obesity, at least in Pima Indian and non-Pima populations living in north-western Mexico, according to a 15-year survey published in this issue of *Diabetes Care* (p. 2075) that looked at prevalence of diabetes, obesity, and lifestyle changes. Pima Indian populations tend to have very high rates of diabetes and obesity that are widely attributed to a genetic predisposition. However, rates have varied over the years, particularly between populations located in southern U.S. and Mexico, suggesting that environmental factors might be involved as well. Esparza-Romero et al. used a population-level study to assess rates of diabetes, obesity, and glucose tolerance and a wide-ranging approach to determine changes in environmental factors such as diet and physical activity over a 15-year period (1995–2010). Both Pima and non-Pima neighbors experienced a significant transition from traditional to more modern lifestyles. At the same time diabetes rates dramatically increased in non-Pima but not Pima men and tended to increase in both groups of women. Obesity rates also increased in all groups over the same period. The authors indicate that general reductions in physical activity (typically occupationally related) and changes in diet away from a more subsistence-based diet to one with more processed, purchased foods are likely to account for the majority of changes in disease rates. The lack of increase in diabetes in Pima men over the study period adds to the evidence for a role of environmental factors, according to the authors. In particular, they suggest that the higher levels of physical activity of this group may offer some protection against the development of diabetes. Commenting on the wider implications of the study, Dr. Schulz stated: “Our challenge in the 21st century is to implement mechanisms for societal modernization that will promote health rather than impair it in order to protect the next generation from the inevitability of increased chronic disease.”

Esparza-Romero et al. Environmentally driven increases in type 2 diabetes and obesity in Pima Indians and Non-Pimas in Mexico over a 15-year period: the Maycoba Project. *Diabetes Care* 2015;38:2075–2082

Insulin Dose in the ACCORD Trial Is Not Independently Associated With Cardiovascular Mortality: Post Hoc Analysis

A post hoc analysis of the ACCORD trial data by Siraj et al. (p. 2000) suggests that there is no support for the hypothesis that insulin dose was independently associated with the increased rates of cardiovascular mortality in the intensive treatment group of the trial. ACCORD examined whether cardiovascular and other outcomes were different following intensive insulin treatment or a standard approach to reduce blood glucose to either near-normal levels or a higher but still acceptable level. Following an interim analysis, however, the intensive treatment group was stopped early due to elevated rates of all-cause and cardiovascular mortality in comparison with the standard treatment group. This prompted Siraj et al. to reevaluate the ACCORD trial data, since no clear explanation had been definitively identified to explain the outcome of the study. Using hazards modeling, the authors examined data from most of the 10,000 participants in the trial, exploring associations between cardiovascular mortality and insulin dose. Adjustments for both baseline and treatment covariates were then made to account for possible confounding factors. Initial analyses showed that higher insulin dose was associated with increased risk of cardiovascular death. However, after adjustments for baseline covariates, the association disappeared and, moreover, adjustments for severe hypoglycemia, weight change, attained HbA_{1c}, and randomization assignment did not alter the result. The authors' conclusions are straightforward: "No support for the hypothesis that insulin dose contributed to [cardiovascular] mortality in ACCORD." Commenting more widely on their analysis, Dr. Siraj stated: "This is reassuring for many physicians and their patients. However, our findings will not lay to rest the ongoing discussion about insulin use and the potential for increased risk, especially at higher doses. There are still unanswered questions, and more studies are needed to answer them definitively."

Siraj et al. Insulin dose and cardiovascular mortality in the ACCORD trial. *Diabetes Care* 2015;38:2000–2008

A Mediterranean Diet Enriched With Olive Oil May Protect Against Retinopathy but Not Nephropathy Associated With Diabetes

A post hoc analysis published in this issue of *Diabetes Care* (p. 2134) suggests that a Mediterranean diet supplemented with extra virgin olive oil may protect against the development of diabetic retinopathy. The analysis by Díaz-López et al. focuses on data from the multicenter randomized PREDIMED nutritional intervention trial that found remarkable effects in terms of prevention of cardiovascular disease following adherence to a Mediterranean diet. Using a subset of 3,614 participants that had type 2 diabetes at baseline but not necessarily any indication of microvascular diabetes complications, the authors found that there was a statistically significant relative reduction in the risk of developing diabetic retinopathy of ~44% when on the Mediterranean diet supplemented with olive oil in comparison with a low-fat diet. This was after a follow-up period of about 6 years. Dr. Salas-Salvadó noted: "The objective of the study was to test if a nutritional intervention based on the Mediterranean diet would have greater protective effect on diabetic retinopathy and nephropathy than a low-fat control diet. Therefore, participants were randomly assigned to one of three dietary interventions: Mediterranean diet supplemented with either extra virgin olive oil or mixed nuts or a low-fat control diet." Although significant effects were noted for the olive oil-supplemented Mediterranean diet, no significant preventive effects on retinopathy could be detected in the case of nut addition, and no effects at all could be detected in either diet on diabetic nephropathy. This was all in comparison with a reasonably healthy low-fat diet. The authors suggest that the discrepancy between the olive oil and nut additions may well be a chance finding because of confounding factors and, in particular, the extra load of nutrients and other compounds that may have been biologically active at the same time during the study. Commenting on the study, Dr. Salas-Salvadó stated: "This study is unique because it demonstrates for the first time, with high degree of scientific evidence, that a healthy dietary pattern, in this case a Mediterranean diet supplemented with extra virgin olive oil, could play a beneficial role in the prevention of diabetic retinopathy in participants at high cardiovascular risk with type 2 diabetes. These results are relevant because diabetic retinopathy is a leading cause of blindness and visual disability in developed countries that can be partly prevented through diet."

Díaz-López et al. Mediterranean diet, retinopathy, nephropathy, and microvascular diabetes complications: a post hoc analysis of a randomized trial. *Diabetes Care* 2015;38:2134–2141