Sleep Disturbances and Glucose Variability

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Summary

Glucose variability is suspected to be among the main causes of diabetic complications.[1] We evaluated the relationship of sleep fragmentation with the level and the variability of the fasting blood glucose values (FBG). We used the Armband an instrument that records the number and the duration of the awakenings during sleep (AW), for six consecutive days in 60 obese type 2 diabetic subjects on diet alone or oral hypoglycemic agents and with a history of sleep disturbance and OSAS (37 M, 23 F); age 61.6+5; BMI=28+1.3 kg/m^2.

Introduction

It has been recently recognized that sleep disruption can cause an increase in glycated (HbA1c), and sleep disturbance is a condition that by definition occurs during the night and may represent a serious stressful condition likely to be reflected on the Fasting Blood Glucose (FBG)[2]. The high level of stress caused by irregular sleep has been clearly defined by numerous studies. Less clear than this is the role of disturbed respiration on sleep fragmentation. Diabetic have many conditions predisposing to heavy snoring and Obstructive Sleep Apnea (OSAS) which represent serious stressors. We thus hypothesized that sleep disturbance might be at least one of the interferences causing a high FBG variability. To this aim we evaluated the data routinely collected from our diabetic population.

Materials and Methods

Among 142 diabetic obese overweight subjects studied for sleep disturbances and inadequate blood glucose control we selected the data of 60 who had no pulmonary or other complications, and were on diet, metformin or gliptins or a combination of them. None of these drugs causes serious hypoglycemia since they do not act on the insulin secretion mechanism. We excluded those on insulin or sulphonylurea drugs and drugs interfering with sleep breathing like benzodiazepines, nonsteroid anti-inflammatory agents or beta blockers. Some of them were on statins, some on antihypertensive agents, a few on anti aggregating agents (Table 1).

To evaluate their sleep disturbance we used the Armband, an extensively validated tool that can measure the characteristics of the sleep and the number of awakenings for as long as seven consecutive nights.3 ,4 ,5 This tool is applied to the forearm and kept in place for seven days, with the exception of the time of the morning shower. Among the different parameters estimated the instrument gives an accurate report of the time spent sleeping (TS), the number (nAW)and the duration of the awakenings (dAW), and the number of daytime sleeping episodes (dtS). To evaluate the impact of the sleep pattern on blood glucose variability we also asked our diabetic patients to record their fasting blood glucose levels upon awakening throughout the period of observation with the home blood glucose monitor using an interference free electrochemical method. We also asked them to duplicate the results at least one morning during this period. The Blood glucose meters were routinely calibrated as per the internal procedure of our department. All the values were downloaded and the Standard Deviation (SD) of the FBG was calculated as an index of glucose variability . The data were log transformed to improve the distribution.

Materials and Methods (continued)

Results

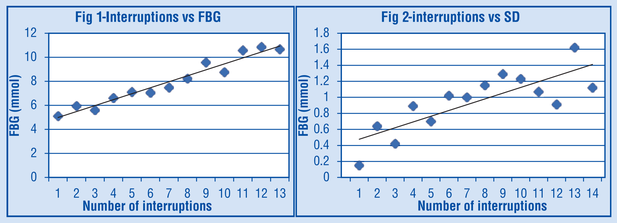
The number of episodes of daytime sleepiness were remarkably few, with a nonsignificant trend to increase with age and inversely to the time spent sleeping. All the available parameters relevant to sleep, TS, nAW, dAW, dtS were entered in the multiple correlation. After removing the effect of the BMI, Age and HbA1c only the number of awakenings remained significantly related to the SD of the fasting blood glucose (corr=.76, p=.001). From our data the time spent sleeping does not seem to have a major role.

We had the same result when the average FBG of the days of observation was substituted for the SD. The ANOVA among the different SD and FBG groups was p=<.001. The data were analyzed with the SPSS package ver 19 (Fig 1 and 2).

Table 1. Characteristics of the subjects

Age	Sex	BMI	Diet	Metformin	Gliptins	Gliptins + Metformin	Statins	Anti aggregant
61.6+5 ys	29	29.8+ 1.2 Kg/m2	17	23	12	8	9	6

Results: number of awakenings vs Fasting Blood Glucose (FBG) or the Standard Deviation (SD) of the FBG throughout the period of observation



Conclusions

We selected 60 subjects treated with metformin or diet alone, thus the possibility of nocturnal hypoglycemia was substantially nil. The high correlation level of the SD with the number of awakenings is not surprising. Any form of nocturnal awakening is a stressful condition and thus can induce an increase in blood glucose. Since the sleep recording time spanned for seven nights it is highly unlikely that an occasional episode of disturbed sleep may have interfered with the statistical analysis. We did not include the HbA1c in our evaluation since this analyte is a long term (3 months) index, and any relationship with the sleeping behavior of only 7 nights out of 90 may be deceptive. The use of the SMBG may be a moot point, since all the available glucose meters have an inherent error that may reach + 15%. However with the most recent meters the error is minimized, and the SMBG is the most affordable way to evaluate the FBG. Furthermore the consistent number of subjects studied for a long period gives substantial statistical support to the results. We chose to use the Standard deviation of the FBG as a proxy for the glucose variability even if this parameter may be influenced by the average, because the SD is the most widely used and reproducible measure available. We also did not include the blood glucose values taken during the waking hours because the variability may be attributable to many other interfering variables, physical activity, meals, driving and any other stressful condition.

Although our observation may add to the growing data linking sleep and glucose metabolism many more aspects remain to be clarified. We do not know the role of disturbed respiration / OSAS that are closely linked to sleep, the role of the different phases of sleep, the role of clock time when sleeping starts, the role of the many drugs that diabetic patients take.

References

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